Long Term Outcome of the Bony Obliteration Tympanoplasty in Cholesteatoma in Children and Adults:

Safety – Hearing – Quality of Life

Joost J.S. van Dinther

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Promotoren:
Prof. dr. C.W.R.J. Cremers
Prof. dr. F.E. Offeciers (European Institute for ORL-HNS, Antwerpen, België)

Manuscriptcommissie:
Prof. dr. C.B. Hoyng
Prof. dr. R. de Groot
Dr. M. Yung (Ipswich Hospital NHS Trust, Verenigd Koninkrijk)

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“My Lord Odysseus,” she said.

“You are home at last. Let me rush to your poor Queen Penelope and

let her know this wonderful news.”

Eurycleia, The Odyssey, Homeros, 8th century BC

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Chapter 1.1

General Introduction

J.J.S. van Dinther

1.1.1 Definition

Cholesteatoma is a hyperproliferative disease of keratinocytes which is characterized by mass formation due to accumulation of continuous desquamation of keratin, leading to local invasive destruction of surrounding tissues.(1)

The correct term for cholesteatoma is keratinocytoma. However, since Müller in 1838 incorrectly described this disease as cholesteatoma, assuming that it was a tumor containing cholesterine and fat, this term became strongly embedded in the otological vocabulary. Therefore, through generations its use still persists today and is broadly and internationally accepted.(2,3)

Two different types of cholesteatoma are distinguished, based on their time and place of origin. This thesis exclusively addresses acquired cholesteatoma, the most common type. It forms during life as a result of migration of skin (ectoderm) from the outer ear canal into the middle ear. A less common type is the congenital cholesteatoma, which arises in the middle ear or in the petrous apex of the temporal bone from a remnant of ectoderm, erroneously left behind during the embryological formative stage. A special variant of congenital cholesteatoma is the epidermoid cyst, which is a remnant of ectoderm entrapped inside the dura mater, medial to the petrous apex.(4,5)

Although the term cholesteatoma may seem to present a clearly defined clinical entity, the clinical literature describes and classifies cholesteatoma in a quite variable way. This presents a problem when comparing the outcome of different therapeutic surgical techniques. Therefore, a Delphi consensus on the definition and classification of cholesteatoma was established in 2015 amongst the members of the European Academy for Otology and Neurotology (EAONO). They agreed on the definition of cholesteatoma as a mass in the middle ear and/or mastoid, formed by keratinising squamous epithelium and subepithelial connective tissue and by the progressive accumulation of keratin debris with or without surrounding inflammatory reaction. Cholesteatoma consists of matrix (keratinising squamous epithelium), perimatrix (a layer of varying thickness of subepithelial connective tissue) and keratin debris.(6)

1.1.2 Anatomy and Function of the Ear

To situate the presence of cholesteatoma in the human body, a short overview of the anatomic subunits of the ear with its respective functions is necessary. The ear, which houses the peripheral auditory and vestibular organs, is divided into three anatomical subunits: the outer ear, the middle ear and the inner ear (Figure 1).

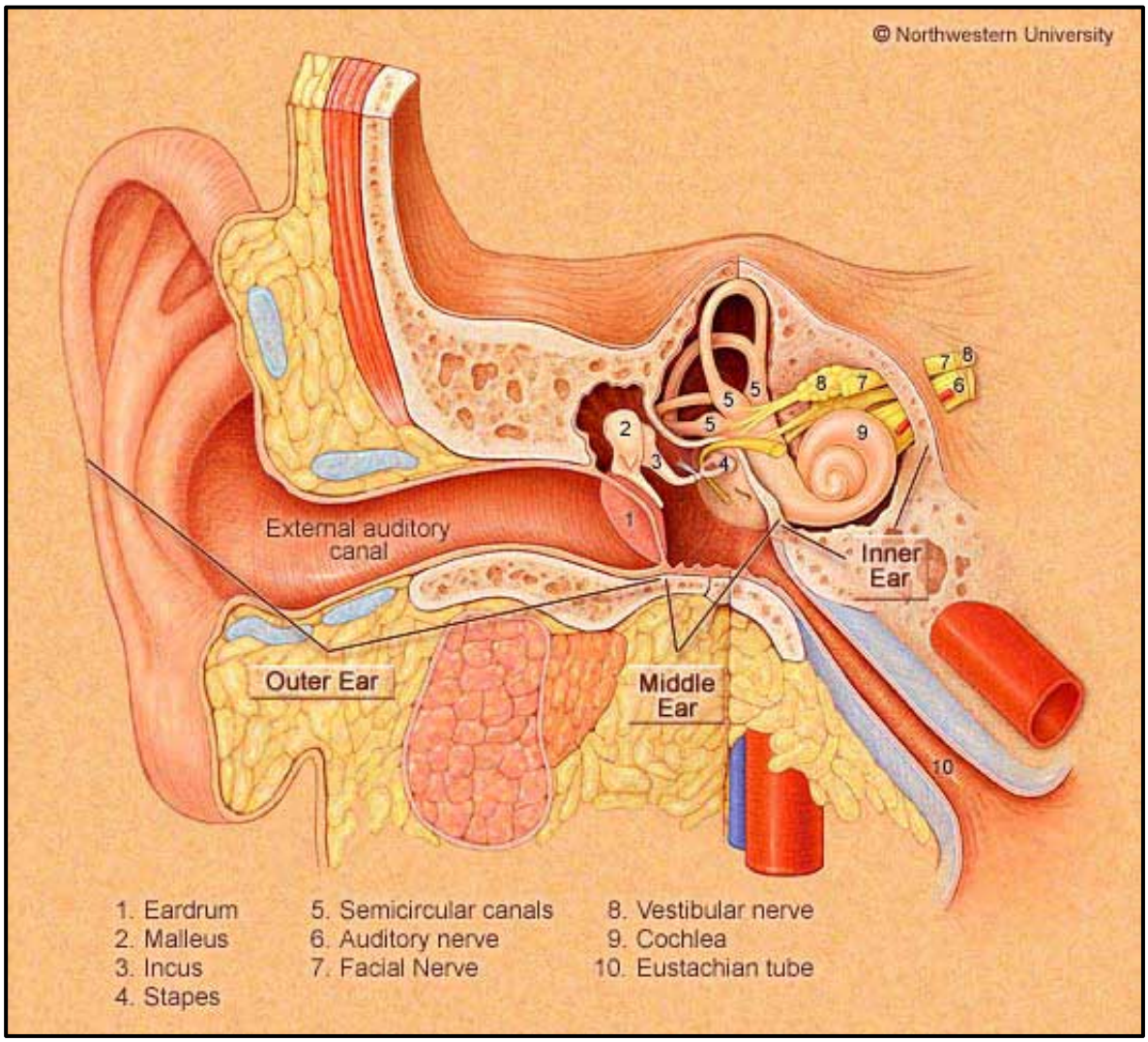

Figure 1. The anatomical subunits of the ear. The **Outer Ear** with the external ear and external auditory canal via the Eardrum (1) connected with the middle ear. The **Middle Ear** with the ossicles: Malleus (2), Incus (3) and Stapes (4) and the Eustachian tube (10). The **Inner Ear** with the Cochlea (9) for the hearing and the Semicircular canals (5) for the equilibrium and the internal auditory canal with the Auditory (6), Facial (7) and Vestibular (8) nerves (Courtesy by Northwestern University).

The auditory system is an evolutionary masterpiece, with in its epicenter an array of acoustical detectors packed into a space no larger than a cubic centimeter. These detectors transduce vibrations as small as the diameter of an atom and respond a

thousand times faster than visual photoreceptors. These rapid auditory responses to acoustical cues facilitate the initial orientation of the head and body to novel stimuli, especially those that are not initially within the field of view. Although humans are highly visual creatures, much human communication is mediated by the auditory system. Hearing loss can therefore be more socially debilitating than blindness. Culturally, the auditory system is essential not only to understand speech, but also to enjoy music, one of the most sophisticated forms of human expression.(7)

The peripheral portion of the vestibular system includes inner ear structures that function as accelerometers and gyroscopes, continuously reporting information about the motion and position of the head and body to integrative centers in the brainstem, cerebellum, and several multisensory cortices. The central vestibular nuclei directly innervate motor neurons controlling extraocular, cervical, and spinal muscles.(8-10) This motor output is especially important for several output functions of the vestibular system: gaze stabilization, perception of self-motion, head position in space and spatial orientation relative to gravity.(8,11-13) The vestibular system is therefore a key component in the prevention of falls and keeping the visual surroundings stable during motion, although its functioning is usually not consciously perceived.(7)

1.1.2.1 The Outer Ear

The outer ear consists of the external ear (auricle or pinna) and the ear canal. The outer ear gathers sound waves and leads them via the ear canal to the eardrum. One consequence of this specific configuration is that it selectively boosts the sound pressure 30- to 100-fold for frequencies around 3 kHz. Most human speech sounds are distributed in the bandwidth around 3 kHz. A second function of the outer ear is a frequency filter for high pitched sounds to produce localisation clues of the elevation level of the sound source.(7)

The external ear is a cartilage structure covered with skin. The outer third of the ear canal skin contains hair and cerumen glands overlying subcutaneous tissue and cartilage. In the medial two third of the ear canal, the bony ear canal is only covered with periost and skin. This skin also covers the eardrum. The ear canal skin has a unique migratory cleaning system, transporting debris outward.

The eardrum or tympanic membrane is an oval membranous partition separating the external auditory canal from the tympanic cavity, measuring 10 mm vertically and 8 mm horizontally. It is formed of a double-layer of epithelial cells across its entire surface: skin or squamous epithelium at the outside and mucosa at the inside. The greater pars tensa has an extra 2 layers of tougher, fibrous epithelial tissue between the previously-

mentioned two layers of cells, to which the long arm of the malleus is attached. The pars tensa transduces the vibrations. Damage to this section of the membrane results in altered hearing. The pars flaccida is the smaller section of the eardrum with only two layers situated above the malleus handle and is flaccid and transparent. The umbo (i.e. the tip of the malleus handle) is the point of deepest recession of the membrane and is the location of genesis of new epithelial cells, which migrate out towards the pinna as new cells are formed behind them. This migration occurs at about the same rate as the growth of fingernails. In addition, the malleus handle is attached to the inner surface and part of the middle ear (Figure 2).(14,15)

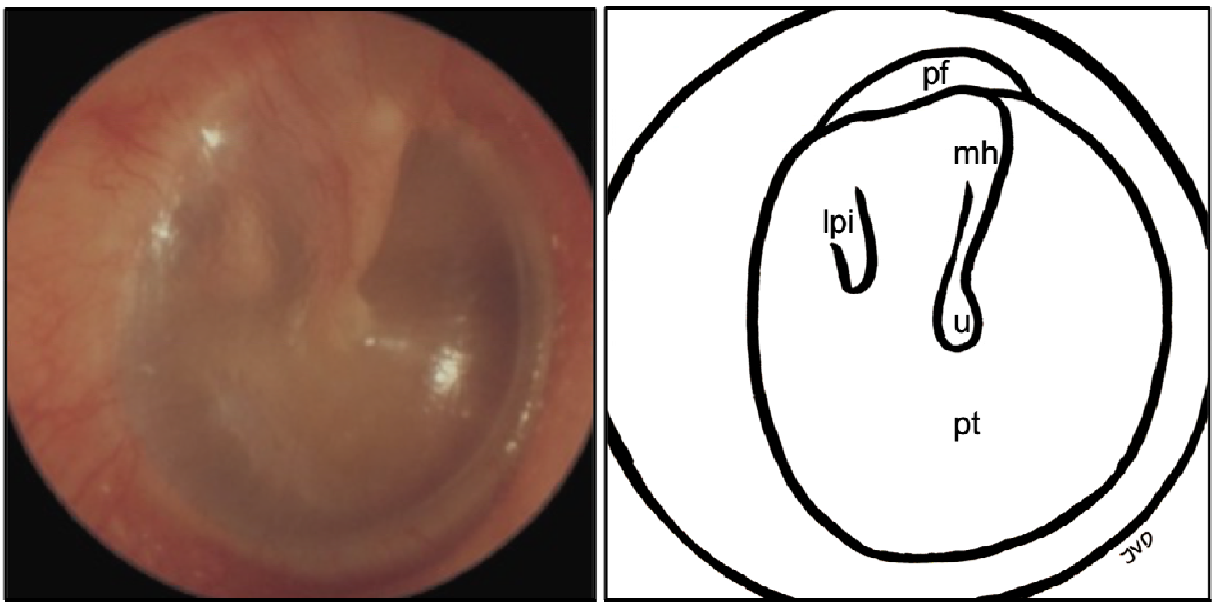

Figure 2. Normal tympanic membrane or eardrum of a right ear with **mh**: malleus handle; **u**: umbo; **pf**: pars flaccida; **pt**: pars tensa; **lpi**: long process incus.

1.1.2.2 The Middle Ear

In the middle ear, the sound waves are captured at the outer surface of the eardrum. Via its connection with the ossicles (malleus, incus, and stapes), the sound waves are led to the oval window. This middle ear sound transport transforms air waves into fluid waves (i.e. from a low to a high impedance or resistance to movement medium), boosting the sound pressure almost 200-fold. This boost is achieved by two mechanisms: the force focusing from a large to a small surface (from tympanic membrane to oval window) and the mechanical lever action of the ossicles, which connects the tympanic membrane with the oval window.(7)

The middle ear is a mucosa-lined gas-filled space. Besides the ossicles other important structures are recognised. The mucosal lining cleans the ear by mucociliary clearance and ventilates the ear by the transmucosal gas exchange. The eustachian tube, which connects the middle ear with the nasopharynx, is able to clear the middle ear with approximately 1cc of air per 24 hours. The middle ear consists of different anatomical subregions which are important in middle ear surgery: the tympanic cavity directly behind the eardrum can be divided into the mesotympanum (with the malleus handle, the long process of the incus and the stapes) the protympanum anteriorly (with the entrance to the Eustachian tube), the hypotympanum inferiorly and the retrotympanum with the sinus tympani posteriorly again with more detailed subunits; the attic superiorly of the mesotympanum with the head of the malleus, the body of the incus and the entrance to the mastoid. The mastoid with antrum and additus ad antrum is via the attic connected with the tympanic cavity. The mastoid forms a relatively spacious ventilated space with gas-exchanging mucosa, posteriorly of the tympanic cavity (Figure 3). A system of ventilated cells connects with the middle ear in the supralabyrinthine, retrolabyrinthine, and infralabyrinthine regions.

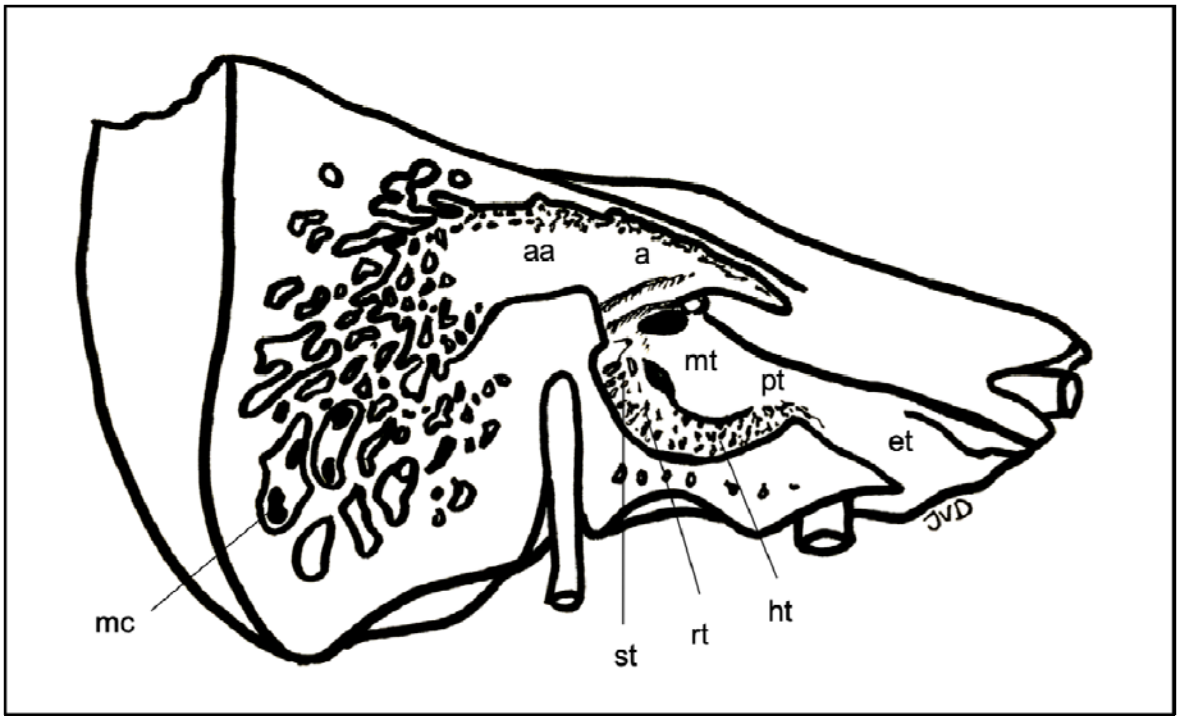

Figure 3. Anatomical subunits of the middle ear cleft. The infero-anterior tympanic cavity with **mt**: mesotympanum; **pt**: protympanum; **ht**: hypotympanum; **rt**: retrotympanum; **st**: sinus tymani; and the supero-posterior tympanic cavity with **a**: attic; **aa**: additus ad antrum; **mc**: mastoid cavity.

1.1.2.3 The Inner Ear

In the inner ear, medial to the stapes footplate in the oval window niche, the acoustic energy is transported through the perilymphatic fluid along the perilymphatic duct (scala vestibuli and scala tympani) of the cochlea. Between these two scalae the endolymphatic duct with the organ of Corti is situated. The hair cells, arranged on the basilar membrane, are tonotopically stimulated (from high to low frequencies) by the sound waves. They connect with and electrically stimulate the dendrites of the cochlear nerve, which transports the electrical signal via the central auditory pathways to the auditory cortex in the brain, where sounds are finally detected, discriminated and identified.

The peripheral vestibular system is also situated in the inner ear. We can distinguish five vestibular suborgans. The semicircular canals (SCCs) are mainly responsible for detecting angular accelerations. Further, the otolith organs (i.e. the utricle and the saccule) are responsible for detecting gravity and linear accelerations.

1.1.3 Milestones in the History of Cholesteatoma

1.1.3.1 The Early Days

The first report on chronic and suppurative infections of the mastoid, possibly due to cholesteatoma, is found in an ancient Greek manuscript by Galenus (129-199).(16) In 1671 Riolan, a French anatomist described mastoid surgery. He recommended the opening of the mastoid or mastoidectomy in case of a potentially lethal acute mastoiditis. (17) A few years later, in 1683, Duverny described a temporal bone tumour probably corresponding to a cholesteatoma.(3,18) Louis and Petit reported in 1750 on multiple cases of mastoid trephinations for acute abscesses.(19,20) It was almost one century later, in 1838, when Müller was the first to use the term “cholesteatoma”.(2,3)

1.1.3.2 About the Origin

In 1855 Virchow considered cholesteatoma to be a tumour arising from the metaplasia of mesenchymal cells transforming to epidermal cells, growing then as tumoral cells.(3,21) Gruber, Wendt and von Troeltsch, in 1868, considered cholesteatoma to be the result of a metaplasia not of bone cells but of tympanic mucosa cells into a malpighian epithelium.(3) In 1869 Politzer assumed that cholesteatoma was a glandular neoplasm of middle ear mucosa.(3) Only in 1889 Bezold and Habermann considered cholesteatoma to be the result of migration of the external ear canal epidermis into the tympanic cavity via a marginal perforation after acute or chronic otitis. It took more than 40 years of discussion before it was finally confirmed that Habermann and Bezold were correct.(3)

1.1.3.3 Systematic Surgical Intervention

Wilde introduced in 1853 the eponymous retro-auricular incision.(22) In 1873 Schwartze and Eysell were the first to describe the cortical mastoidectomy with the systematic description of how and under what conditions the procedure should be performed, recommending the use of a chisel and hammer to remove the bone to inspect and drain the antrum.(23) Küster and von Bergmann, both general surgeons, were credited in 1888 for the development of the radical surgery, which was known as the Küster-Bergmann procedure. They advocated a single stage procedure combining the dissection of the attic, antrum, and middle ear, transforming these into a single large cavity.(24-26) Zaufal described the first radical mastoidectomy in 1893, removing the superior and posterior bony ear canal, tympanic membrane, and ossicles in an attempt to eliminate the infection, to externalize the disease, and to create a dry ear.(27) In 1910 Bondy popularised the modified radical mastoidectomy in which all the middle ear structures were preserved if possible, in order to attempt to preserve the hearing.(28) One should realise that in this period people did still die from the intracranial complications as a result of the natural course of cholesteatoma disease. (29)

1.1.3.4 Microscopic Revolution

The introduction of the otologic operating microscope in 1953 by Zeiss was an enormous step forward in middle ear surgery. It made more precise otological dissection possible. In 1958 Wullstein described the first attempts of the reconstruction of the tympanic membrane via tympanoplasty.(30) In the same year Jansen introduced the canal wall up (CWU) mastoidectomy procedure. This led to tympano-ossicular reconstructions with mastoidectomy (the so-called closed cavity mastoidectomy or intact canal wall tympanomastoidectomy or canal wall up (CWU) mastoidectomy and to the use of traditional mastoidectomy for the treatment of chronic suppurative and cholesteatomatous otitis. Since then, many variations of the mastoidectomy have been described.(31) The following 50 years the canal wall up versus down discussion filled up many programs of conferences on cholesteatoma surgery, with safety versus dry and self-cleaning capacity being the most crucial priorities. Improvement of imaging by means of CT-scan contributed to a more reliable preoperative planning and counselling of patients.

1.1.3.5 Game-changers of the 2nd Millennium

In 1987 Mercke published his one-year results of canal wall down (CWD) surgery with canal wall reconstruction and bony obliteration of the mastoid for cholesteatoma. In 1991 he presented the five-year safety results of the same series with no recurrences and a low residual rate.(32,33) In 1997 Offeciers performed the first canal wall up with bony obliteration procedure in Antwerp for extensive cholesteatoma in cholesteatoma recurrence cases. Soon they systematically implemented the obliteration technique in all cases of extensive cholesteatoma.(34,35) Parallel to this evolution, in order to exclude residual cholesteatoma in a non-invasive way, the value of diffusion-weighted magnetic resonance imaging (MRI) was investigated. In 2002, Maheshwari published a case in which echo planar diffusion-weighted MRI was able to differentiate cholesteatoma from granulation tissue.(36) Until then, echo planar diffusion-weighted MRI was mainly used for the early detection of brain ischemia. The first results using echo planar diffusion-weighted MRI for the detection of residual and recurrent cholesteatoma seemed promising.(37-39) but in 2006, Vercruysse showed that echo planar diffusion-weighted MRI is not able to replace second look surgery, since echo planar diffusion-weighted MRI is unable to detect cholesteatoma smaller than 5 mm, and so missing the majority of all residual cholesteatoma.(40) Dubrulle reported in 2006 a high sensitivity, specificity, negative and positive predictive value of a non-echo planar diffusion-weighted MRI in the detection of postoperative recurrent cholesteatoma.(41) In the same year, in a technical report, De Foer described the difference between echo-planar diffusion-weighted MRI and non-echo planar diffusion-weighted MRI (non-EP DW MRI) in a case of a middle ear cholesteatoma, scanned with both techniques.(42) In 2007, it was first described that non-EP DW MRI was able to detect middle ear cholesteatoma as small as 2 mm.(43) Using

non-EP DW MRI with its higher resolution, lack of artefacts and thinner slice thickness, it became possible to replace second look surgery.(44) The use of non-EP DW MRI made the use of intravenous gadolinium contrast administration for the detection of residual cholesteatoma obsolete.(45) Later, numerous metanalysis confirmed the high sensitivity, specificity, positive predictive and negative predictive value of non-EP DW MRI in the detection of residual cholesteatoma proving that non-EP DW MRI is able to replace second look surgery.(46-51) The introduction of both game-changers – bony obliteration of the paratympanic spaces and the cholesteatoma MRI diffusion sequence – contributed to an enormous drop in the re-operative rates in both children and adults. Today various other authors reported on bony obliteration of the mastoid after canal wall up tympanoplasty in both children and adults with systematic good results.(34,35,52,53)

1.1.4 Classification

Today there is not one universal used classification system for cholesteatoma. Different, mostly overlapping, systems are used. There is a very high consensus on classifying cholesteatoma into two general categories: i.e. congenital and acquired cholesteatoma.(6)

1.1.4.1 Congenital Cholesteatoma

Cholesteatoma can occur in the middle ear with a normal tympanic membrane and external auditory canal. This is termed “congenital cholesteatoma” or ‘primary cholesteatoma’ and is most commonly found in the anterosuperior mesotympanum in children.(5) Congenital cholesteatoma is an expanding cystic mass with keratinising squamous epithelium located medially to the intact tympanic membrane, assumed to be present at birth but usually diagnosed during infancy or in early childhood in patients with no prior history of otorrhea, perforation, or previous surgery.(6) Congenital cholesteatoma can also be situated in the petrous apex. An intradurally located congenital cholesteatoma is called an epidermoid cyst.

1.1.4.2 Acquired Cholesteatoma

Primary acquired cholesteatoma is a subcategory of chronic otitis media that is not present at birth. It is characterised by clinical symptoms that are the result of growth with or without the destruction of adjacent structures (i.e., with or without tympanic membrane perforation, otorrhea and/or hearing deterioration). On CT-scan and MRI images it appears as a soft tissue mass, with adjacent areas of bony erosion of the middle ear and mastoid (6). Various classifications, based on otoscopic findings, were proposed. These classifications divide the acquired disease into attic, sinus and pars tensa cholesteatoma. Combinations of sites are possible. Recently, EAONO performed a Delphi consensus procedure on the classification of cholesteatoma (6) (Figure 4). To this EAONO classification, the presence of cholesteatoma after cholesteatoma surgery (i.e. recurrent and residual cholesteatoma), and after trauma (secondary acquired cholesteatoma) was added.

1. **Attic Cholesteatoma** arising from a retraction of the pars flaccida of the tympanic membrane (Figure 5). This type of cholesteatoma is divided into an anterior ad posterior subtype, respectively deriving from the anterior or posterior pouch.
2. **Sinus Cholesteatoma (marginal disease)** arising from a retraction of the posterosuperior quadrant of the pars tensa of the tympanic membrane (Figure 6).
3. **Pars Tensa Cholesteatoma (central disease)** arising from the central region of the pars tensa of the tympanic membrane (Figure 7).

4. **Cholesteatoma after Cholesteatoma Surgery**
   Cholesteatoma is notorious for its tendency to recur after initial cholesteatoma surgery. This includes both residual and recurrent cholesteatoma. It is essential to differentiate them.
   a. **Recurrent Cholesteatoma** originates from the reformation of retraction pocket after complete surgical removal of the previous cholesteatoma.(6)
   b. **Residual Cholesteatoma** results from incomplete surgical removal of the cholesteatoma matrix.(6)
5. **Traumatic Cholesteatoma** is the result of a complication after trauma to the temporal bone. This category includes surgical trauma, resulting in a "iatrogenic or secondary acquired cholesteatoma". This is an inclusion of epithelium behind a closed tympanic membrane or canal skin (after a healed traumatic perforation; after the restoration of the eardrum in myringoplasty).(54)

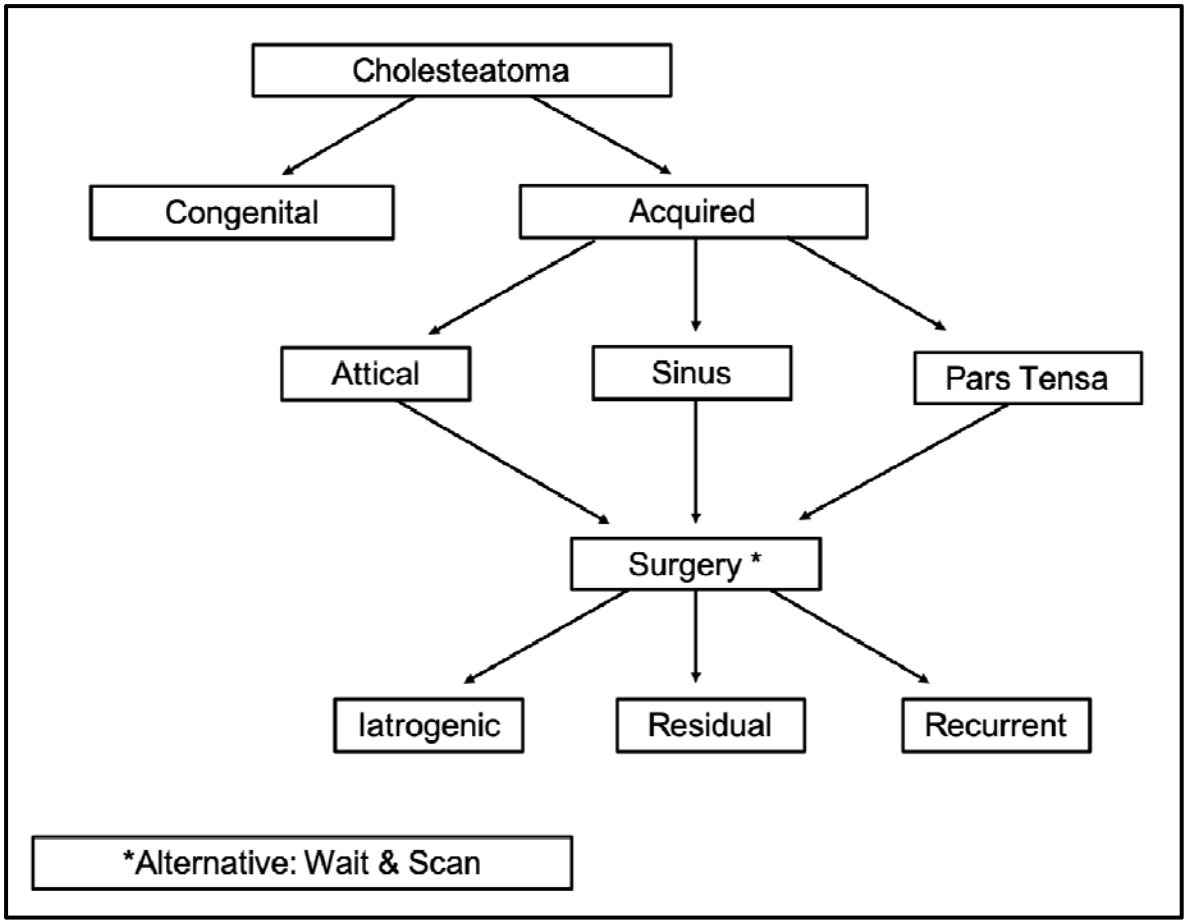

Figure 4. Cholesteatoma classification. Different combinations of acquired types of cholesteatoma and types after surgery are possible (adapted from the EAONO Steering Group 2015).

1.1.4.3 Cholesteatoma of the External Auditory Canal

Cholesteatoma of the external auditory canal is a separate entity. This disease can be congenital in atresia, or acquired, or iatrogenic after ear surgery. When cholesteatoma is thought of predominantly as a disease of the underlying supporting tissue (that is mucosa in the mucosal traction theory) we can understand how it relates to external auditory canal (EAC) cholesteatoma. In the case of EAC cholesteatoma the underlying structure is bone. Local osteitis develops with local inflammatory cytokines, enhancing bone resorption but also stimulating keratinocyte proliferation. Both tympanic membrane and external auditory canal cholesteatoma may be primarily driven by disease which damages the undersurface of the epithelium.(55)

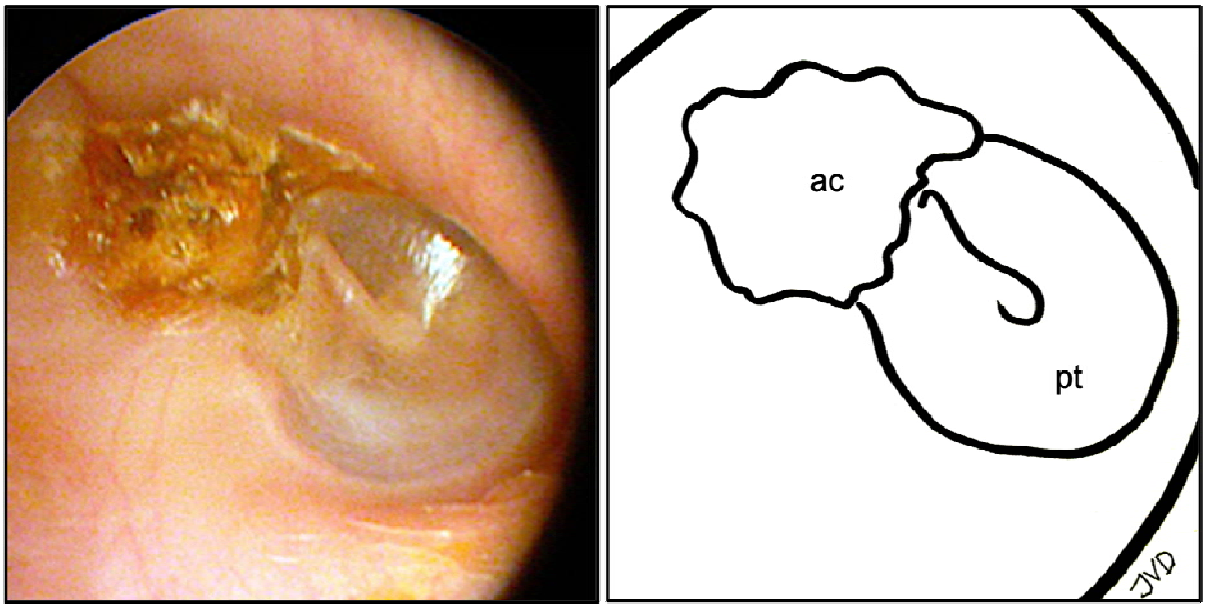

Figure 5. Otoscopy of a right ear with an **ac**: attic cholesteatoma; **pt**: pars tensa.

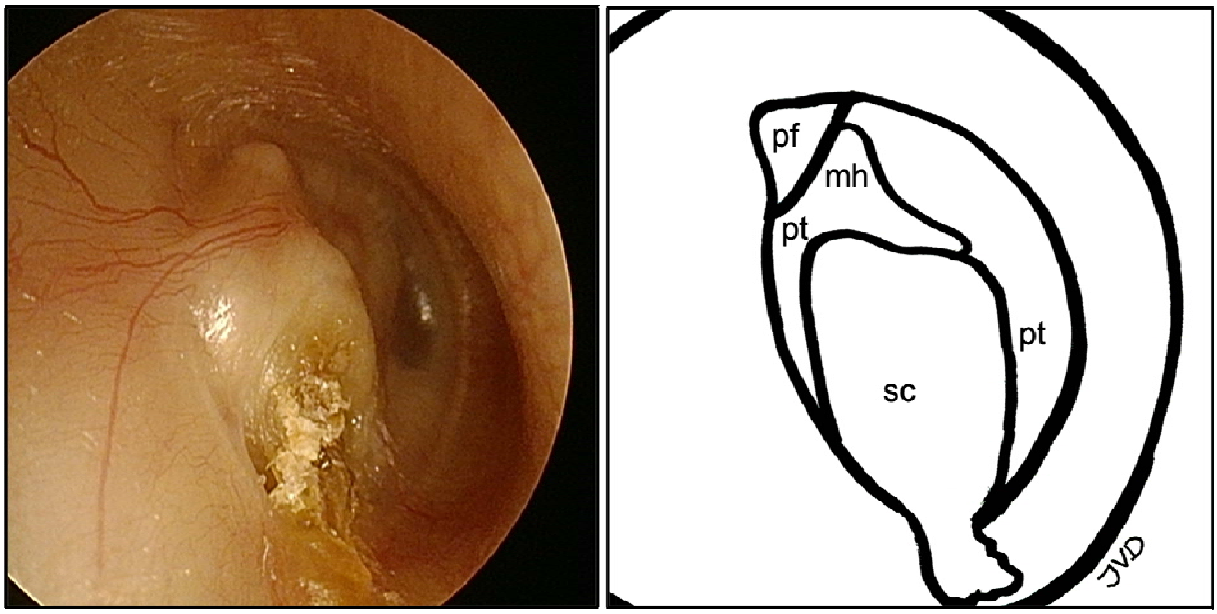

Figure 6. Otoscopy of a right ear with a **sc:** sinus cholesteatoma; **pt**: pars tensa; **mh**: malleus handle; **pf**: pars flaccida.

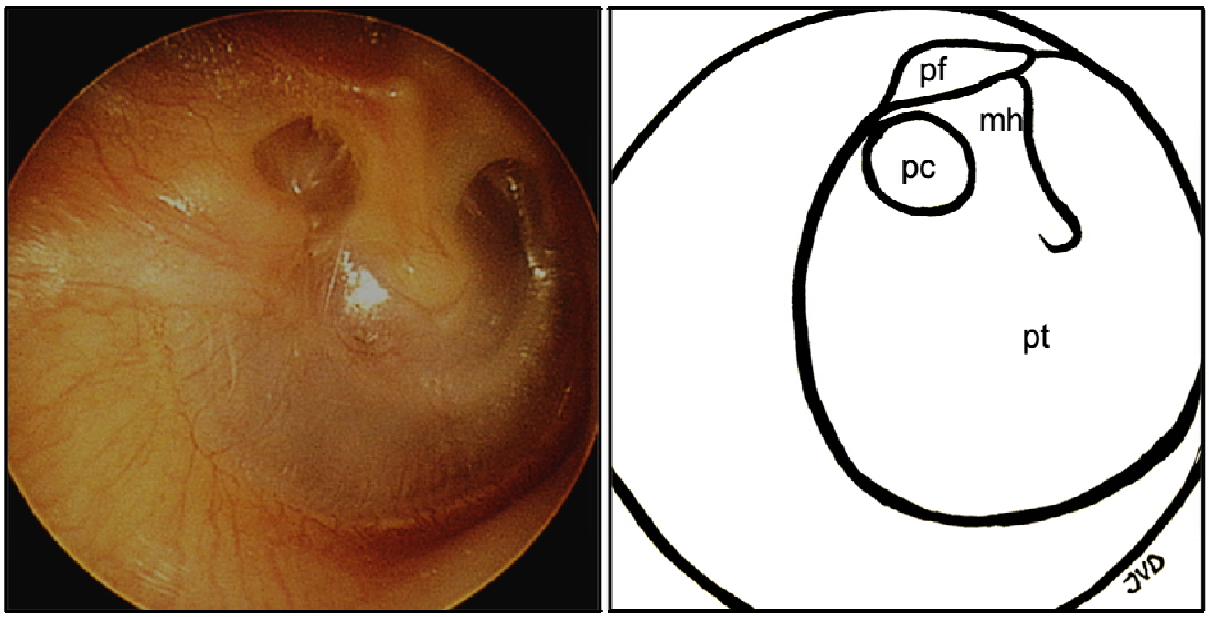

Figure 7. Otoscopy of a right ear with a **pc**: pars tensa cholesteatoma; **pt**: pars tensa; **mh**: malleus handle; **pf**: pars flaccida.

1.1.5 Epidemiology

The incidence of cholesteatoma in adults is 9.2 per 100.000 per year, with a male predominance of 7/5. In children it is estimated at 3 per 100.000 per year. There is a higher prevalence among Caucasian individuals. Cholesteatoma is rarely found in the Asian, American Indian and Alaskan Eskimo population.(56,57) Kemppainen found no influence of social status.(56)

In a retrospective study of cholesteatoma patients (n=54) Van Cauwenberge and Vermeersch found that all cases except one previously had a middle ear problem, recurrent acute otitis being the most important problem. Cholesteatoma rarely developed after tympanostomy tube insertion.(58) In the Kemppainen study of cholesteatoma patients (n=500), 72% of cholesteatoma patients had prior otitis media episodes. Tympanostomy had been carried out in 10%, and adenoidectomy or adenotonsillectomy in 16% of all cholesteatoma ears prior to cholesteatoma surgery. Four % of patients had prior ear trauma and 9% had prior ear surgery. In 1.4% of the cholesteatoma patients a cleft palate was present. Whereas in the cleft palate patient group 8% developed a cholesteatoma. In only 4% of cholesteatoma patients bilateral disease was found.(56)

Various underlying situations such as tuba dysfunction, might create a predisposition for the development of acquired cholesteatoma. A 20-fold higher risk for cholesteatoma is found in non-syndromic cleft palate.(59) Syndromes characterised by craniofacial anomalies, such as Turner syndrome, have a higher prevalence of cholesteatoma.(60) Down syndrome carries a higher risk for otitis media with effusion. This is possibly responsible for later arriving complications such as cholesteatoma.(61) Down ears often shows specific anatomical features, such as a narrow external auditory canal, an anteriorly curved scutum in relation to the canal wall, a hypoplastic mastoid and a low tegmen tympani. While these anatomical features may facilitate cholesteatoma formation, they also make its surgical treatment more challenging.

Congenital cholesteatoma of the middle ear represents 2% of all middle ear cholesteatomas.(5) In the paediatric cholesteatoma population up to 16% of congenital cholesteatoma is found.(62) Kemppainen found cholesteatoma behind an intact tympanic membrane without a previous otitis media history in 0.6%., which suggests an embryological pathogenesis.(56)

1.1.6 Etiopathogenesis

1.1.6.1 Etiopathogenesis of Congenital Cholesteatoma

In 1953 House reported the first case of a congenital or 'primary cholesteatoma'.(4) Derlacki and Clemis described another six cases in 1965 and were the first to establish clinical criteria for the diagnosis of congenital cholesteatoma. It was then defined as an epithelial inclusion cyst behind an intact tympanic membrane in a patient without a prior history of otitis media.(5) Later, Levenson et al. concluded that the diagnosis of a congenital cholesteatoma could not be excluded by prior otitis media.(63) Different theories on the etiopathogenesis exist.

The Ectoderm Migration Theory

In the ectoderm migration theory, the ectoderm from the primitive ear canal passes through or around the tympanic ring to enter the middle ear space.(64)

The Metaplasia Theory

The metaplasia theory suggests that otitis media or other inflammatory middle ear processes result in squamous metaplasia leading to keratin formation.(65)

The Amniotic Cell Migration Theory

The amniotic cell migration theory of the group of Northrop suggested that viable squamous epithelial cells found in amniotic fluid in the middle ear could be a potential source for congenital cholesteatoma.(66)

The Invagination or Acquired Inclusion Theory

The invagination or acquired inclusion theory of Tos states that inflammation in the middle ear causes a portion of the tympanic membrane to invaginate, trapping epithelium in the middle ear space.(67)

The Epidermoid Formation Theory

In Michaels' epidermoid formation theory, epithelial cells identified in the lateral walls of the embryonic cavity should normally disappear by 33 weeks of gestation. If these cell remnants do not involute, a congenital cholesteatoma forms.(68)

Although the epidermoid formation theory is the most widely accepted for the middle ear cavity, it has not been quoted for the deeper temporal bone structures in which congenital cholesteatoma can also occur. An epidermoid cyst or congenital petrosal cholesteatoma originates at the time of neural tube closure due to entrapment of

ectoderm – the later skin – in the head. If the entrapment takes place inside the dura, the lesion is called epidermoid or epidermoid cyst. The most frequent location of an epidermoid cyst is the cerebellopontine angle where it is reported to be the third most frequent mass lesion after vestibular schwannoma and meningioma. If the ectoderm gets trapped outside the dura, but inside the petrous bone, it is called a congenital petrosal cholesteatoma. Histologically, an epidermoid cyst and a congenital cholesteatoma are exactly the same, consisting of entrapped ectoderm or skin. As the skin is gradually exfoliating, the lesion very slowly but gradually starts to grow. Depending on its location, clinical symptoms may arise.(69)

When situated in the middle ear cavity the cholesteatoma is mostly found in the anterosuperior part in contact with the malleus head and incus body. From that point extension towards the antrum and mastoid is possible. In the mesotympanum extension along the long process of the incus, the incudostapedial joint and the crura, the facial nerve, the footplate, the promontory and the sinus tympani is possible with subsequent bony erosion. If the congenital cholesteatoma is arising from the temporal bone near the otic capsule it is very often found near the geniculate ganglion and from there on invading all adjacent structures.(5,62,70)

1.1.6.2 Etiopathogenesis of Acquired Cholesteatoma

The Squamous Metaplasia Theory

In the squamous metaplasia theory, inflammation in the middle ear leads to transformation of the middle ear mucosal lining. Squamous metaplasia from middle ear mucosa has been observed in animal models, but no histological or experimental evidence exists demonstrating that metaplasia can results in cholesteatoma. All current evidence suggests an ectodermal origin.(71)

The Squamous Immigration or Invasion Theory

The squamous immigration theory refers to squamous keratinising epithelium migration along the margin of a tympanic membrane perforation, thus entering the middle ear cavity. The main dilemma regarding this theory is the discrepancy between the incidence of tympanic membrane perforations and the incidence of cholesteatoma. The great majority of cholesteatomas develops from an intact tympanic membrane.(72,73)

The Squamous Basilar Hyperplasia or Papillary Ingrowth Theory

Following the basilar hyperplasia theory, the basal keratinocytes are thought to proliferate and penetrate the basal membrane, with extending elongated pseudopodia

into the subepithelial space. Although inflammation can drive proliferation, there is no supporting evidence to explain why these basal cells migrate medially rather than laterally. Another requirement for pathogenesis of cholesteatoma in this setting would be the weakening of the supporting structures and inward retraction exerted on these basal cells.(74,75)

The Retraction Pocket Theory

The retraction pocket theory is the most widely accepted theory today. Other terms for the same theory are the "Squamous Obstruction-Vacuum-Retraction" or "Ex Vacuo" theory. A dysfunction of the ventilation of the middle ear causes a vacuum of the tympanic cavity, which causes retraction of the tympanic membrane. This theory is mainly based on the following observations: cholesteatoma formation in 75% of cases after ligation of the Eustachian tube in a gerbil model; the observation of increased cholesteatoma incidence in cleft palate patients; and the occurrence of retraction pockets in the epitympanum.(76-78) In this theory the formation of two different subtypes of cholesteatoma is explained depending on the location of the retraction: the attical or pars flaccida cholesteatomas and the pars tensa cholesteatomas. Most frequently, these retraction pockets are situated in the pars flaccid, further expanding into the lateral epitympanic space, the so-called Prussack space. Gradually exfoliating, the retraction pocket enlarges, eroding the surrounding bony structures such as the malleus head, the incus body and the lateral epitympanic wall. A defective self-cleaning capacity of the external auditory canal skin causes the accumulation of keratin leading to the formation of a cholesteatoma. When the cholesteatoma further grows, it will expand and fill up the attic, possibly eroding the tegmen tympani, the bony delineation of the tympanic segment of the facial nerve and the lateral semicircular canal. The cholesteatoma may then invade the middle cranial fossa or the membranous labyrinth and it may also enter the petrous apex. Less frequently, the retraction pocket will originate at the posterosuperior pars tensa of the tympanic membrane and will expand around the long process of the incus, extending further medially to the stapes, the aditus, antrum and mastoid. This type of cholesteatoma is called a sinus or marginal type pars tensa cholesteatoma. If it originates more centrally, it is called a central or true pars tensa cholesteatoma. A pars tensa cholesteatoma usually expands medial to the ossicular chain and moves upwards displacing the ossicles laterally.

The Mucosal Traction Theory

Recently, Jackler et al. described the mucosal traction theory. He defined the shortcomings in the way the invagination of the tympanic membrane evolves to a cholesteatoma is explained by the different theories.(55)

Shortcomings in Other Theories

Some serious shortcomings mainly concerning the retraction pocket theory were defined: there are animal models with Eustachian tube dysfunction which do not induce cholesteatoma; cleft lip repair and transtympanic drain placement does not reduce the incidence of cholesteatoma; a vacuum can initiate tympanic membrane retraction but is not a sustaining force for the progression since the epitympanum, aditus and antrum become blocked early in the course of the disease with mucus and inflammatory tissue (granulation, polyps) and gas reabsorption is difficult in these circumstances; wide-mouthed pockets empty of keratin debris, can progressively invaginate into a nonaerated epitympanum and mastoid; endoscopy of the Eustachian tube in cholesteatoma patients shows a lack of pathological changes; ears with tubal occlusion rarely develop cholesteatoma; it has long been maintained that the pars flaccida which is the most common segment of the tympanic membrane to generate cholesteatoma was thinner than the pars tensa but the opposite is actually true; transtympanic ventilation drains (tubes) do not prevent cholesteatoma formation and recurrence after canal wall up tympanoplasty.(55)

Observations not explained with former theories

Why cholesteatoma arise from the pars flaccida, superior and posterior pars tensa quadrants of the tympanic membrane and not anteriorly or inferiorly

How cholesteatoma growth can be driven into nonaerated spaces such as a disease filled epitympanum and antrum

Why some ears develop stable atelectasis and others develop cholesteatoma

The frequent lack of abnormality of the Eustachian tube and protympanum

Why anatomical obstruction of the Eustachian tube does not routinely lead to cholesteatoma formation

Why functioning transtympanic drains (tubes) do not prevent cholesteatoma recurrence

Why cholesteatomas arise in older children and young adults, but not in infants and seldom in young children

Why cholesteatoma is strongly associated with mastoid hypopneumatization

Figure 8. Observed unexplained behavior of cholesteatoma in the retraction theory (adapted from Jackler 2015).(55)

The authors stated that the vast majority of acquired cholesteatoma arise when a pouch of the tympanic membrane draws into the attic and/or posterior mesotympanum. The migration of the squamous outer surface of the tympanic membrane and the aggressive keratin behavior has been well characterised but there is a paucity of data available concerning the migratory behavior of its medial surface, the mucosa. The existing theories of primary acquired cholesteatoma do not adequately explain the observed

characteristics of the disease. A comprehensive theory for the pathogenesis of primary acquired cholesteatoma needs to explain all aspects of its observed behavior (Figure 8).

The Middle Ear Mucosa

Jackler proposed a new hypothesis which states that the mucosal membrane interactions are the driving force in cholesteatoma formation. Given the role of the mucosa in this new theory, it is important to review what is known about the mucociliary system of the middle ear. The tympanum is lined by a respiratory epithelium, which is low and cuboidal in many areas, columnar in others, with a variable distribution of secretory (goblets) cells and cilia. Cilia are also present on the under surface of the tympanic membrane. Sade described two different pathways to clear the middle ear towards the Eustachian tube: the inferior or lower hypotympanic pathway via the floor of the middle ear (most prominent) and an upper or superior pathway with a tract along the anterior tympanic cavity, a tract along the roof, and a tract over part of the promontory.(79) In contrast to the migration of the epithelial surface of the tympanic membrane, little is known about the movement of the mucosal undersurface of the eardrum. The mucociliary apparatus consists of three functional compartments: the cilia, a protective mucus layer, and an airway surface liquid layer.(80) Respiratory mucosal surfaces are well known to migrate upon their basal lamina in the nose, trachea and bronchi. Jackler et al. in their rat study could prove ink migration but not if this was done by the mucosa itself or its mucous blanket.(55) It is likely that mucosa in the ear behaves in a similar way as in the other respiratory mucosal surfaces. It is likely that human mucosal migration on the tympanic membrane directs the secretion to join the superior or inferior Sade pathways. The mucosal migration pattern of the ossicles has not been well studied but this is presumably via the superior pathway. The mucous blanket presumably bridges to the floor of the epitympanum via the mucosal surfaces of the suspensory ligaments.(55) mucociliary clearance in the middle ear is rapid and efficient in expelling material from the tympanum to the Eustachian tube.(79) In the rat study, the ink migrated from the tympanic membrane surface towards the Eustachian tube via a predictable pathway. If the mucosa of the undersurface of the tympanic membrane leads to trapped mucosal elements such as mucin or secretory cells, this possibly results in inflammation.(55)

The Mucosal Coupling and Traction Theory

When, after an initial retraction, the mucosa of the under surface of the tympanic membrane comes in contact with the mucosa of the lateral surface of the ossicles, these two mucosal layers may get coupled. Once coupled the mucosal migratory propulsion of the conjoined layers could drag the pliable tympanic membrane superiorly. Theoretically the upward traction could be generated by different potential types of mucosal

interaction: i.e. mucous blanket migration, mucosal migration, and/or sequential adhesion.(55)

Therapeutic Implications

The theory implies to avoid fascia and use hermetic cartilage placement during tympanic membrane reconstruction at the level of the posterosuperior tympanic membrane and the scutum to prevent retraction, mucosal traction and recurrent cholesteatoma.(55)

1.1.7 Diagnosis and Follow Up of Cholesteatoma

1.1.7.1 Diagnosis

Clinical Diagnosis

Otorrhea, hearing deterioration, vestibular signs and facial nerve palsy are the potential initial symptoms caused by cholesteatoma, although it can initially develop silently for quite a long period. These clinical symptoms are the result of expansion of the lesion, leading to destruction of adjacent structures, inflammation and periodic surinfection. The presence of a cholesteatoma needs to be excluded when one of these symptoms is present and especially when there are signs of meningitis or a brain abscess.

Acquired cholesteatoma is mainly diagnosed by micro-otoscopic confirmation after suction cleaning or “nettoyage" of the ear. Various signs can be seen: whitish non-migrating desquamation, retraction pockets with or without tympanic membrane perforation, inflammation with polyp formation, bone destruction, ossicular erosion all in different combinations (Figure 9).

Evaluation of the hearing, the vestibular function, if necessary, the facial function, and the quality of life is performed during this initial stage.

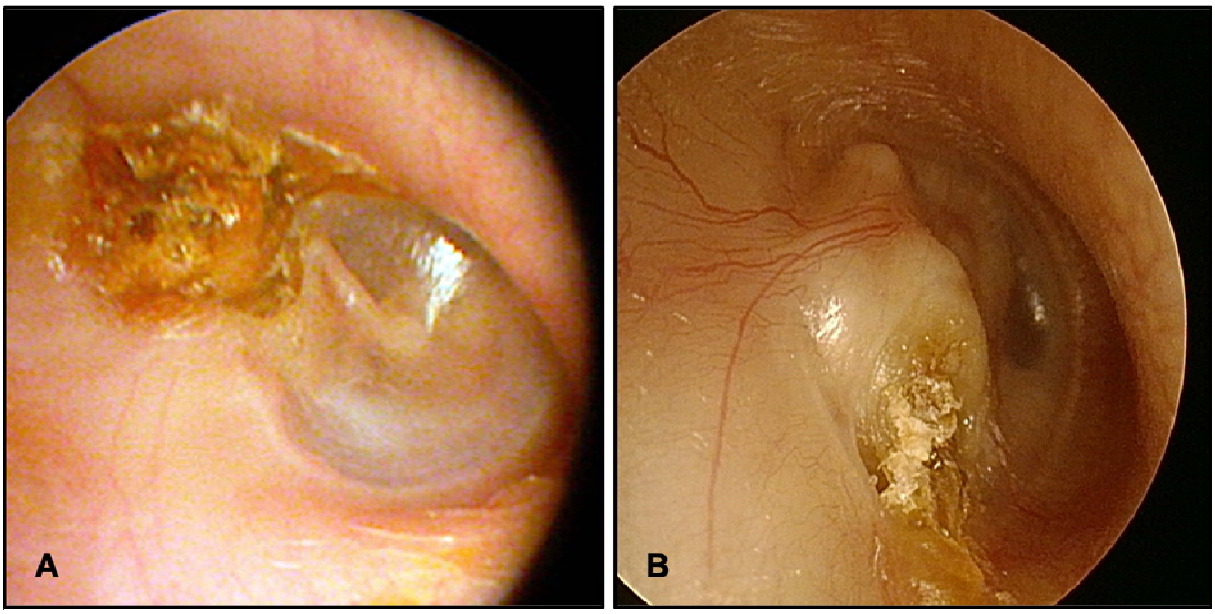

Figure 9. Otoscopic view. **A,** view of right ear with an attic cholesteatoma. **B,** view of a right ear with a sinus (marginal pars tensa) cholesteatoma.

Imaging Diagnosis

Although micro-otoscopic evaluation remains the first step in the diagnosis of acquired cholesteatoma, imaging plays an important supporting role (Figure 10).

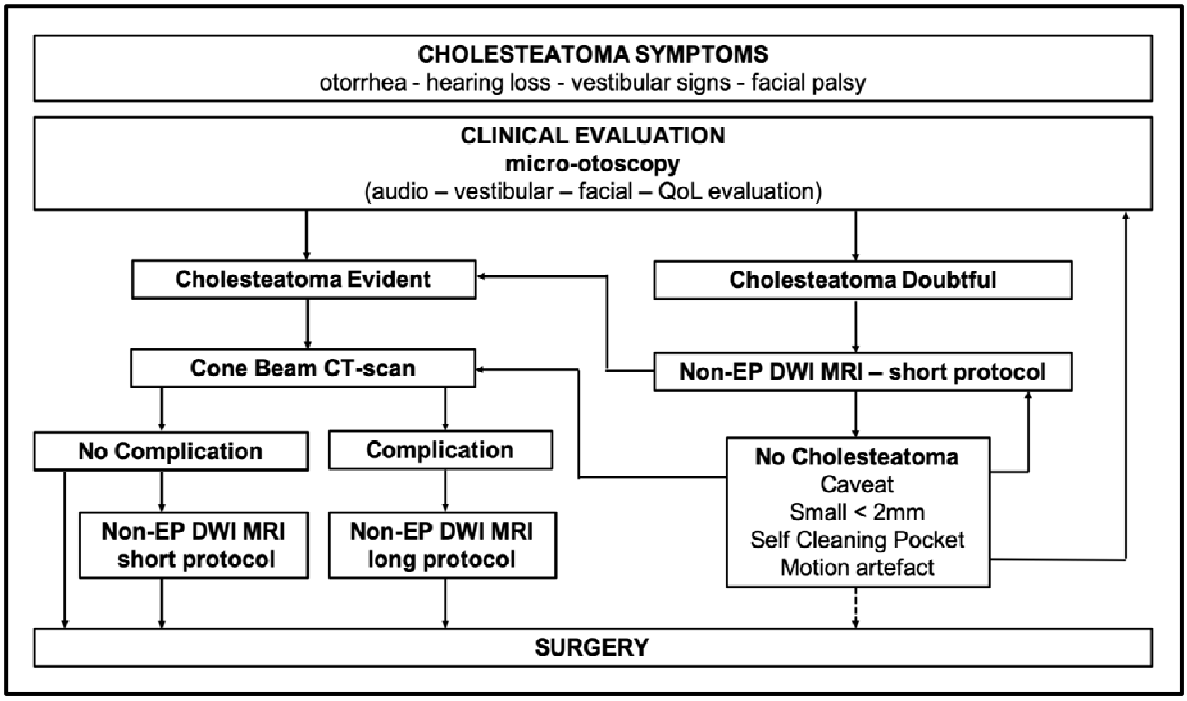

Figure 10. Possible diagnostic flowchart for cholesteatoma. From cholesteatoma symptoms to surgery or re-evaluation with all possible diagnostic tools available.

Nowadays non-EP DW MRI is the most sensitive type of imaging for the radiological diagnosis of cholesteatoma, depicting its exact location and extent. If one corrects for motion artefacts and (auto) evacuated cholesteatoma the sensitivity and specificity is extremely high. CT-scan is added for the pre-operative planning and as a “road map” during surgery.(69,81) The MRI and CT images can be fused into one image to facilitate detailing the location of the lesion and to plan the surgical approach.

Many surgeons still only use CT-scan to confirm their clinical diagnosis. This can be misleading. When a typical soft tissue mass with focal areas of bony erosion of the middle ear (including ossicles) and mastoid is seen on CT-scan, the presence of a cholesteatoma is confirmed. However, when there is no bony erosion and only “opacification” of the middle ear spaces is present, it is impossible to distinguish between inflammation tissue, scar tissue, cholesterine granuloma, fat, liquid and cholesteatoma. This fact makes MRI rather than CT the imaging technique of choice to confirm the diagnosis in case of clinical doubt. To avoid unnecessary radiation, a CT-scan should only be performed once the decision for surgery has been taken. It yields useful information for the pre-operative

planning (urgent versus not urgent, as in case of fistula to the inner ear) and provides an excellent surgical “road map” (Figure 11).(69)

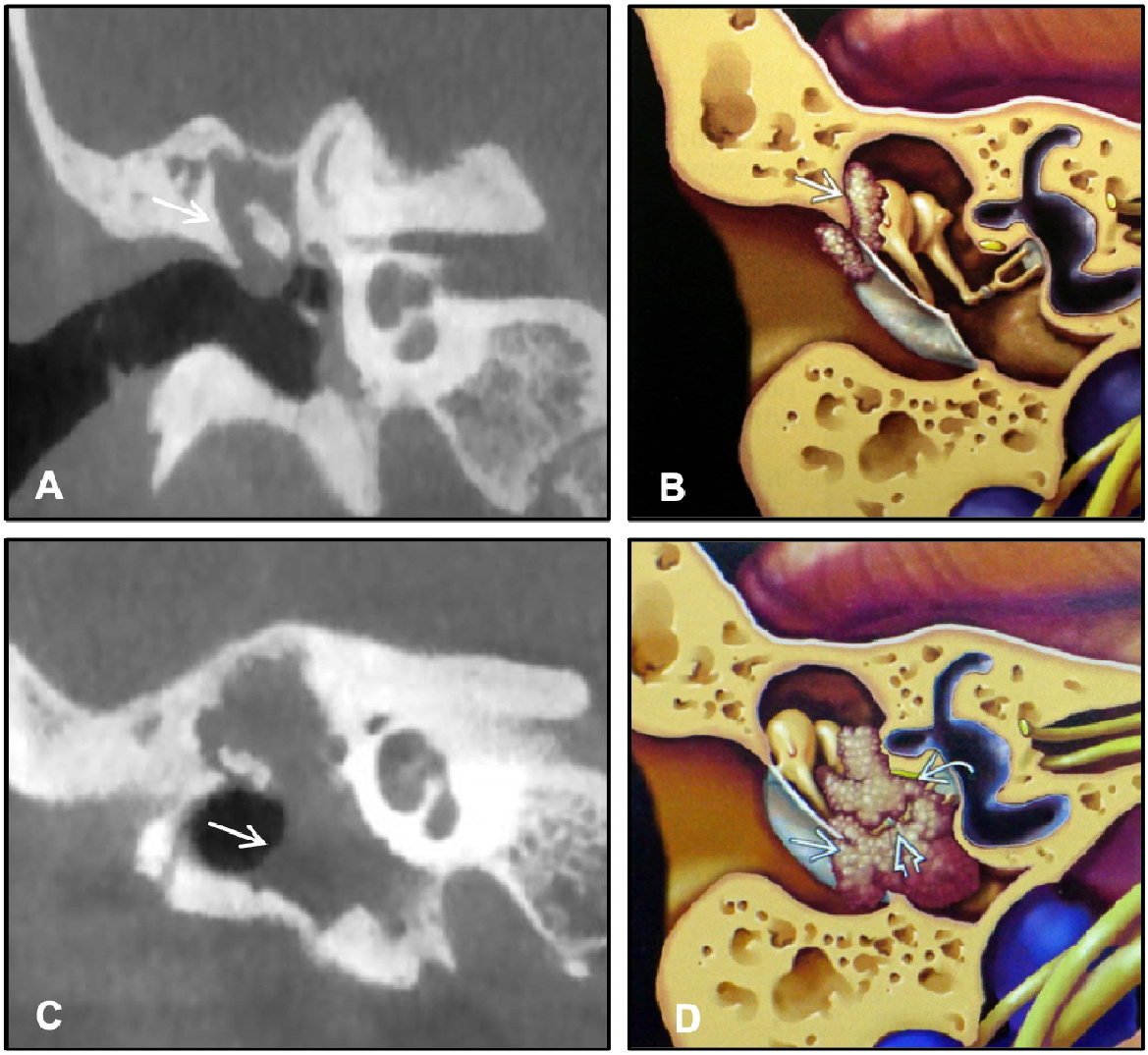

Figure 11. Cone Beam CT-scan preoperative, cases of acquired cholesteatoma, coronal views. **A,** attic cholesteatoma with erosion of the malleus head. **B,** schematic overview of attic cholesteatoma (Courtesy: Diagnostic Imaging, Head and Neck, Amirsys). **C,** sinus (pars tensa) cholesteatoma with erosion of stapes. **D,** schematic overview of sinus (pars tensa) cholesteatoma (Courtesy: Diagnostic Imaging, Head and Neck, Amirsys).

If the initial diagnosis of cholesteatoma is still doubtful a “short-protocol” non-EP DW MRI can be performed. If the non-EP DW MRI is positive for the presence of cholesteatoma, then a CT-scan can be performed, this again to prevent unnecessary irradiation, especially in children (Figure 12).

If the CT-scan shows destruction of important structures: the facial nerve, the inner ear, the tegmen tympani or certain regions are doubtful regarding invasion by the cholesteatoma, a non-EP DW MRI should always be performed during the pre-operative

radiological workup. If the status of the inner ear needs to be evaluated (i.e. fluid in the cochleae, the vestibulum, the lateral canal) and/or a complication or fistulisation is suspected, a complete MRI or "long-protocol" non-EP DW MRI with heavily-weighted T2 images and gadolinium-enhanced T1-weighted images is needed (Figure 13).(69)

Congenital cholesteatoma is an exception. At micro-otoscopic examination a with mass can sometimes be seen anterior and later posterior of the malleus behind an intact tympanic membrane. If there is conductive hearing loss a (Cone Beam) CT-scan is indicated since surgical intervention with a functional aim is likely. If the hearing is normal, a non-EP DW MRI can be performed to exclude a congenital cholesteatoma. If MRI is positive, a (Cone Beam) CT-scan is then performed for the surgical planning (Figure 14).

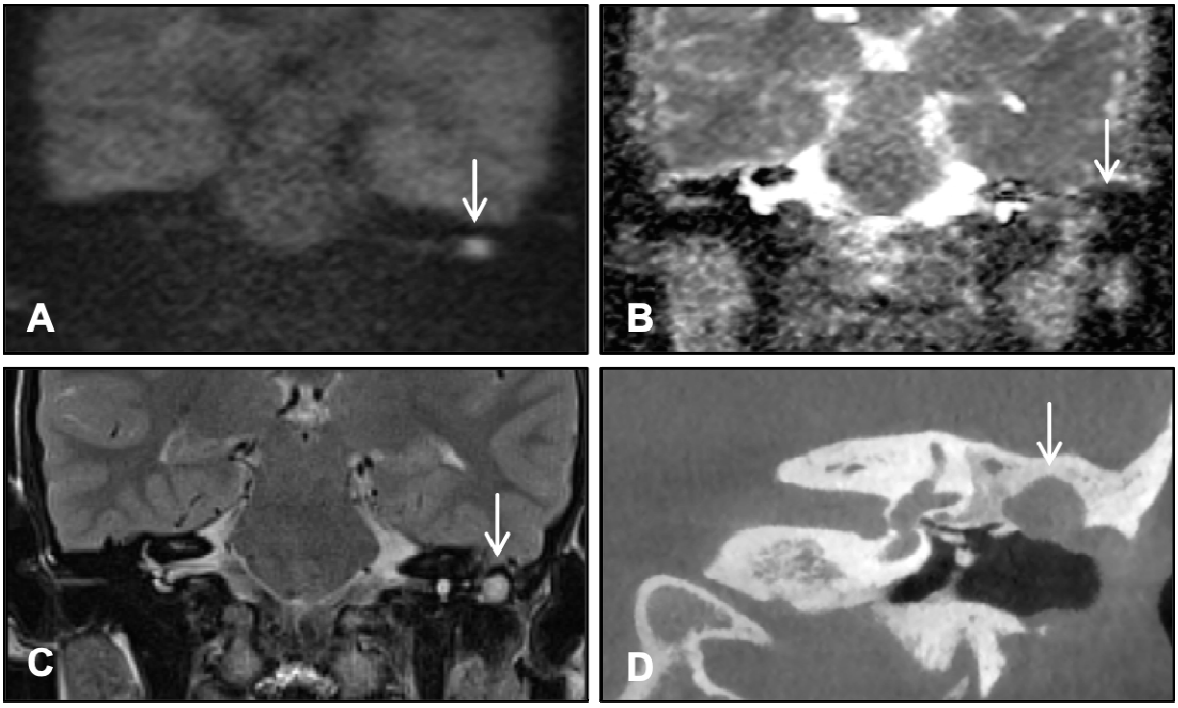

Figure 12. Short-protocol non-EP DW MRI. Follow up MRI protocol with recurrent cholesteatoma in the left ear after a left-sided bony obliteration. **A,** MRI, coronal b 1000 non-EP DWI, showing the cholesteatoma as a bright spot. **B,** MRI coronal ADC map. The cholesteatoma shows a clear drop in signal and become hypo-intense. **C,** MRI coronal TSE T2. The cholesteatoma displays moderate hyperintensity. **D,** Cone Beam CT-scan performed after positive MRI as pre-operative road map, showing the lesion originating from the roof of the external auditory canal.

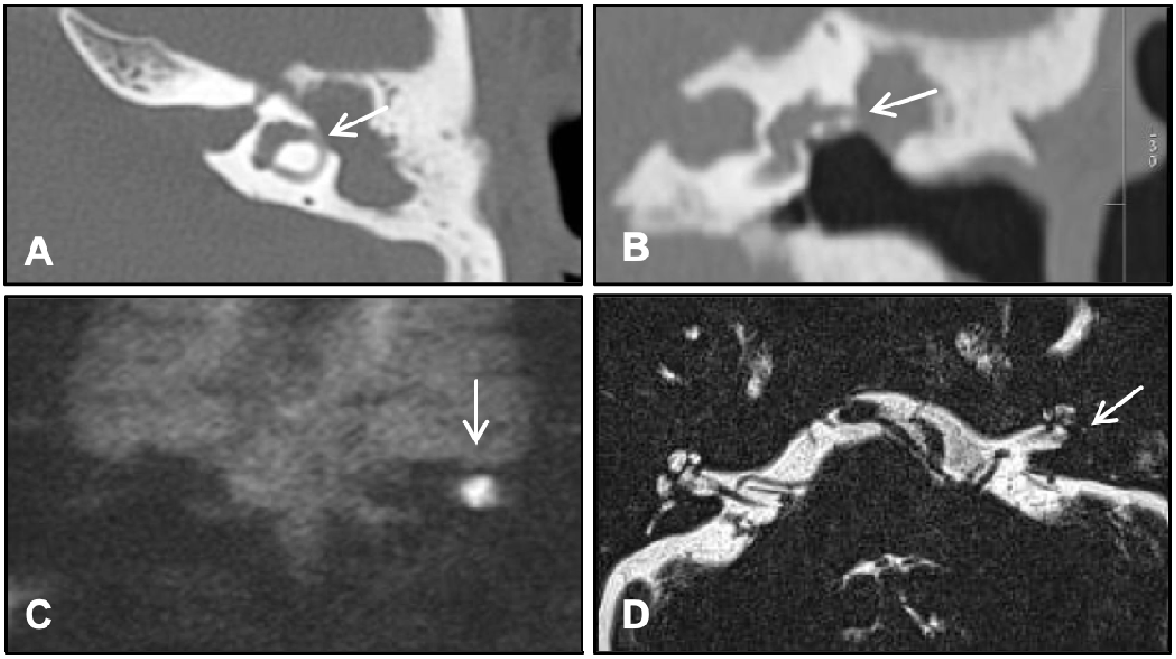

Figure 13. Complicated acquired cholesteatoma case: preoperative imaging work-up. **A,** Axial CT image at the level of the lateral semicircular canal: the ossicular chain can no longer be discriminated in the opacified middle ear and there seems to be a communication towards the lateral semicircular canal (arrow). **B,** Coronal CT reformation showing the communication with the lateral semicircular canal (arrow). **C,** MRI coronal b 1000 non-EP DWI. The cholesteatoma is seen as a hyperintense nodule, under the left temporal lobe (arrow). **D,** MRI axial 3D TSE T2, showing signal loss in the left cochleovestibular labyrinth due to labyrinthitis and subsequent fibrosis of the membranous labyrinth (arrow).

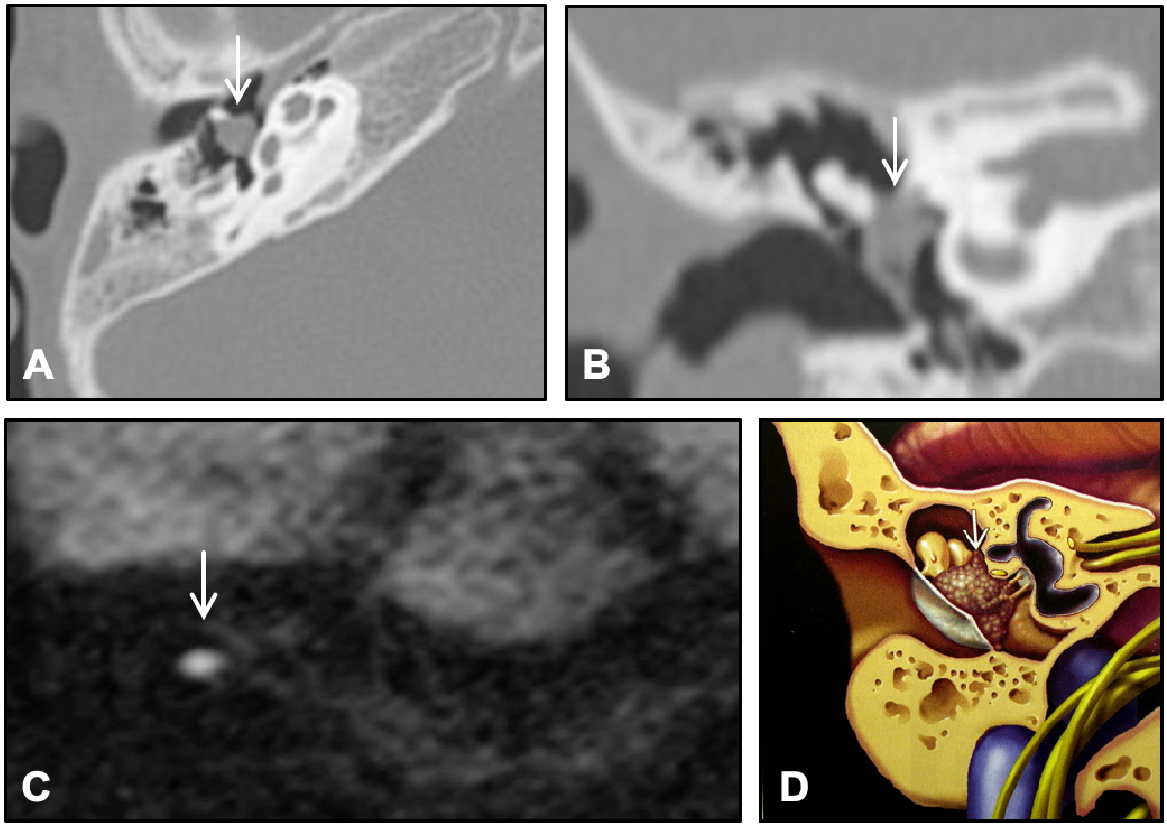

Figure 14. Congenital cholesteatoma. **A,** Axial CT image at the level of the basal turn of the cochlea showing a small sharply delineated nodule medial to the ossicles (arrow). **B,** Coronal CT reformation shows a sharply delineated soft tissue mass medial to the ossicles (arrow). **C,** Coronal b1000 non-EP DW MRI shows the congenital cholesteatoma as a small hyperintense nodule (arrow). **D,** Schematic overview of a congenital cholesteatoma (Courtesy: Diagnostic Imaging, Head and Neck, Amirsys).

1.1.7.2 Follow Up

Because of the risk for residual disease and the tendency for recurrence, patients need to be strictly followed up after surgical removal of the cholesteatoma.

Clinical Follow Up

Screening for recurrent disease, i.e. a newly formed cholesteatoma, is done by yearly micro-otoscopy for at least 10 years. This is combined with evaluation of the hearing, the vestibular function, if necessary, the facial function, and the quality of life by standardised questionnaire.

Imaging Follow Up

Screening for residual disease is done by repeated MRI imaging, using the non-EP DW MRI sequence, up to five years post-operatively (Figure 15). Residual cholesteatomas, smaller than 2 mm, are not yet detectable on the non-EP DWI sequence. Therefore, repeated MRI

imaging up to 5 years is advised.(69,82) We want to catch residual disease early on so it can be easily removed without disturbing the reconstructed ear too much. However, this necessitates follow up imaging to catch the initially missed small residual (< 2 mm) that has grown in the meantime (Figure 16). The frequency of imaging follow up during this period is determined by the surgeon, depending on the observed aggressivity of the pathology, the age of the patient and the subjectively perceived certainty by the surgeon of complete removal of the cholesteatoma.

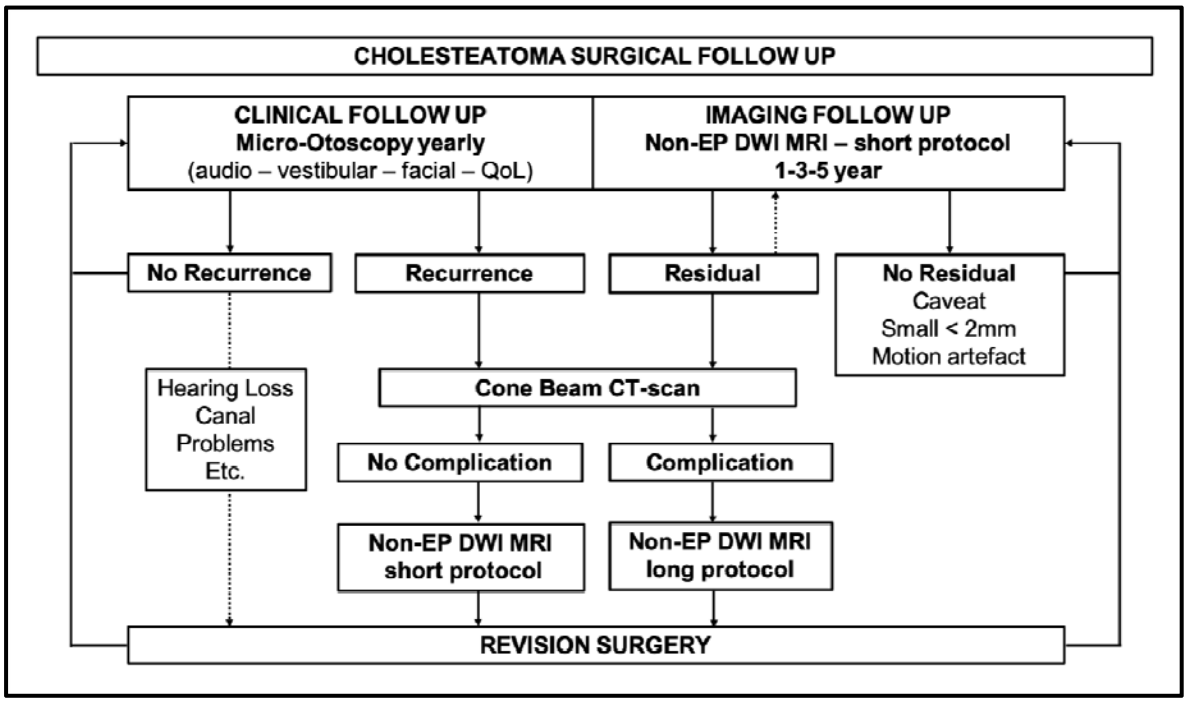

Figure 15. Possible follow up flowchart for cholesteatoma. Clinical, audiovestibular and radiological evaluation with all possible diagnostic tools available.

One should be careful with a negative interpretation of the non-EP DW MRI in case of motion artifacts or the presence of dental fixtures which can disturb the image. In case of doubt the MRI must be repeated after removal of the dental fixtures.

If during micro-otoscopy follow up a retraction pocket is observed which cannot be totally overseen, MRI is performed to exclude cholesteatoma recurrence. However, if the pocket is still self-cleaning, the non-EP DW sequence will be negative, since there is no mass of keratin present. In such a case a CT-scan is helpful to visualise the depth of the retraction and determine the advisability of revision surgery. If a residual cholesteatoma is found, again a pre-operative CT-scan (road map) should be performed to prepare for surgery.
If the ear is free of cholesteatoma on MRI follow up, but the audiogram shows a remaining conductive hearing loss and the patient wants hearing improvement by surgery, a CT-scan is warranted to determine the feasibility of surgical improvement, by

showing aeration of the middle ear space and possibly visualising the cause of the conduction loss (Figure 17).

Today we preferably use Conebeam CT instead of the conventional multidetector CT, since it gives a much lower radiation dose to the patient and has a much higher resolution power. This requires strict immobilisation of the head during the examination. This can be problematic in young children and in the elderly population (tremor).

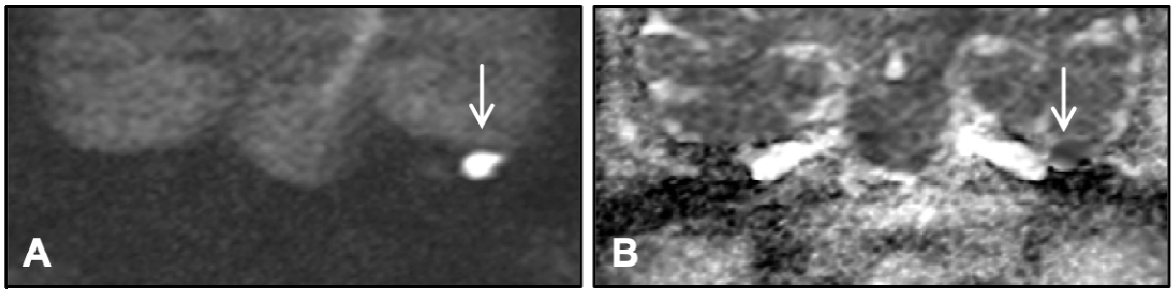

Figure 16. Follow up MRI images. **A,** Coronal b 1000 non-EP DW MRI with residual cholesteatoma presenting as a nodular hyperintensity in the left ear (arrow). **B,** Coronal ADC map confirming the presence of a residual cholesteatoma as a clear signal drop (arrow).

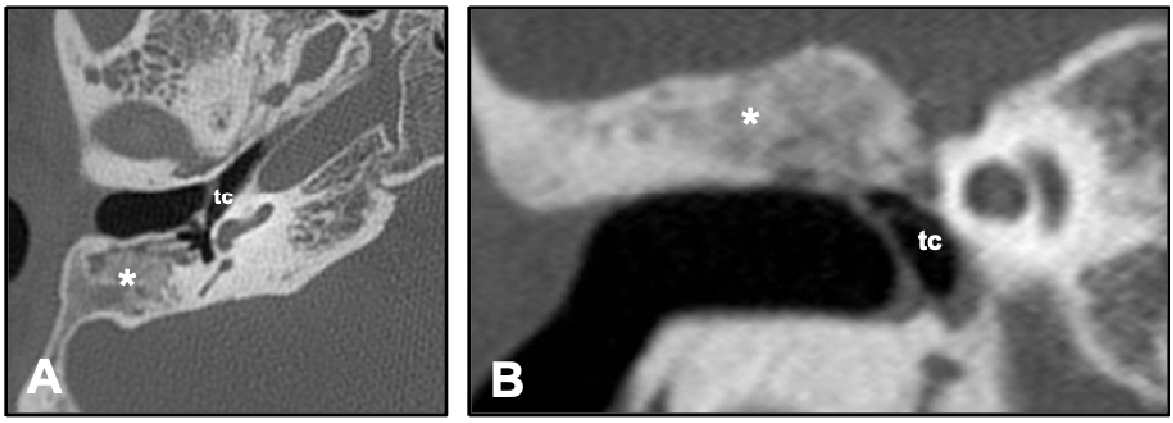

Figure 17. CT-scan after bony obliteration tympanoplasty indicated for the evaluation of aeration and ossicular status prior to middle ear inspection for hearing improvement. **A,** Axial view with bony obliteration tympanoplasty (*****) of the mastoid and a well aerated **tc**: tympanic cavity. **B,** Coronal CT reformation with bony obliteration tympanoplasty (*****) of the mastoid and a well aerated **tc**: tympanic cavity.

1.1.8 Goals and Outcome in Cholesteatoma Treatment

In the industrialised world we tend to forget about the days when cholesteatoma patients died from intracranial complications. In the early days of the otological history, when antibiotherapy was not yet available, cholesteatoma needed surgery to save lives.(29) Today the main indication for treatment of cholesteatoma is still the safety of the patient, aiming to prevent potentially serious, even lethal complications. Fortunately, antibiotics and effective surgical procedures make a lethal outcome extremely rare. Nowadays, cholesteatoma management has a much wider scope than just safety, including hygienic and functional aims, thus vastly improving the patient's quality of life.

The primary goal of the surgical treatment of cholesteatoma is the complete eradication of the disease (i.e. prevention of residual disease) while avoiding operative complications, whereas the secondary goals are the prevention of recurrent disease, the improvement of the hygienic status of the ear, and the preservation or improvement of the hearing and vestibular function. An optimal disease specific quality of life status is achieved when both the primary and the secondary goals are fulfilled.
Many variables influence the long-term outcome of surgery. The more extensive the disease and damage at initial presentation, the poorer the outcome. An important variable influencing the outcome of surgery for chronic otitis media with cholesteatoma is the quality of the surgical act, which depends on different factors including the surgeon's personal experience and skills, the choice of the surgical technique, and choice of the material used for the reconstruction.

1.1.8.1 Safety

To achieve all the safety goals various aspects concerning safety are important in all the stages of the disease and its treatment and follow up, starting with the best possible preoperative diagnostics and surgical planning.

Residual Disease

Residual cholesteatoma disease is due to remnants of cholesteatoma matrix (skin) left behind in the cavum tympani and/or paratympanic spaces behind the reconstructed tympanic membrane and canal skin. A residual cholesteatoma could again lead to all the possible complications of the natural course of cholesteatoma. Therefore, the complete eradication of the cholesteatoma should always be aimed for.

Recurrent Disease

Recurrent cholesteatoma disease is the new formation of a cholesteatoma by retraction of skin from the tympanic membrane or the canal. A recurrent cholesteatoma could again lead to all the possible complications of the natural course of cholesteatoma. A recurrent cholesteatoma should be prevented as much as possible by choosing the best possible surgical techniques in the given socio-economic setting.

Surgical Complications

During the eradication and reconstructive surgical procedure, the safety concerning facial nerve, hearing, vestibular function, vascular and dural integrity must be guaranteed to avoid all possible surgical complications.

Re-operative Rate

The number of re-operations (re-operative rate) needed to reach a certain safety, hygienic status, hearing and quality of life levels should be taken into account. Both the surgical technique and adequate follow up tools such as non-EP DW MRI are significant re-operative rate decreasing game-changers.

1.1.8.2 Hygienic Restoration

To have a dry, self-cleaning, waterproof ear, fit to receive a hearing aid and free of frequent ambulant care is in an important goal. The use of a closed technique, which means that at the end of the surgical reconstruction there is an intact bony or cartilaginous canal wall, avoiding all types of open cavities, is therefore mandatory. In certain situations meatocanalplasty can be very helpful.

1.1.8.3 Functional Hearing

Functional hearing means an almost intact inner ear function with a minimal air-bone gap, offering sufficient hearing levels to hear without the need for a hearing aid. In certain cases the inner ear function is decreased before initial surgery. Frequently the biological and mechanical status of the tympanic cavity is unfavorable to achieve good results with ossicular chain reconstruction (fibrosis or lack of aeration of the middle ear cavity, ossicular fixation due to tympanosclerosis or scarring of the ossicles, concomitant stapes fixation due to otosclerosis, etc.). So hearing improvement still remains an great challenge in cholesteatoma surgery. However, these patients can still be helped by fitting a conventional hearing aid, on condition that the surgery has provided a dry, self-cleaning external ear canal. More invasive alternatives are a bone anchored implant, or an active middle ear implant. This being said, some reconstructive techniques tend to be more efficient in improving the natural hearing than others.

1.1.8.4 Quality of Life

From both the clinical and research perspective, in chronic ear disease a well balanced appraisal of patient symptoms is needed to assess disease severity and to appreciate the results of both surgical and non-surgical interventions (83,84), since it is associated with material morbidity and it affects approximately 2% of the population.(85)

Measures of health-related quality of life (HRQoL) allow a systematic replicable appraisal of need for and benefit from treatment. In current healthcare policy, emphasis has been on remedying the past lack of outcome information as a tool of quality assurance (86), giving rise to the concept of patient-reported outcome measures (PROMs) or patient-reported outcomes (PROs) in the United States, mostly intended for routine administration and therefore very short.

Health-related quality of life (HRQoL) and patient-reported outcome measures (PROMs) are not interchangeable terms. HRQoL assesses a patient's overall health status while PROMs, in their requirement to monitor the outcome of interventions, may also include specific symptom items not necessarily of broad value to health in general.

In 2014 the Chronic Otitis Media Questionnaire (COMQ-12), a health-related quality of life questionnaire for the assessment of active chronic otitis media was published by Phillips.(87) It described the development and initial validation of a mixed generic and specific health-related quality of life questionnaire, ultimately for use as a patient-reported outcome measure. For consistency throughout, the term health-related quality of life was used in the original text. In the preliminary study described within that work, the outcome of a particular intervention was not considered; thus, to refer to that health-related quality of life questionnaire at that stage as a patient-reported outcome measure was considered to be premature.

Phillips performed a literature search and review of questionnaires on symptoms associated with chronic otitis media. This yielded three questionnaires: the Chronic Ear Survey (CES) (85), the Chronic Otitis Media Outcome Test 15 (COMOT-15) (88), and the Chronic Otitis Media 5 (COM-5) (89). All questions were amalgamated to create an initial ''long list'' containing 33 questions categorised by theme. This long list was then further reduced. Sufficient consistency and initial validity information was obtained to justify clinical use of a reduced item set of questions. Acquisition of further data to refine scoring in both a clinical and research setting was then an issue to be addressed in future research. At that time, the COMQ-12 was subject to satisfactory evaluation of various forms of validity including responsiveness (i.e., contrast between pre-intervention and

post-intervention data). It was hoped for that the COMQ-12 would be a useful health-related quality of life questionnaire, particularly as a patient-reported outcome measure.(87)

In 2015 the COMQ-12 was translated and validated for the Dutch language. In this study a cut-off value between normal individuals and COM was calculated. Acceptable validity, diagnostic accuracy, and test-retest reliability was achieved making it a reliable evaluation tool in clinical evaluation studies for assessing the impact of surgery on patients' complaints.(90)

The COMQ-12 was used preoperatively and at two-year post-intervention in a group of patients who underwent a canal wall up with bony obliteration tympanoplasty (CWU+BOT) for extensive cholesteatoma. Two years after the surgical intervention 50% of patients had a normal COMQ-12 quality of life score, the other 50% improved to a level very close to normal. Improvement was significant on almost all subscales. The authors expect more significant improvement in a more extensive sample with longer follow up. Questions regarding hearing satisfaction were the most negatively influencing factor in this group of patients.(91)

In 2016 the role of patient-reported outcome measures for the assessment of chronic ear disease was rigorously appraised in a systematic review by Phillips.(92) This and the conclusions from national audit data (93), suggested that the at that time current health-related quality of life questionnaires lack documented ability to assess ''responsiveness,'' i.e. changes in outcome or the contrast between pre-intervention and post-intervention data. Dynamic assessment tools which measure a change, such as the somewhat generic Glasgow Benefit Inventory (GBI) (94), already existed as popular ''one-shot'' instruments. At that time, a tool which is both dynamic and semi-specific, focusing on the chief domains affected in chronic middle ear disease, did not exist.

In 2017 a new partly generic and partly specific dynamic (i.e., change-oriented) patient-reported outcome measure for adult middle ear disease, named the Chronic Otitis Media Benefit Inventory (COMBI) was developed and validated.(95) At the level of item content, the preliminary version of the COMBI was constructed from the basic 12 item wording in the static COMQ-12. At the level of item format, when ''before'' and ''after'' data are not collected on separate occasions, items have to elicit a retrospective comparison between two defined occasions or periods. The COMQ-12 item wording was, therefore, adapted to allow the respondent to report any perceived change in symptoms. Other intervening events are conceivable, but here the prime application envisaged was consequences of a

surgical intervention. The COMBI's one-shot format offers convenience over available single-occasion status instruments for chronic middle ear disease that require completion both at pre-intervention and post-intervention. Differences obtained by subtraction or baseline adjustment may be more bias-free for research but there are situations where simpler and more accessible methods of questionnaire completion are desired and acceptable. The COMBI should not be considered as an exact replacement for the COMQ-12, but as a complementary tool for use where very simple pre- versus post- comparison is required. The COMBI's brevity and consistent psychometric properties make it potentially useful for simple applications such as clinical audits.(95)

In 2018 the COMQ-12 was translated and validated in Dutch. In this study a cut-off value between normal individuals and individuals with chronic otitis media (COM) was calculated.(96)

1.1.9 Surgical Treatment of Cholesteatoma

1.1.8.1 Mastoidectomy - Basic Techniques

Cortical Mastoidectomy

After a question mark shaped retro-auricular incision 2 separate anteriorly based dermal and musculoperiosteal flaps are created, thus exposing the mastoid cortex. In a simple cortical mastoidectomy the mastoid cortex is removed with a cutting burr, posterosuperior to the external auditory canal wall, inferior to the mastoid tegmen and anterior to the sigmoid sinus. The underlying air cells are removed. The dissection can be superficial or may continue medially to the mastoid antrum. The simple cortical mastoidectomy is mainly used to drain an inflamed mastoid or subperiosteal abscess in acute mastoiditis. Although it is the first step in most of the other mastoidectomy types, a simple cortical mastoidectomy doesn't suffice for cholesteatoma removal.(97-99)

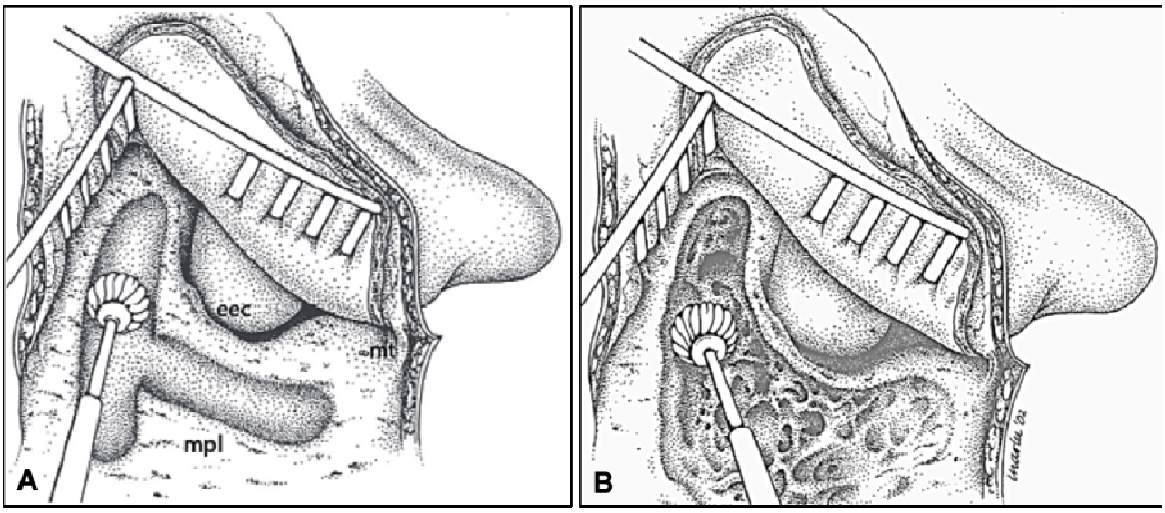

Figure 18. Cortical mastoidectomy in a right ear. **A,** before opening mastoid cells, with **eec**: external ear canal; **mt**: mastoid tip; **mpl**: mastoid plane. **B,** opening of some mastoid cells (Courtesy by Cremers and Mulder, Kugler publications, Amsterdam 2011).

Canal Wall Up Mastoidectomy

The canal wall up or classic intact canal wall mastoidectomy involves removing the mastoid air cells lateral to the facial nerve and otic capsule bone while preserving the posterior and superior external auditory canal wall. Using this technique, the epitympanum can be accessed while maintaining the natural bony and epithelial barrier between the external auditory canal and mastoid cavity. This approach can be combined with a posterior tympanotomy by drilling away the bone between the facial nerve canal posteriorly and the chorda tympani canal anteriorly, for removal of cholesteatoma from the facial recess, for a better exposure of the posterior mesotympanum, and for

visualising the round window, the incudostapedial joint and the oval window, the access to the sinus tympani and the tympanic segment of the facial nerve. If increased exposure is necessary, the posterior tympanotomy can be extended inferiorly to gain complete access to the hypotympanum or anterosuperiorly for wider access to the epitympanum.(97-101)

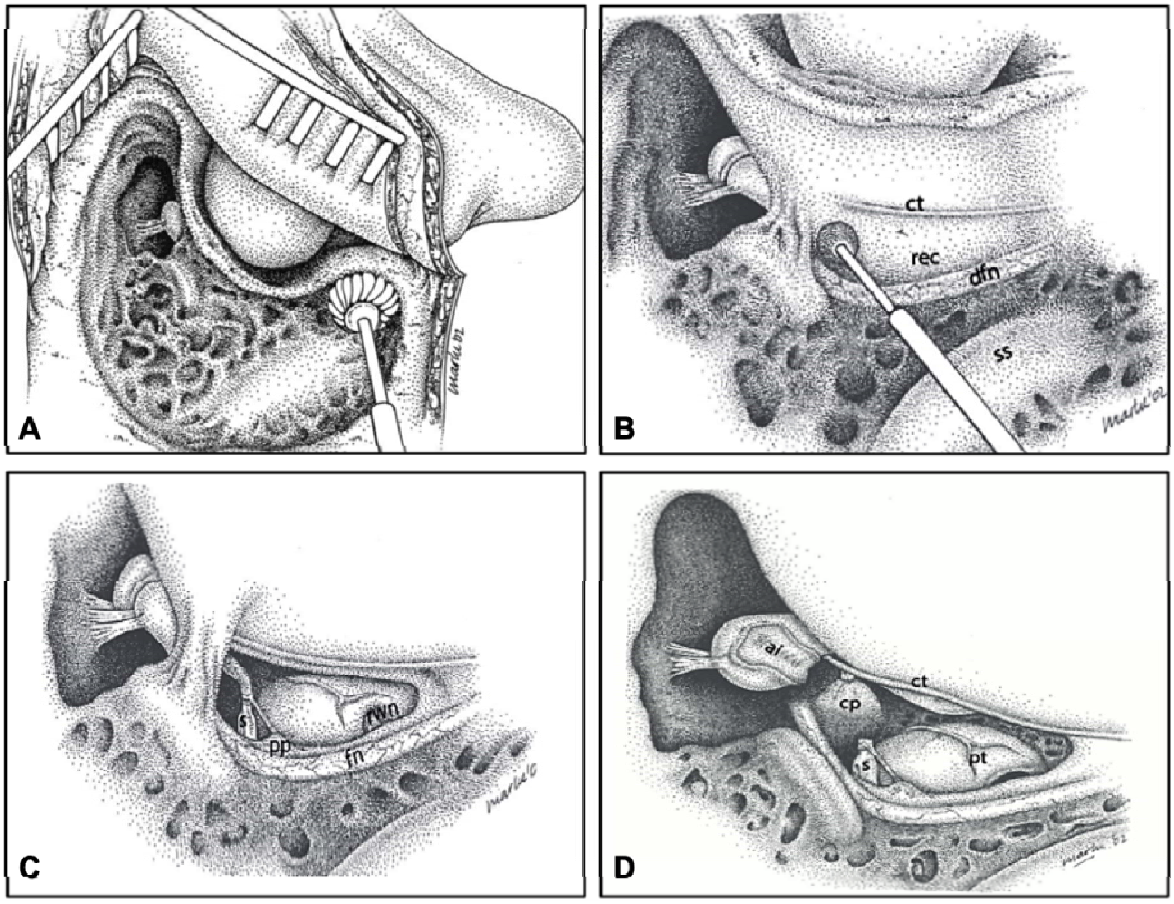

Figure 19. Mastoidectomy with a posterior tympanotomy in a right ear. **A,** opening of additus ad antrum. **B,** identification of **ct**: chorda tympani; **dfn**: descending part of the facial nerve canal; opening of **rec**: facial recess; and identification of **ss**: sigmoid sinus. **C,** posterior tympanotomy with identification of **pp**: pyramidal process; **rwn**: round window niche; and **s**: stapes crura. **D,** removal of buttress and incus, **ai**: articular groove for the incus; **cp**: cochleariform process; **pt**: promontory (Courtesy by Cremers and Mulder, Kugler publications, Amsterdam 2011).

Canal Wall Down or Modified Radical Mastoidectomy

Although the classic description of a modified radical mastoidectomy is the atticotomy described by Bondy (28), most surgeons currently use the term to describe a canal wall down mastoidectomy with removal of the external auditory canal wall combined with tympanic membrane reconstruction. There are both preoperative and intraoperative indications to remove the auditory canal. Preoperative indications for a modified radical mastoidectomy include poor general health with anesthetic risk and problematic long-term follow up. Some surgeons still advocate a canal wall down technique after multiple

failed attempts at canal wall intact surgery, in case of an extensive posterior external auditory canal defect, in the presence of a labyrinthine fistula where the surgeon prefers not to dissect the matrix from the fistula and in case of a low-positioned middle fossa dura limiting epitympanic access.(101-103)

Some surgeons perform a radical mastoidectomy in patients with insufficient aeration of the middle ear space, irreversible middle ear disease, or unresectable cholesteatoma or tumor. In this procedure the middle ear and mastoid air cells are exteriorised as a single cavity without attempt to reconstruct.(99,104)

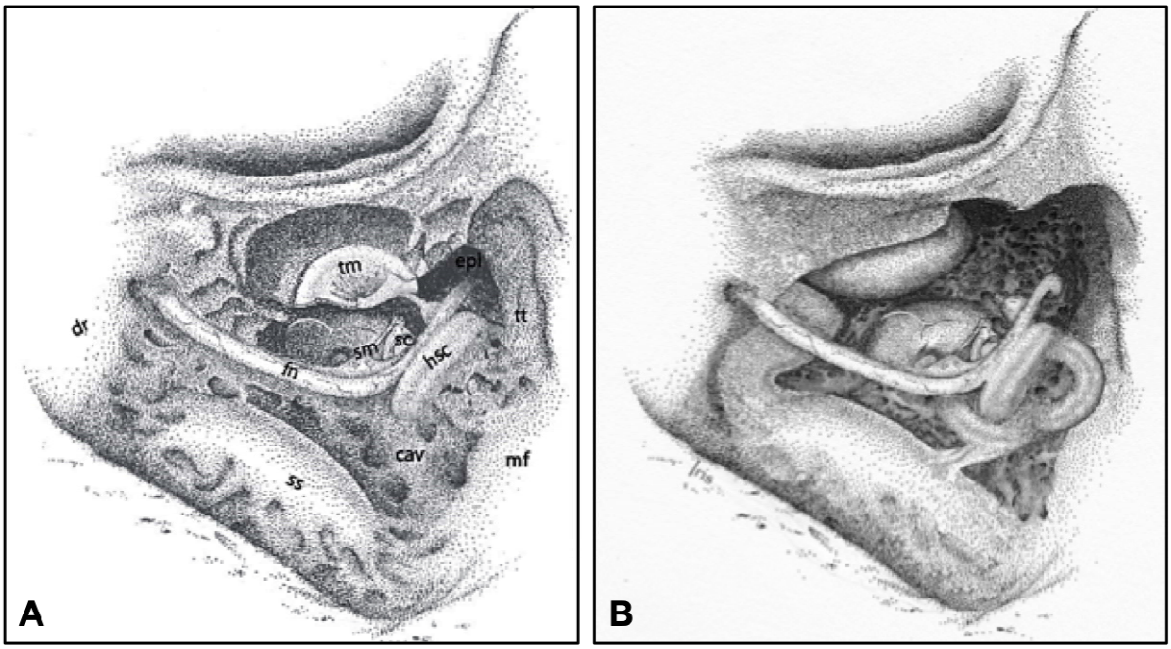

Figure 20. A radical mastoidectomy in a left ear. **A,** tympanic membrane remnant in situ, **cav**: mastoid cavity; **dr**: digastric ridge; **epi**: epitympanum; **fn**: facial nerve; **hsc**: horizontal semicircular canal; **mf**: middle fossa dural plate; **sc**: stapes crura; **sm**: stapedial muscle; **ss**: sigmoid sinus; **tm**: tympanic membrane; **tt**: tegmen tympani. **B,** further stage as in a subtotal petrosectomy, in which all remnants of the tympanic membrane and external auditory canal skin are removed and all attainable cells are opened and cleaned (Courtesy by Cremers and Mulder, Kugler publications, Amsterdam 2011).

Retrograde Mastoidectomy

Various reports have been published related to surgical techniques that involve temporary removal of the canal wall for better exposure of the cholesteatoma and its easier elimination, followed by reconstruction of the canal wall using autologous (bone, cartilage) or alloplastic (hydroxyapatite cement, titanium) graft materials.(105-113)

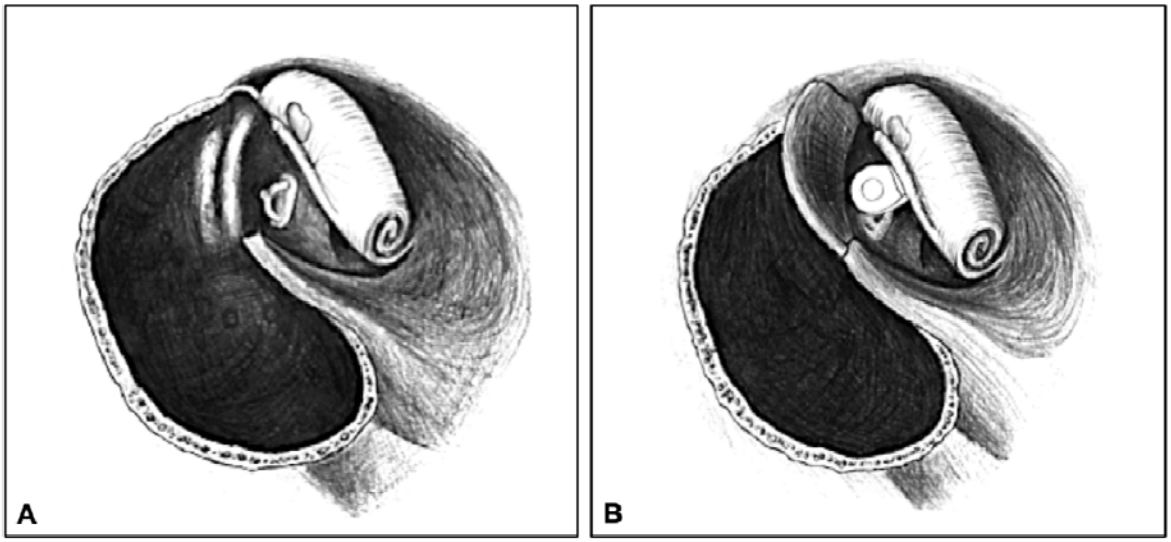

Figure 21. Retrograde mastoidectomy in a right ear. **A,** removal of the posterosuperior canal wall. **B,** reconstruction of the posterosuperior canal wall with cartilage (Courtesy by Dornhoffer, Otol Neurotol 2004).

Subtotal Petrosectomy

This procedure is described by various authors and has been given various names. It was popularised by Fisch who introduced the term subtotal petrosectomy. It is a canal wall down procedure (Figure 20B) starting via a retro-auricular skin incision and the development of anteriorly based dermal and musculoperiosteal flaps. Then follows the complete exenteration of the pneumatic cell tracts of the temporal bone, while preserving the otic capsule, the facial nerve canal, the dural plate and the cell tracts medial to the cochleovestibular labyrinth. All remnants of the tympanic membrane and the medial part of the skin of the external canal are removed. The external auditory canal is closed by everting and suturing the lateral part of the canal skin. The protympanum and access to the Eustachian tube is blocked, usually by freeing the musculus tensor tympani from its canal and turning it into the protympanum, thus firmly separating the ear from its connection with the nasopharynx. Finally, the remaining cavity is filled with abdominal fat harvested around the umbilicum (Figure 22).(114)

This procedure is indicated when an ear presents with invalidating symptoms such as chronic pain and discharge which couldn't be solved by less invasive surgical and medical treatment, or when the ear with chronic otitis is deaf or can't be fitted with a conventional hearing aid because of uncontrollable otorrhea. Subtotal petrosectomy is frequently used as a preliminary procedure to prepare the ear for ulterior implantation with a cochlear implant or an active middle ar implant.

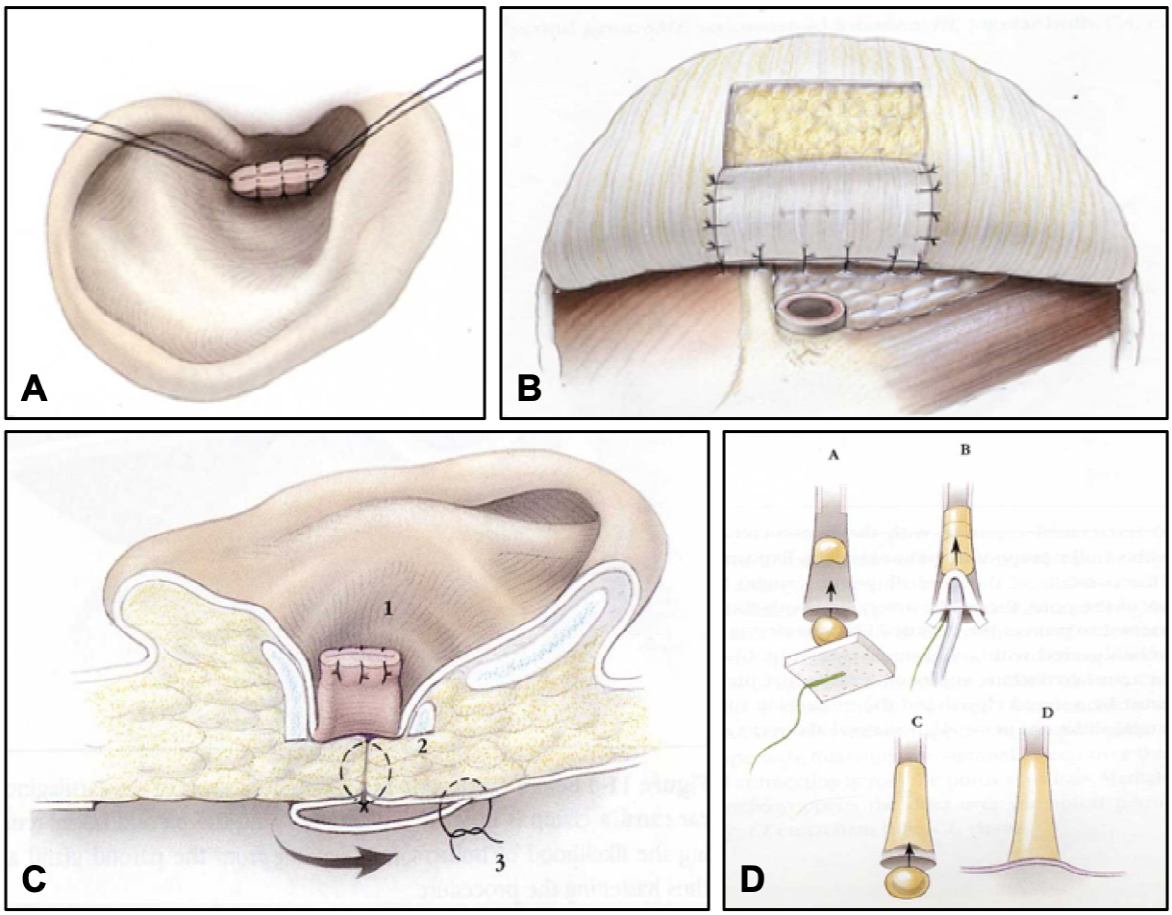

Figure 22**.** Subtotal Petrosectomy. **A,** closure of the external canal. **B,** section of the external canal skin and retroposition of the anterior based periostal flap. **C,** different layers of closure of the external canal. **D,** closure of the Eustachian tube with bone wax and fascia (Courtesy by Jackler, 1996).

1.1.9.2 Mastoid Obliteration

History

Mastoid obliteration techniques were initially introduced to treat chronically discharging and problematic cavities. Blake (1898) was the first to attempt obliteration of a mastoid cavity, using a blood clot as a medium to induce fibrous growth and thus reduce the cavity size.(115) The mastoid obliteration technique was introduced in 1911 by Mosher in order to promote the healing of a mastoidectomy defect using a superiorly based post-auricular soft tissue flap.(116) Subsequent to his first description, a variety of surgical techniques have been developed in the 20th and 21st century, using different types of autologous material such as fascia (117-119), fat (120,121), cartilage (122), cortical bone chips (123), bone pâté (124), vascularised musculo-periosteal flaps (116,125-128) or biocompatible materials such as hydroxyapatite (129), demineralised bone matrix (130), ionomeric cements (131,132), and calcium phosphate ceramics (133,134). The most final

obliteration is the subtotal petrosectomy with exclusion of the external auditory canal and fat obliteration of the cavity with closure of the protympanum.(114)

The second, more recent indication for mastoid obliteration is cholesteatoma surgery, with its specific aim to reduce the recurrence rate. Mercke was the first to apply the mastoid and epitympanic bony obliteration after complete eradication of the pathology in a consecutive series of cholesteatoma cases. He reported a strong decline in the rate of recurrent disease.(32,33) Other authors confirmed these results.(35,52,135,136)

A drop in residual rate in obliterated mastoids is also found in the former reports and could be explained by the absence of (diseased) mucosa. The Hinohira experiment with skin remnants placed in the otic bulla of guinea-pigs obliterated with plaster of Paris shows that skin remnants did survive but could hardly grow into a dermal cyst (i.e. residual cholesteatoma) compared to controls without obliteration. They conclude that this is due to a severe inflammation induced by the plaster of Paris.(138)

Currently Used Bony Obliteration Techniques

In the cholesteatoma literature, the choice to use canal wall up (CWU) versus canal wall down (CWD) procedures is often described as a trade-off between comfort versus safety. Indeed, the reported residual and recurrence rates after CWD procedures are in the mean substantially lower than after CWU procedures, thus offering higher safety, while the postoperative hygienic and hearing results are in the mean substantially better after CWU than after CWD procedures, thus offering better hearing and comfort to the patient.

More recently, a systematic review of the literature on the recurrent and residual disease rates after either CWU or CWD tympanoplasty combined with mastoid obliteration in one single stage showed to be qualitatively similar to, if not better than, previously reported rates of non-obliterative techniques. In this study the lowest recurrent and residual rates were found when the CWU procedure was combined with mastoid obliteration, on average 0.28 and 4.2%, respectively.(53)

In his series, Mercke obliterated the mastoid after a CWD tympanoplasty with autologous cortical bone chips and bone pâté.(32) Offeciers performs the Antwerp bony obliteration tympanoplasty, which is a CWU technique combined with the exclusion of the tympanic cavity from the attic and mastoid by autologous cortical bone chips and the obliteration of the attic and mastoid cavity with autologous bone pâté.(34) In the case of a reconstruction of previous performed CWD procedure, the reconstruction of the canal wall is performed with more extensive bone chips. Gantz removes the posterior canal wall

temporarily to facilitate removal of the pathology. He replaces the bony wall and fixes it with titanium screws at the end of the procedure and fills the attic and mastoid space with autologous bone pâté.(135)

Hydroxyapatite or glass granules have been proposed as an alternative to bone pâté for obliteration, using similar surgical approaches as described by Mercke, Offeciers and Gantz. CWD techniques with cartilage canal wall reconstruction and obliteration with bone pâté, hydroxyapatite granules, glass granules or the combination of these different materials for the attical and mastoid obliteration are also effective. In cases of canal wall reconstruction and/or defective posterior canal skin, a mid temporal artery flap can be very helpful in the healing process.(138-141)

The Antwerp Bony Obliteration Technique

This surgical procedure is performed under general anaesthesia using facial nerve monitoring. A classic “question mark” shaped retro-auricular incision is followed by the elevation of anteriorly based dermal and musculoperiosteal flaps. Cortical bone chips are harvested using a thin, broad, flat chisel and put aside. A bone dust collector and a cutting burr are used to collect healthy bone dust from the cortex of the mastoid process and/or the squama of the temporal bone. Care is taken not to harvest soft tissue or diseased bone. The bone dust is mixed with an antibiotic solution (rifamycin solution, 500 mg/10 ml) forming a semisolid paste, i.e. bone pâté. A cortical mastoidectomy and a wide posterior tympanotomy using the CWU technique are performed. In contrast to the original Mercke technique (32) and the technique described by Gantz (135), the posterior canal wall is left intact during the whole procedure. The aim is to preserve maximum vitality of the remaining bony canal wall in order to speed up the healing process. The cholesteatoma, the diseased soft tissue, the ossicular remnants (eroded incus/malleus) and diseased bone are then completely removed, and all accessible cell tracts are cleaned (Figure 23A, 24A). Bone chips are sculpted and placed at the tympano-attical barrier and posterior tympanotomy to completely seal off the epitympanum and mastoid from the middle ear cavity (Figure 23B, 24B). Lesions of the scutum and the bony canal wall are carefully reconstructed with sculpted solid cortical bone. The paratympanic space is thus completely isolated from the middle ear cavity by a solid bony partition. It is then progressively and completely filled up with bone pâté, up to the level of the cortex (Figure 23C, 24C).(34)

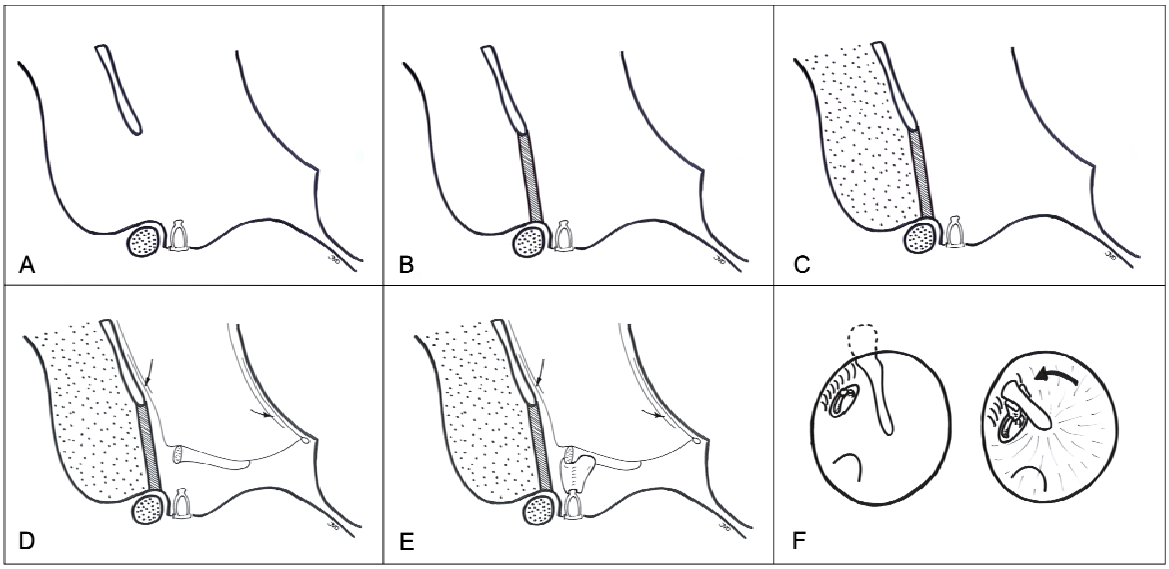

Figure 23. Surgical principles of the CWU-BOT with intact stapes superstructure. **A,** tympano-ossicular remnants removed with intact canal wall up. **B,** tympanoattical barrier and posterior tympanotomy sealing with cortical bone chips. **C,** paratympanic space obliteration with bone pâté. **D,** tympano-ossicular allograft placement. **E,** allograft incus (or malleus head) interposition between malleus handle and stapes head. **F,** counter clockwise tympano-ossicular graft rotation (right ear) with malleus handle above oval window.

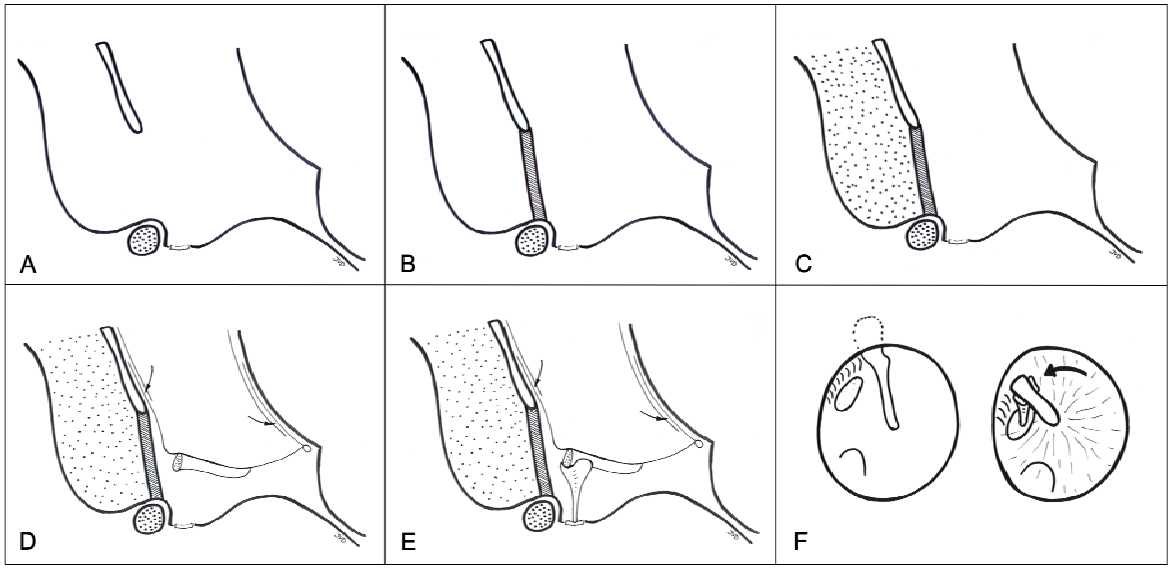

Figure 24. Surgical principles of the CWU-BOT with absent stapes superstructure. **A,** tympano-ossicular remnants removed with intact canal wall up. **B,** tympanoattical barrier and posterior tympanotomy sealing with cortical bone chips. **C,** paratympanic space obliteration with bone pâté. **D,** tympano-ossicular allograft placement. **E,** allograft incus or malleus interposition between malleus handle and stapes footplate. **F,** counter clockwise tympano-ossicular graft rotation (right ear) with malleus handle above oval window.

In our department, the middle ear reconstruction is frequently performed by using a tympano-ossicular allograft (TOA) (Figure 25).(142) The allograft consists of a meatal

periosteal cuff in continuity with the tympanic membrane (TM) and malleus handle. The malleus head and neck of the graft are removed with a malleus nipper at the level of the lateral process of the malleus. The allograft TM (with malleus handle) is rotated clockwise (left ear) or counterclockwise (right ear) to place the malleus in an advantageous position, perpendicularly centered above the oval window (Figure 23F, 24F, 25B). This allows for the most effective columellar energy transduction between the implanted malleus handle and stapes or stapes footplate (Figure 23D-F, 24D-F, 25). The ossicular reconstruction is executed using a remodeled allograft incus or malleus (Figure 23E, 24E). If needed a thin silastic sheet (0.5 mm) is placed in the middle ear cleft, extending from the protympanum to the retrotympanum, to avoid fibrous adhesions and to promote the regrowth of healthy middle ear mucosa during the postoperative healing. A M-meatoplasty (143), frequently with an antero-superior oblique conversion, the MO-meatocanalplasty (144), is often performed to optimize the size of the external meatus, thus stimulating the self-cleaning capacity of the outer ear canal. The meatoplasty is performed either as a preliminary procedure, or simultaneously with the BOT, or as a separate second stage. Perioperative antibiotics (cefazoline) are continued intravenously (IV) for 24 hours. Patients are sent home with amoxicillin-clavulanate or, in case of penicillin allergy, cefuroxime, for 5 days. It is important to mention that great care is taken in pre-operatively preparing the ear by suction cleaning, repeatedly if necessary. In case of persistent otorrhea, topical anti-inflammatory and antibiotic eardrops are used, or antibiotics are administered orally and even IV, in order to make the ear as dry as possible before admission for surgery.

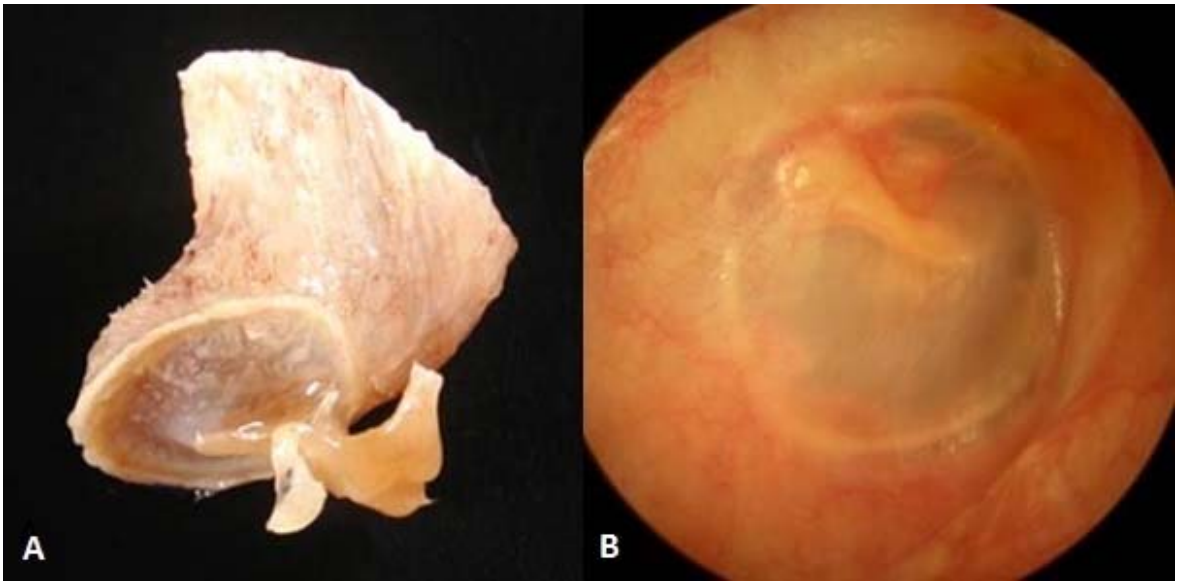

Figure 25. Tympano-ossicular allograft (TOA). **A,** tympanic view on eardrum and ossicular chain of TOA. **B,** Post-operative otoscopic view of a right ear with a TAO reconstruction with an intact posterior canal wall and counterclockwise rotated malleus handle.

1.1.10 Aims of this thesis

The scope of this thesis is to report on the long-term outcome measures of the bony obliteration tympanoplasty for chronical otitis media with cholesteatoma in children and adults. Supporting techniques are explained and evaluated.

In **Chapter 2** a cohort of children who underwent a single stage canal wall up tympanoplasty with bony obliteration of the mastoid and epitympanic space for chronic otitis media with extensive cholesteatoma with allograft reconstruction is evaluated. In **Chapter 2.1** we retrospectively analysed the long-term safety and hygienic results. The residual rate is evaluated using non-EP DW MRI 5-year postoperatively. The recurrent rate and the hygienic status are evaluated by micro-otoscopic evaluation 5-year postoperatively. The re-operative rates, i.e. the number of operations per patient in these 5-year, are calculated. In **Chapter 2.2** the long-term hearing results are evaluated in the same cohort of children. Various hearing outcome measures are analysed to be able to compare with the literature and previous results of canal wall up surgery using allografts without bony obliteration. The Amsterdam Hearing Evaluation Plots are used to evaluate safety concerning inner ear hearing function and successful hearing result in terms of air bone gap closure.

In **Chapter 3** an adult cohort of patients undergoing single stage canal wall up surgery with bony obliteration for extensive cholesteatoma performed by a single surgeon (different from the cohort of chapter 2) is evaluated. The safety, hygienic and hearing results of autograft and allograft reconstruction of the tympanic membrane are evaluated.

In **Chapter 4** the long-term clinical outcome of the bony mastoid and epitympanic obliteration technique with canal wall reconstruction is analysed, including the long-term safety issues (the residual rate by non-EP DW MRI; the recurrent rate by micro-otoscopy), the hygienic status, the tympanic membrane status and the hearing outcome.

In **Chapter 5** we introduce Dutch disease-specific health-related quality of life questionnaires for the evaluation of bony obliteration tympanoplasty. In **Chapter 5.1** we report on the translation to a Dutch version of the Chronic Otitis Media Questionnaire 12 (COMQ-12), a disease-specific patient-reported outcome measure (PROM) designed by Philips, a tool to evaluate health-related quality of life in patients with chronic otitis media. This Dutch version is validated, the test-retest reliability is checked, and a cut-off between normal and abnormal quality of life is calculated. In **Chapter 5.2** we retrospectively analysed a cohort of patients who underwent a canal wall up

tympanoplasty with bony obliteration for chronic otitis media with extensive cholesteatoma. We compared the pre-operative with the two-year postoperative result to evaluate the effect of the surgical intervention on the health-related quality of life (HRQoL). In **Chapter 5.3** we report on the translation to a Dutch version of the Chronic Otitis Media Benefit Inventory (COMBI), a single shot disease-specific questionnaire for the evaluation of change in health-related quality of life in patients with chronic otitis media. This Dutch version is validated, and the test-retest reliability is checked.

In **Chapter 6** we report on useful supporting techniques in cholesteatoma surgery with bony obliteration. In **Chapter 6.1** the MO-meatocanalplasty technique, which is very useful in chronic otitis media with cholesteatoma surgery, is step by step explained. In **Chapter 6.2** the long-term effect of the MO-meatocanalplasty technique is evaluated in a cohort of patients undergoing the MO-meatocanalplasty for a narrow external auditory canal with recurrent otitis externa or the inability to wear a hearing aid. In **Chapter 6.3** we describe a case of a patient with chronic otitis media with extensive cholesteatoma with supralabyrinthine petrosal extension operated via the Subarcuate Supralabyrinthine Approach (SaSLA).

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Chapter 2

Bony Obliteration in Canal Wall Up Tympanoplasty with Tympano Ossicular Allografts for Cholesteatoma in Children

Chapter 2.1

The Bony Obliteration Tympanoplasty in Pediatric Cholesteatoma: Long-term Safety and Hygienic Results

van Dinther JJS, Vercruysse JP, Camp S, De Foer B, Casselman J, Somers T, Zarowski A, Cremers CW, Offeciers E.

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Abstract

Objective: To present the safety and hygienic results of a 5-year longitudinal study in a pediatric population undergoing surgery for extensive cholesteatoma using a canal wall up approach with bony obliteration of the mastoid and epitympanic space.
Study Design: Retrospective consecutive study.
Patients: Thirty-three children (≤18 yr) undergoing surgery for cholesteatoma (34 ears) between 1997 and 2009.
Interventions: Therapeutic.
Setting: Tertiary referral center.
Main Outcome Measures: 1) Residual and recurrent cholesteatoma rates at 5-year postsurgery, 2) postoperative waterproofing and hygienic status of the ear, and 3) required operation rate to achieve the safety and hygienic goals.
Results: At 5 years no patients were lost in follow up. This consecutive series design is rare in chronical otitis media treatment reporting. The standard residual rate at 5 years was 5.8%, representing two residual cholesteatomas in the middle ear. The standard recurrence rate at 5 years was 2.9%, representing one recurrent cholesteatoma. At 5-year followup all ears were free of otorrhea and waterproof and all external ear canals were patent and self-cleaning. The operation rate to reach this safety and hygienic status was 1.5 operations per ear at 5-year follow up.
Conclusion: The use of a canal wall up approach with obliteration of the mastoid cavity and epitympanic space to surgically treat cholesteatoma in children results in low residual and recurrence rates and a high rate of trouble-free ears in the long term.

The pediatric subgroup of cholesteatoma patients forms a special challenge. The incidence of cholesteatoma in children is lower compared with the average population (1,2). Various authors have reported on the inferior outcomes of cholesteatoma surgery in children compared with the adult population regarding residual and recurrent disease (3–9).

The literature on pediatric cholesteatoma indicates that the canal wall up technique carries a higher risk for residual and recurrent cholesteatoma, however meticulously it is executed (3–10). The question arises whether combining it with bony obliteration of the mastoid and epitympanic space might improve the outcome.

Mercke was the first to report on excellent systematic results with the obliteration of the mastoid and epitympanic space in adults. The residual and recurrent rates of his bony obliteration technique (BOT) were comparable to the canal wall down (CWD) results (11). Mercke's results led us to design our own version of the BOT. The essential differences

with his technique are 1) keeping the bony canal wall intact during the dissection of the pathology and 2) the use of tympano-ossicular allografts for reconstruction of the middle ear. We first applied the single-stage canal wall up bony obliteration technique (CWU-BOT) with tympano-ossicular allograft (TOA) reconstruction of the middle ear to the adult population (12).

The introduction and validation of non-echo-planar diffusion-weighted magnetic resonance imaging (non-EP DW MRI) for the detection of residual disease in our department proved to be an important step forward for cholesteatoma surgery and follow up (13,14). It allowed us to abandon routine, often unnecessary, second-look operations, thus reducing the number of reoperations in cholesteatoma surgery (15), and made it possible to safely follow up the obliterated mastoid and epitympanic space in a noninvasive way. CT scanning is not a viable alternative, given the accumulating irradiation dose, especially in children, and the fact that CT cannot discriminate between the various soft tissues in the middle ear (12).

Arguments to use the CWU-BOT technique in extensive cholesteatoma in children are as follows: 1) the unsatisfactory residual and recurrent rates in our own pediatric population using the CWU technique without obliteration, as compared with the CWD technique (8); 2) the good hygienic and functional results in CWU populations (3–9), 3) the introduction of the non-EP DW MRI for follow up of the obliterated mastoid and epitympanic space (15), 4) the rewarding results of the CWU-BOT in adults (12), and 5) convincing good results with obliteration reported by other authors (11,16–19).

This study presents the long-term complete 5-year follow up results on safety and hygiene in children operated for extensive cholesteatoma with the CWUBOT technique (20).

Materials and methods

A consecutive series of 34 ears in 33 children (≤18 years) who underwent a one-stage canal wall up bony obliteration tympanoplasty (CWU-BOT) for acquired extensive cholesteatoma was retrospectively evaluated. Cases in which the ossicular chain could be left intact and in which the epitympanum was therefore not obliterated were excluded from this series. All children were operated at the European Institute for ORL-HNS at the Antwerp Sint-Augustinus Hospital (Antwerp, Belgium) between September 1997 and August 2009. All patients had at least 5-year otoscopic and radiological follow up and/or a second-stage transmeatal tympanotomy 1 year after the CWU-BOT procedure during revision. Seventeen of these ears presented with a primary acquired cholesteatoma, and another 17 ears were operated for recurrent disease. The surgical procedures were all

performed by the senior author (E. O.). The following outcome measures were analysed: cumulative recurrence rate, residual rate, hygienic status, and long-term safety issues. For this purpose our BOT database was consulted.

The parameters investigated were age at surgery, sex, side, surgical history, surgical findings, reconstructive, as well as otoscopic, radiological, and surgical follow up details. The postoperative anatomical status of the external auditory canal (EAC) and the tympanic membrane (TM) was evaluated by yearly micro-otoscopy, controlling for the presence of tympanic membrane retraction, retraction pockets, canal wall breakdown, and recurrent cholesteatoma. Recurrent cholesteatoma is defined as a new cholesteatoma, developing from an unsafe, non-self-cleaning retraction pocket, identified by micro-otoscopy. All 34 ears were followed up by yearly micro-otoscopy.

Residual cholesteatoma is defined as keratinizing squamous epithelium left behind during the first-stage CWU-BOT surgery, which has regrown into a cholesteatoma, identified by direct vision during a planned transmeatal second stage procedure or by non-EP DW MRI follow up.

During the first-stage surgery, bony reconstruction of the canal wall and the tympano–attical barrier, as well as immediate obliteration of the mastoid and epitympanic space with bone pâté, was performed. After satisfactory validation of the non-EP DW MRI sequence for the detection for residual cholesteatoma (13–15), the systematic second-stage transmeatal tympanotomy with middle ear inspection (n = 14) at 12 months for the evaluation of residual cholesteatoma was abandoned. Of these 14 staged ears only two early cases were not followed up subsequently by non-EP DW MRI. In total, 32 of the 34 ears were thus followed up by non-EP DW MRI sequence at 1 and ≥5 years after surgery.

Adequate long-term imaging follow up of obliterated mastoids is compulsory to prevent late complications because of residual cholesteatoma. However, up to now, we have only detected residual cholesteatomas in the middle ear, at the barrier between the obliterated attic and the middle ear, and lateral to the mastoid obliteration, but never in the obliterated attic or mastoid itself (12). Therefore, our initial strategy of a two-stage CWU-BOT, in which the bony reconstruction of the canal wall and the tympano-attical barrier is performed in the first stage and the obliteration of the attic and mastoid with bone pâté is postponed to the second stage, is nowadays only performed in some complicated patients with labyrinthine fistulas or petrosal cholesteatomas.

Surgical Technique

Surgery was performed under general anaesthesia using facial nerve monitoring. A classic ‘‘question mark’’ shaped retroauricular incision was followed by the elevation of anteriorly based dermal and musculoperiosteal flaps. Cortical bone chips were harvested using a thin, broad, flat chisel, and put aside. A bone dust collector and a cutting burr

were used to collect healthy bone dust from the cortex of the mastoid process and/or the squama of the temporal bone. Care was taken not to harvest soft tissue or diseased bone. The bone dust was mixed with an antibiotic solution (rifamycin solution, 500 mg/10 ml) forming a semisolid paste, i.e., bone pâté.

A cortical mastoidectomy and a wide posterior tympanotomy using the CWU technique were performed. In contrast to the original Mercke technique (11) and the technique described by Gantz (16), the posterior canal wall was left intact during the whole procedure. Our aim was to preserve maximum vitality of the remaining bony canal wall to speed up the healing process. The cholesteatoma, the diseased soft tissue, the ossicular remnants (eroded incus/malleus), and diseased bone were completely removed and all accessible cell tracts were cleaned (Figs. 1A and 2A). Bone chips were sculpted and placed at the tympano–attical barrier and posterior tympanotomy to completely seal off the epitympanum and mastoid from the middle ear cavity (Figs. 1B and 2B).

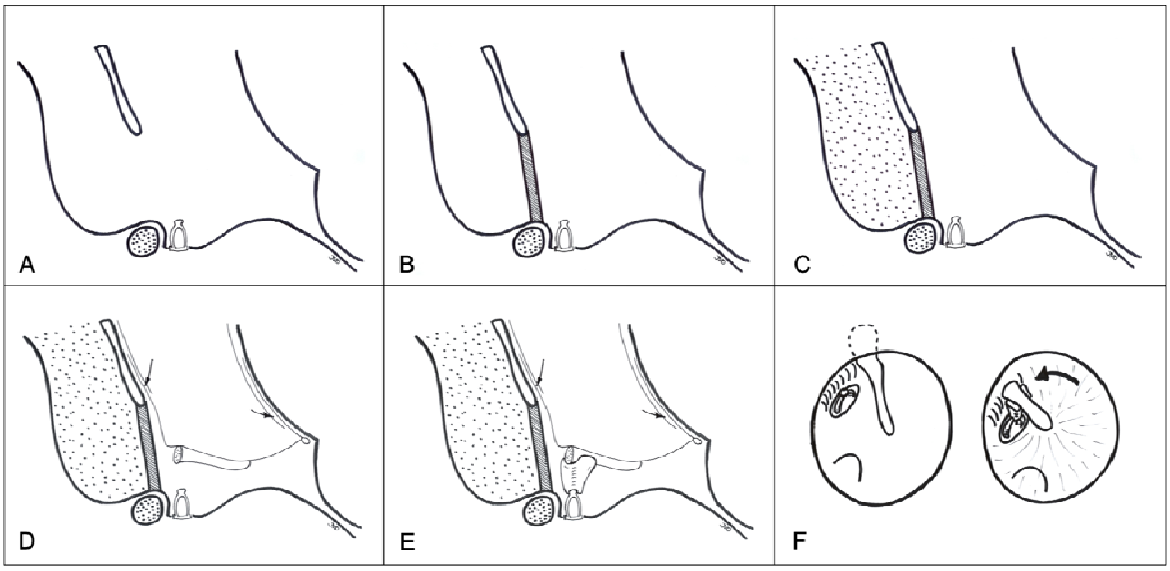

Figure 1. Surgical principles of the CWU-BOT with intact stapes superstructure. A, Tympano-ossicular remnants removed with intact canal wall up. B, Tympanoattical barrier and posterior tympanotomy sealing with cortical bone chips. C, Paratympanic space obliteration with bone pâté. D, Tympano-ossicular allograft placement. E, Allograft incus (or malleus head) interposition between malleus handle and stapes head. F, Counter clockwise tympano-ossicular graft rotation (right ear) with malleus handle above oval window.

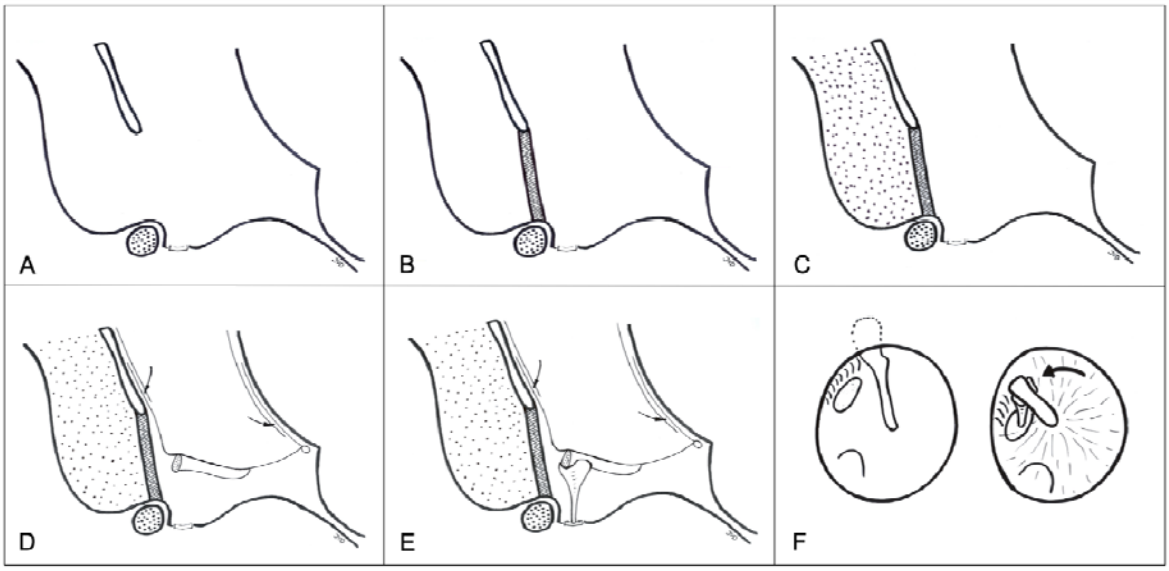

Figure 2. Surgical principles of the CWU-BOT with absent stapes superstructure. A, Tympano-ossicular remnants removed with intact canal wall up. B, Tympanoattical barrier and posterior tympanotomy sealing with cortical bone chips. C, Paratympanic space obliteration with bone pâté. D, Tympano-ossicular allograft placement. E, Allograft incus or malleus interposition between malleus handle and stapes footplate. F, Counter clockwise tympano–ossicular graft rotation (right ear) with malleus handle above oval window.

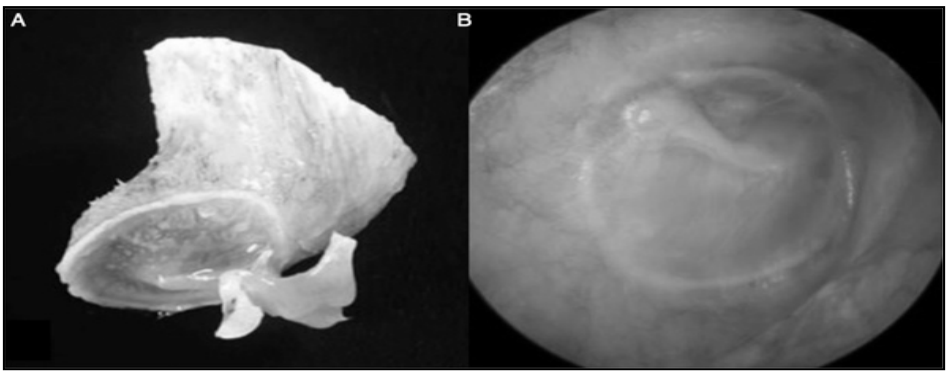

Figure 3. Tympano-ossicular allograft (TOA). A, Tympanic view on eardrum and ossicular chain of TOA. B, Postoperative otoscopic view of a right ear with a TAO reconstruction with an intact posterior canal wall and counterclockwise-rotated malleus handle.

Lesions of the scutum and the bony canal wall were carefully reconstructed with sculpted solid cortical bone. The paratympanic space was thus completely isolated from the middle ear cavity by a solid bony partition. It was then progressively and completely filled up with bone pâté, up to the level of the cortex (Figs. 1C and 2C) (21).

The middle ear reconstruction was mostly performed by using a tympano-ossicular allograft (TOA) (Fig. 3) (22). The allograft consisted of a meatal periosteal cuff in continuity with the TM and malleus handle. The malleus head and neck of the graft were removed with a malleus nipper at the level of the lateral process of the malleus. The allograft TM (with malleus handle) was rotated clockwise (left ear) or counter clockwise

(right ear) to place the malleus in an advantageous position, perpendicularly centered above the oval window (Figs. 1F, 2F, and 3B). This allows for the most effective columellar energy transduction between the implanted malleus handle and stapes or stapes footplate (Figs. 1D-F, 2D-F, and 3). The ossicular reconstruction was executed using a remodelled allograft incus or malleus (Figs. 1E and 2E). If needed, a thin silastic sheet (0.5 mm) was placed in the middle ear cleft, extending from the protympanum to the retrotympanum, to avoid fibrous adhesions and to promote the regrowth of healthy middle ear mucosa during the postoperative healing.

A M-meatoplasty (23), frequently with an antero-superior oblique conversion, the MO-meatocanalplasty (24), was often performed to optimize the size of the external meatus, thus stimulating the self-cleaning capacity of the outer ear canal. The meatoplasty was performed either as a preliminary procedure, or simultaneously with the BOT, or as a separate second stage.

Perioperative antibiotics (cefazoline) were continued intravenously (IV) for 24 hours. Patients were sent home with amoxicillin-clavulanate or, in case of penicillin allergy, cefuroxime, for 5 days. It is important to mention that great care was taken in preoperatively preparing the ear by suction cleaning, repeatedly if necessary. In case of persistent otorrhea, topical anti-inflammatory and antibiotic eardrops were used, or antibioticis were administered orally and even IV, to make the ear as dry as possible before admission for surgery.

Results

Thirty-four ears (n = 34) in 33 patients were operated using the one-stage canal wall up bony obliteration tympanoplasty (CWU-BOT), 19 right ears (55.9%), and 15 left ears (44.1%). Twenty-one male (61.8%) and 13 female (38.2%) ears were treated. One case had a cleft palate. The mean age was 12.6 years (range 6.0-18.5 yr). Seventeen ears were primary cholesteatoma cases, the other 17 were revision cases. All children had a follow up period of at least 5 years (Table 1).

Table 1. Patient characteristics (n = 34)

Mean age	12.6 yr (range 6.0-18.5 yr)
Sex (M:F)	21:13
Side (R:L)	19:15
Primary surgery	17 (50%
Revision surgery	17 (50%)

During the first 5-year follow up there were no major complications. A safe, dry, and trouble-free graft was present in 28 ears (82.4%). Of the 34 ears 33 (97.1%) remained without recurrent disease and 32 ears (94.2%) were free of residual disease. The standard 5-year recurrent rate is 2.9%, and the standard residual rate is 5.8%. This is in line with our previously published adult CWU-BOT population with residual and recurrent rates of both 2.9% after a mean follow up of 6.4 years (range 4.5-9.5) with good hygienic outcome (12).

Complications

Only one early patient in this series needed re-admission for wound infection. Following this early event in our series, peri- and postoperative antibiotics administration became the rule. No other postoperative complications (regarding, e.g., facial nerve, sensorineural hearing loss, bone resorption, or canal breakdown) occurred.

Perforation

There were three postoperative perforations of the tympanic membrane. The first (ear 1) and third perforation (ear 30) occurred in a retracted tympanic membrane during the fourth postoperative year. Both these perforations were closed with a perichondrium/ cartilage graft in underlay during the fourth year. The second perforation (ear 22) occurred during the third postoperative year and was surgically closed in the fourth year after the initial obliteration, 2 years after revision surgery for a recurrent cholesteatoma. It was closed with a perichondrium/cartilage graft in underlay.

Retraction

At 5 years the otoscopic follow up revealed the presence of a stable, self-cleaning, safe mesotympanic retraction in seven ears. During this 5-year follow up another eight retractions in seven ears were temporarily present. One retraction (ear 1) perforated and was surgically corrected with a perichondrium/cartilage graft. In one ear (ear 22) a retraction pocket evolved into a recurrent cholesteatoma. The ear was revised and corrected with a perichondrium/cartilage graft, but subsequently re-retracted and perforated. In one ear (ear 5) the self-cleaning retraction pocket was surgically corrected using perichondrium/cartilage reinforcement during elective functional surgery. In four patients, the retraction was mild and resolved spontaneously.

Recurrent

Disease One of the retraction pockets became a recurrent cholesteatoma (ear 22) in the second year. In this primary cholesteatoma patient, revision surgery showed the presence of a mesotympanic atelectatic TM, partial resorption of the tympanoattical barrier with

extension of the retraction into the attic toward a dehiscent facial nerve and also to the retrotympanum. Reclosure of the epitympanum by cartilage in combination with perichondrium and cartilage tympanoplasty was performed.

Residual Disease

Second staging by means of second-look transmeatal tympanotomy (n = 14) or/and follow up by non-EP DW MRI (n = 32) revealed in two patients the presence of a residual cholesteatoma pearl. The first residual patient (ear 11) was a revision case. The residual pearl (<2 mm) was found in the retrotympanum at year one during second-stage surgery. The second patient of residual disease (ear 23) was a primary case in an only hearing ear (contralateral ear with congenital deafness), in which the residual disease (3-4 mm) was detected at year one by non-EP DW MRI at the barrier between the middle ear and the anterior attic. So both residuals were found in the middle ear space. No residual cholesteatoma was detected to date within the bony obliterated paratympanic spaces.

Other Issues

Myringitis was temporary present in two ears (ears 2 and 33). We found lateralization of the graft in one ear (ear 31), and blunting of the graft in two ears (ears 9 and 32), (Table 2).

Table 2. 2 Five-year follow up details

Postoperative wound infection	1
Perforation (successfully closed)	3
Myringitis temporary	2
Graft blunting	2
Graft lateralization	1
Chronic discharge	0
Mesotympanic self-cleaning retraction	7
Retraction correction	1
Meatoplasty revision	4
Canal wall correction	2
Residual cholesteatoma	2
Recurrent cholesteatoma	1
Ears with residual or recurrent disease	3

Table 3. Meatocanalplasty details, n = 25 (73.5%)

As a preliminary procedure	6
At first stage	8
As a second stage	11

External Ear Canal

As noted after 5-year follow up, a M-meatoplasty or MO-meatocanalplasty had been performed in 73.5% of the patients, to widen the external meatus and canal to improve the self-cleaning capacity of the external ear canal skin. This was either performed as a preliminary procedure (n = 6), or during the first stage in combination with the BOT (n = 8), or as an elective second stage (n = 11) (Table 3). A canal wall correction was needed in two patients (ears 8 and 16) to get rid of an ear canal irregularity hampering the self-cleaning capacity of the skin. At 5-year otoscopic follow up all external ear canals were patent and self-cleaning.

Operation Rate

The numbers of operations to reach the eradication, safety, and hygienic goals at 5-year follow up were as follows: 6 preliminary M-plasties, 34 CWU-BOTs (including 8 M-meatoplasties), 12 revision operations were performed (three revision tympanoplasties for cholesteatoma disease, three revisions for tympanic membrane perforation, one revision for retraction, two revisions for ear canal irregularity, 11 second-stage M-meatoplasties). These 12 revision patients comprised a combination of revision types in most patients. In total, 52 operations were performed to reach the presented eradication, safety and hygienic level, with an operation rate per ear of 1.5 at 5-year follow up.

Discussion

We present our first complete 5-year follow up results of the single-staged canal wall up bony obliteration tympanoplasty (CWU-BOT) with tympano-ossicular allograft (TOA) reconstruction in our pediatric cholesteatoma patient population. The pediatric cholesteatoma patients are a subgroup and form a special challenge (1-9). Most authors have reported inferior outcomes in children compared with the adult cholesteatoma patient population regarding residual and recurrent disease (3-9). Various studies regarding CWU techniques in children without obliteration (3-10) reported inferior results concerning residual and recurrent rate compared with the obliteration techniques (16-20). In our adult population, the single-stage CWU-BOT technique with TOA reconstruction also markedly improved the results concerning safety. The residual and recurrent rates were both 2.9% after a mean follow up of 6.4 years (range 4.5-9.5) with good hygienic outcome (12). The 5-year results of this long-term monitored cohort of pediatric patients operated with the single-stage CWU-BOT with TOA reconstruction performed by a single surgeon show that this is a reliable and safe technique. It reduces the number of operations needed to reach the safety and hygienic goals we set ourselves.

These results indicate that in pediatric cholesteatoma patients it is safe 1) to obliterate the mastoid and epitympanic space in one stage, 2) to abandon the routine exploratory second-look operation and replace it by yearly micro-otoscopy and non-EP DW MRI follow up. In our residual cholesteatoma patients, the residual disease was found to result in the middle ear cleft, never in the obliterated paratympanic space. One could argue that the reduction in the residual rate compared with the formerly used CWU technique without obliteration is partially because of the Hinohara effect (25). This effect makes it unlikely for residual skin to develop into a cholesteatoma in a bony obliterated space and is in itself an argument in favor of bony obliteration. Another factor contributing to the reduction of the residual disease rate could be that, when preparing the mastoid and epitympanic space for obliteration, one is more thorough in eliminating all soft tissues from the cavity, thus reducing the likelihood that keratinocytes are left behind. In the majority of cases the technique resulted in a dry and trouble-free graft and in safe, dry, self-cleaning, and waterproof ears. A normal-sized external meatus, a canal protected by a solid bony wall, and a well-placed tympanic membrane in its normal position form an ideal basis for a stable hygienic condition of the ear. Moreover, if the functional result remains insufficient, a conventional hearing aid with an ear canal occlusion mould can be safely worn. In this way, the more costly and less well-received hearing rehabilitation with (percutaneous) bone-anchored hearing device solutions can be avoided. The use of TOAs for middle ear reconstruction allows for the combination with other reconstructive materials in revision surgery, such as cartilage reinforcement of the retraction pockets in the tympanic allograft or in case of a threatening recurrence. As an alternative for the TOAs, a cartilage-perichondrium graft and a columellar reconstruction with a partial or total ossicular reconstruction prosthesis can be used. Recently, we started using hydroxyapatite bone cement as a complement for the fixation and the reconstruction of the canal wall. The results in this pediatric series indicate that the mastoid and epitympanic bony obliteration technique is a valuable addition to the combined approach tympanoplasty technique to lower residual and recurrence rates. On the basis of our 5-year results, we can conclude that the CWU-BOT offers an excellent surgical solution in pediatric cholesteatoma patients. If well executed, the likelihood of residual cholesteatoma in the bony obliterated spaces is low. However, for reasons of long-term safety, the application of non-EP DW MRI monitoring remains mandatory, if alone to exclude residual disease in the middle ear cleft. We typically perform this at 1 and 5 years post-op, and in case of doubt we repeat the examination. Also clinical monitoring by micro-otoscopy and audiometry remains mandatory to exclude recurrent disease, even later than 5 years post-op. Therefore, we advise yearly otoscopy for at least 10 years on an annual basis, and 3-yearly micro-otoscopic and audiometric follow up after 10 years

post-op. The complete 10-year follow up of the pediatric cohort presented in this article is planned in the foreseeable future.

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Chapter 2.2

The Bony Obliteration Tympanoplasty in Pediatric Cholesteatoma: Long-term Hearing Results

van Dinther JJS, Coopman R, Vercruysse JP, Somers T, Zarowski A, Vanspauwen R, Maryn Y, Cremers CW, Offeciers E.

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Abstract

Objective: To present the hearing results of a 5-year longitudinal study in a pediatric population undergoing surgery for extensive cholesteatoma using a canal wall up (CWU) approach with bony obliteration of the mastoid and epitympanic space, with a standard residual rate of 5.8%, a recurrence rate of 2.9%, and all ears waterproof, free of otorrhea and all external ear canals patent and self-cleaning.
Study Design: Retrospective consecutive study.
Patients: Thirty-three children (<=18 yr) undergoing surgery for cholesteatoma (34 ears) between 1997 and 2009.
Interventions: Therapeutic.
Setting: Tertiary referral center. Main Outcome Measures: Hearing and gain in hearing at 1- and 5-year postsurgery: (1) pure-tone average (PTA), (2) pure-tone average high frequency, (3) pure-tone average including 3 kHz, (4) bone conduction at corresponding frequency averages, (5) gain at corresponding air conduction and bone conduction (gain at corresponding air conduction) frequency averages. (6) The Amsterdam Hearing Evaluation Plots were used to study the individual cases.
Results: The Amsterdam Hearing Evaluation Plots at 5-year showed in 58.8% of patients a positive gain air conduction. In 23.5% a successful functional result was achieved, defined as an air-bone gap closure to 20 dBHL or less. In 6 patients (17.6%) a limited bone conduction deterioration was shown all limited to maximum 20 dBHL.
Conclusion: The CWU bony obliteration tympanoplasty in a consecutive series of pediatric extensive cholesteatoma shows a similar to slightly improved hearing outcome as compared with CWU surgery without BOT. Although the series shows a clearly reduced reoperation rate and a significantly improved safety and hygienic outcome as compared with CWU without BOT, better hearing outcomes remain desirable in this group of children.

The pediatric subgroup of cholesteatoma patients forms a special challenge. The incidence of cholesteatoma in children is lower compared with the average population (1,2). Various authors have reported on the inferior outcomes of cholesteatoma surgery in children compared with the adult population (3-9). Excellent systematic results for extensive cholesteatoma surgery in children with different techniques of obliteration of the mastoid and epitympanic space concerning the residual and recurrent cholesteatoma rates, the hygienic situation, and the operative rates have been reported (10-14). Only a few short-term reports on the functional outcome of obliteration techniques in children with incomplete data have been published (11,12,14). It may be wishful to study a long-

term evaluation of a possible highly negative biased subpopulation concerning the hearing, with possible continuing negative influencing factors even many years after the initial surgical procedure. A 1-year follow up is too short for measuring an effect necessary for a complete life spell. It might be useful for both counseling and improvement of future hearing results to identify subgroups in which the long-term hearing is better than in others, improves, stabilizes, or deteriorates in time. In our institution, we systematically use the canal wall up bony obliteration tympanoplasty (CWU-BOT) technique in extensive cholesteatoma in children. This technique is an adaptation of the canal wall up approach with keeping the bony canal wall intact during the dissection of the pathology. The mastoid and epitympanic space are sealed off with cortical bone chips and then obliterated with bone pate. Tympano-ossicular allografts (TOA) are used for the reconstruction of the middle ear. These ears are followed up by yearly micro-otoscopy for the detection of recurrent disease; and by 1 and 5-year non-echo-planar diffusion-weighted magnetic resonance imaging (non-EP DW MRI) for the detection of residual disease (12,13,15,16). The non-EP DW MRI use allowed us to abandon routine, often unnecessary, second-look operations (17-19). This combined with the excellent results concerning the residual and recurrent rates, importantly decreased the number of necessary reoperations in cholesteatoma surgery in children (16). With improving the safety and hygienic situation and the reoperative rates in children, the hearing becomes more and more an important and still an often-unresolved issue in these extensive cholesteatoma cases. Some authors state that unilateral hearing loss is negatively influencing the development of children and adolescents and prevention of this possible irreversible lifelong developmental damage by restoring the binaural situation is therefore urgent and mandatory (20). Since routine second look surgery tends to be more and more replaced by non-EP DW MRI, a second opportunity for a routine functional revision during this second look procedure at 1 year postoperatively is lost (17-19). An ossicular reconstruction could potentially be more successful in second stage surgery after healing of the former reconstructed tympanic membrane. Parents could tend to decline an elective functional revision when the ear is safe, dry and the contralateral hearing is acceptable even after thorough counseling of the possible impact of unilateral hearing loss. A long-term follow up with nonfunctional, pure functional and combined revision types at different points in time could provide a more adequate view on their long-term hearing status. Different, functional, and outcome-determining factors in chronical middle ear surgery are described. Conventional middle ear surgery can hardly overcome negative outcome influencing factors such as an impaired inner ear function, a reduced middle ear aeration, a stapes footplate fixation and severe ossicular chain destruction. These factors will influence the functional result. In children, the preoperative hearing level is an important predictor for the postoperative hearing

outcome (21). This study presents the long-term 5-year follow up results on the hearing in children operated for extensive cholesteatoma with the CWU-BOT technique.

Methods

A consecutive series of 34 ears in 33 children (<=18 yr) who underwent a one-stage CWU-BOT for acquired extensive cholesteatoma was retrospectively evaluated. Cases in which the ossicular chain could be left intact and in which the epitympanum was therefore not obliterated were excluded from this series. Those latter ears are known for having better postoperative hearing outcome (22). All children were operated at the European Institute for ORL-HNS at the Antwerp Sint-Augustinus Hospital (Antwerp, Belgium) between September 1997 and August 2009. All patients had at least 5-year otoscopic, radiological, and audiological follow up. During the beginning of this study the nowadays routinely used non-EP DW MRI was proven to be reliable and shorter sequences without gadolinium were used. The second stage transmeatal tympanotomy for the detection of residual disease became quickly obsolete. It was therefore only used in the early beginning of this study at 1 year after the CWU-BOT procedure, mostly during revision surgery. At 5-year all ears were followed up for residual disease by non-EP DW MRI only. Seventeen of these ears presented with a primary acquired cholesteatoma, and another 17 ears were operated for recurrent disease. The surgical procedures were all performed by the senior author (E.O.). The following outcome measures were analyzed at 1- and 5-year postoperative: pure-tone average (PTA = 0.5 + 1 + 2 kHz/3); pure-tone average high frequency (PTA-HF = 1 + 2 + 4 kHz/3); pure-tone average with 3 kHz (PTA-3 kHz = 0.5 + 1 + 2 + 3/4); bone conduction (BC) at the corresponding frequency averages (BC-PTA, BC-PTA-HF, BC-PTA-3 kHz) and gains for all the air conduction (AC) and bone conduction (BC) averages (PTA-gain, PTA-HF-gain, PTA-3 kHz-gain, BC-PTA-gain, BC-PTA-HF-gain, BC-PTA-3 kHz-gain). For this purpose, our BOT database was consulted. The parameters investigated were age at surgery, sex, side, surgical history, surgical findings, surgical functional interventions, otoscopic, and surgical follow up details. The postoperative anatomical status of the external auditory canal and the tympanic membrane (TM) were evaluated by yearly micro-otoscopy, controlling for the presence of tympanic membrane retraction, retraction pockets, canal wall breakdown, and recurrent cholesteatoma. All 34 ears were followed up by yearly micro-otoscopy. Residual cholesteatoma was identified by direct vision during a planned transmeatal second stage procedure or by non-echoplanar diffusion-weighted magnetic resonance imaging (non-EP DW MRI) follow up at 1- and 5 year. During the first-stage surgery, bony reconstruction of the canal wall and the tympano-attical barrier as well as immediate obliteration of the mastoid and

epitympanic space with bone pate was performed. After satisfactory validation of the non-EP DW MRI sequence for the detection for residual cholesteatoma (17-19), the systematic second-stage transmeatal tympanotomy with middle ear inspection (n = 14) at 12 months for the evaluation of residual cholesteatoma was abandoned.

Surgical Technique

Surgery was performed under general anaesthesia using facial nerve monitoring. A classic "question mark" shaped retro-auricular incision was followed by the elevation of anteriorly based dermal and musculoperiosteal flaps. Cortical bone chips were harvested using a thin, broad, flat chisel, and put aside. A bone dust collector and a cutting burr were used to collect healthy bone dust from the cortex of the mastoid process and/or the squama of the temporal bone. Care was taken not to harvest soft tissue or diseased bone. The bone dust was mixed with an antibiotic solution (rifamycin solution, 500 mg/10 mL) forming a semisolid paste, i.e., bone pate. A cortical mastoidectomy and a wide posterior tympanotomy using the CWU technique were performed. In contrast to the original Mercke technique (10) and the technique described by Gantz et al. (11), the posterior canal wall was left intact during the whole procedure. Our aim was to preserve maximum vitality of the remaining bony canal wall to speed up the healing process. The cholesteatoma, the diseased soft tissue, the ossicular remnants (eroded incus/malleus), and diseased bone were completely removed and all accessible cell tracts were cleaned. Bone chips were sculpted and placed at the tympano-attical barrier and posterior tympanotomy to completely seal off the epitympanum and mastoid from the middle ear cavity. Lesions of the scutum and the bony canal wall were carefully reconstructed with sculpted solid cortical bone. The paratympanic space was thus completely isolated from the middle ear cavity by a solid bony partition. It was then progressively filled up with bone pate, up to the level of the cortex (15,16). In mostly all ears (94%) the malleus was absent or could not be preserved and the middle ear reconstruction was performed by using a TOA (23). The allograft consisted of a meatal periosteal cuff in continuity with the TM and malleus handle. The malleus head and neck of the graft were removed with a malleus nipper just below the level of the lateral process of the malleus. The allograft TM (with malleus handle) was rotated clockwise (left ear) or counter clockwise (right ear) to place the malleus in an advantageous position, perpendicularly centered above the oval window (15,16). This allows for the most effective columellar energy transduction between the implanted malleus handle and stapes or stapes footplate (15,16). In only two ears (6%) there was still a malleus handle which could be preserved. In the first case the tympanic membrane was partially reconstructed with a fascia autograft, in the second case with a tympanic membrane allograft. In all cases the ossicular reconstruction was executed using a remodeled allograft incus or malleus (15,16). Depending on the degree

of diseased mucosa removal a thin silastic sheet (0.5 mm) was placed in the middle ear cleft, extending from the protympanum to the retrotympanum, to avoid fibrous adhesions and to promote the regrowth of healthy middle ear mucosa during the postoperative healing. A M-meatoplasty (24), frequently with an antero-superior oblique conversion, the MO-meatocanalplasty (25), was often performed to optimize the size of the external meatus, thus facilitating the self-cleaning capacity of the outer ear canal. The meatoplasty was performed either as a preliminary procedure, or simultaneously with the BOT, or as a separate second stage.

Statistical Analysis

The statistical analysis was performed using SPSS 24.0.0 (SPSS Inc., Chigaco, IL). Not all parameters were normally distributed, therefore the difference between the measurements performed preoperatively and 1 and 5 years postoperatively was determined by using the nonparametric Wilcoxon signed rank test (with Bonferroni correction). For all analyses $p < 0.05$ was used as a criterion of statistical significance. Only statistical significant p values are mentioned in the Results section. To evaluate the amount of variance of the 12 dependent outcome measures (air or bone conduction gain in PTA, PTA 3 kHz, and PTA-HF after 1 and 5 yr) that is accounted for by the different independent factors (sex, primary versus revision, side, stapes status, stapes mobility, silastic use, meatocanalplasty, staging surgery, cholesteatoma type, eardrum, aeration, mucosal pathology, age, functional revision), coefficients of determination (i.e., R^2) were determined. However, with the dependent outcome measures at interval data level, choice of R^2 was determined by the independent factor: squared point-biserial correlation coefficient when dichotomous category (i.e., sex, side, primary versus revision, silastic use, stapes status, stapes mobility, staging surgery, and meatocanalplasty), squared eta statistic when more than two nominal levels (i.e., cholesteatoma type, aeration, eardrum), squared Spearman rank-order correlation coefficient when ordinal data (i.e., mucosa pathology), and squared Pearson product-moment correlation coefficient when interval level (i.e., age, functional revisions) (26). Higher R^2 values indicate higher percentages of explained variance of the dependent variable by the independent variable, and vice versa.

Results

Thirty-four ears (n = 34) in 33 patients were operated using the one-stage CWU-BOT, 19 right ears (55.9%), and 15 left ears (44.1%). Twenty-one male (61.8%) and 13 female (38.2%) ears were treated. One case had a cleft palate. The mean age was 12.6 years

(range 6.0-18.5 yr). Seventeen ears were primary cholesteatoma cases, the other 17 were revision cases. All children had a follow up period of at least 5 years. During the first 5-year follow up period, there were no major complications. A safe, dry, and trouble-free graft was present in 28 ears (82.4%). Of the 34 ears 33 (97.1%) remained without recurrent disease and 32 ears (94.2%) were free of residual disease. The standard 5-year recurrent rate is 2.9%, the standard residual rate is 5.8%. Between 1 and 5-year after the initial surgery 19 functional revisions were performed in 16 ears, in 3 ears a second functional revision was performed. In only 3 out of 19 patients the revision was performed solely for a functional purpose. This was in case of a hearing problem with no other indications for revision surgery, and if the patient or parents wanted an operation for functional reasons, and if it was safe and technically feasible to gain hearing (aeration of the middle ear, normal mucosal status, mobile stapes footplate). In 16 out of 19 cases the functional revision was combined with other indications for revision surgery, e.g., meatoplasty. In 10 out of the 14 planned second look surgeries to check for residual disease, there was a combination with functional revision. In three ears a second functional revision was performed. These three second functional revisions were combined with other types of revision surgery. In two functional revisions (combined with other revision types) the footplate was fixed. These combined procedures are potentially less ideal for functional revision. No possible long-term negative influence by bony overgrowth of the CWU-BOT was detected during any of the revisions in this series. No ossicular chain fixation to any of the bonechips was observed.

The Preoperative Hearing

Preoperatively the median PTA was 48.3 dBHL (Fig. 1: Air pre) with a median BC of 7.5 dBHL (Fig. 1: Bone pre) and a median air-bone gap (ABG) of 38.3 dBHL. The median preoperative AC and BC thresholds for each evaluated frequency were calculated (Fig. 2). The median PTA of the contralateral ear was 15.0 dBHL. There were 7 ears (6 patients) with otological surgery performed at the contralateral side (ears 1, 9, 11, 15, 20, 29, 30). For 1 patient, both ears (ear 29, 30) were included in this study.

The 1-year Postoperative Hearing

A total of 33 ears (32 patients) were evaluated 1-year postoperatively. The median PTA for AC was 53.3 dBHL with a median BC of 8.3 dBHL and a median ABG of 43.3 dBHL. The median gain in PTA was -1.7 dBHL (Fig. 1: Gain Air 1-year). The median gain in BC was -1.7 dBHL (Fig. 1: Gain Bone 1-year). There were no significant changes at 1 year. The median 1-year postoperative AC and BC thresholds for each evaluated frequency were calculated (Fig. 2). There were no significant differences compared with the preoperative values. The Amsterdam Hearing Evaluation Plots (AHEPs) 1-year postoperatively (n = 33) were

generated (Fig. 3). The preoperative BC plotted against the 1-year postoperative BC for each operated ear to check for significant cochlear damage (i.e., > 10 dBHL) showed only one case with bone conduction deterioration, i.e., < 20 dBHL (Fig. 3. A). The 1-year postoperative gain plotted against the preoperative ABG for each operated ear (both at PTA-3 kHz frequencies) showed in 45.4% of patients a positive gain in AC (>0 dBHL). In 3% a successful functional result was achieved, defined as an ABG closure to 20 dBHL or less (Fig. 3 B).

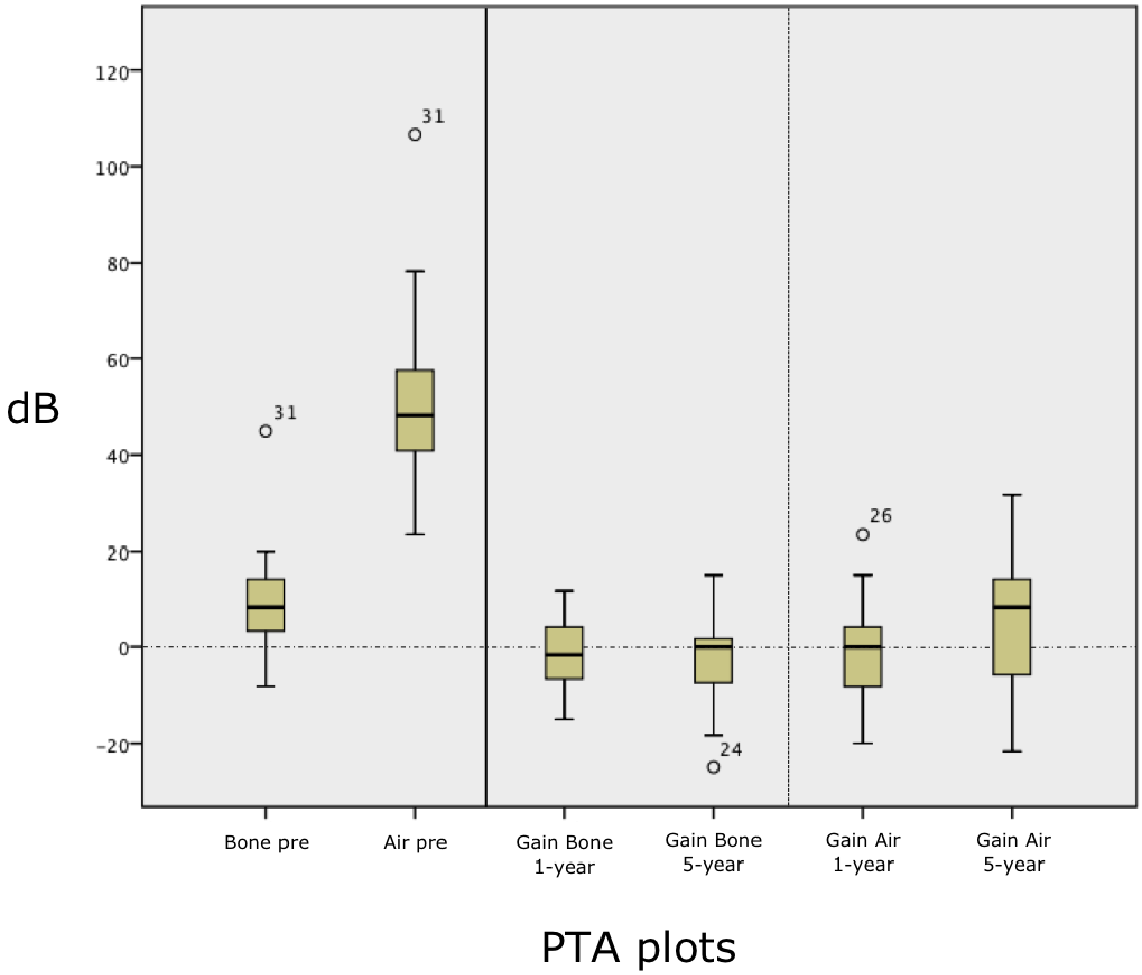

Figure 1. Pre- and postoperative hearing levels. Box and Whisker plots. The pre- and postoperative hearing thresholds (PTA) are shown: Bone pre, the preoperative bone conduction threshold; Air pre, the preoperative air conduction threshold; Gain Bone 1-year, difference between pre- and postoperative bone conduction threshold at 1 year; Gain Bone 5-year, difference between pre- and postoperative bone conduction threshold at 5 year; Gain Air 1-year, difference between pre- and postoperative air conduction threshold at 1 year; Gain Air 5-year, difference between pre- and postoperative air conduction threshold at 5 year; Bars, minimum to maximum values; rectangles, 25th to 75th percentile, bars in rectangles, median value; dots outlying values.

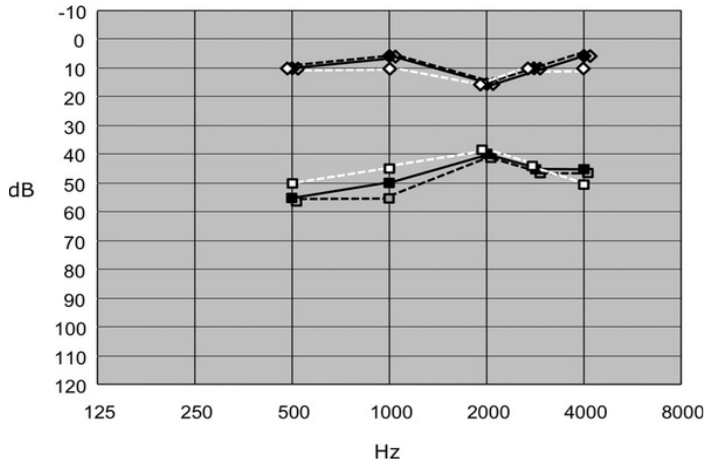

Figure 2. Median pre- and postoperative hearing levels at 1 and 5 years. Black solid line with black boxes, median preoperative air conduction thresholds; black solid line with black diamonds, median preoperative bone conduction thresholds; black dotted line with gray boxes, median postoperative air conduction at 1 year; black dotted line with gray diamonds, median postoperative bone conduction at 1 year; white dotted line with white boxes, median postoperative air conduction thresholds at 5 years; white dotted line with white diamonds, median postoperative bone conduction thresholds at 5 years.

The AHEPs at 5-year

The AHEPs 5-year postoperatively (n = 34) were generated (Fig. 4). The preoperative BC plotted against the 5-year postoperative BC for each operated ear to check for significant cochlear damage (i.e., > 10 dBHL) showed six patients (17.6%) with bone conduction deterioration all limited to 20 dBHL or less (Fig. 4B). The 5-year postoperative gain plotted against the preoperative ABG for each operated ear (both at PTA-3 kHz frequencies) showed in 58.8% of patients a positive gain in AC (>0 dBHL). In 23.5% a successful functional result was achieved, defined as an ABG closure to 20 dBHL or less (Fig. 4B).

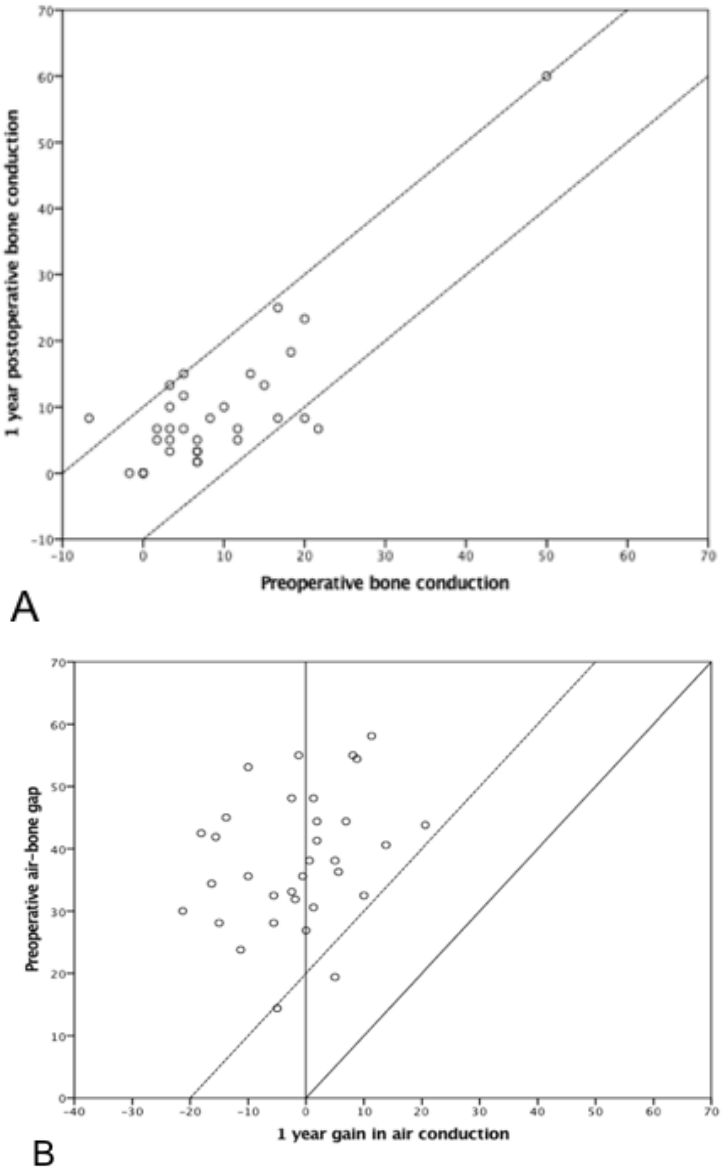

Figure 3. The 1-year postoperative Amsterdam Hearing Evaluation Plots (AHEPs) in 33 ears (n = 33). A, Preoperative bone conduction plotted against 1-year postoperative bone conduction for each operated ear (both in PTA high frequency or Fletcher Index). The two diagonal lines enclose the area in which bone conduction did not change over more than 10 dB, n = 30 (90.9%). The area above the upper dotted line encloses the cases with postoperative cochlear damage > 10 dB, n = 1 (3.0%). The area below the lower dotted line encloses the cases with postoperative "improvement" of the bone conduction, n = 2 (6.1%). B, Postoperative gain at 1 year in air conduction plotted against the preoperative air-bone gap for each operated ear (both in PTA 3 kHz). The solid diagonal line indicates total closure of the gap between preoperative air conduction and bone conduction. Every point below this line is defined as overclosure, n = 0 (0%). A successful functional result regarding air conduction is defined as a positive change in air conduction or a change in air conduction which was enough to close the gap between post-operative air conduction and preoperative bone conduction to 20 dB or less. This is indicated by the dotted diagonal line (at the right side from the solid vertical line) n = 1 (3.0%). The solid vertical line indicates no change in air conduction, n = 1 (3.0%). Every point at the right side from this line and above the dotted diagonal line is defined as an improvement in air conduction between 0 and 20 dB, n = 14 (42.4%). Every point at the left side of the vertical line is defined as a deterioration of air conduction (more than 0 dB), n = 17 (51.5%).

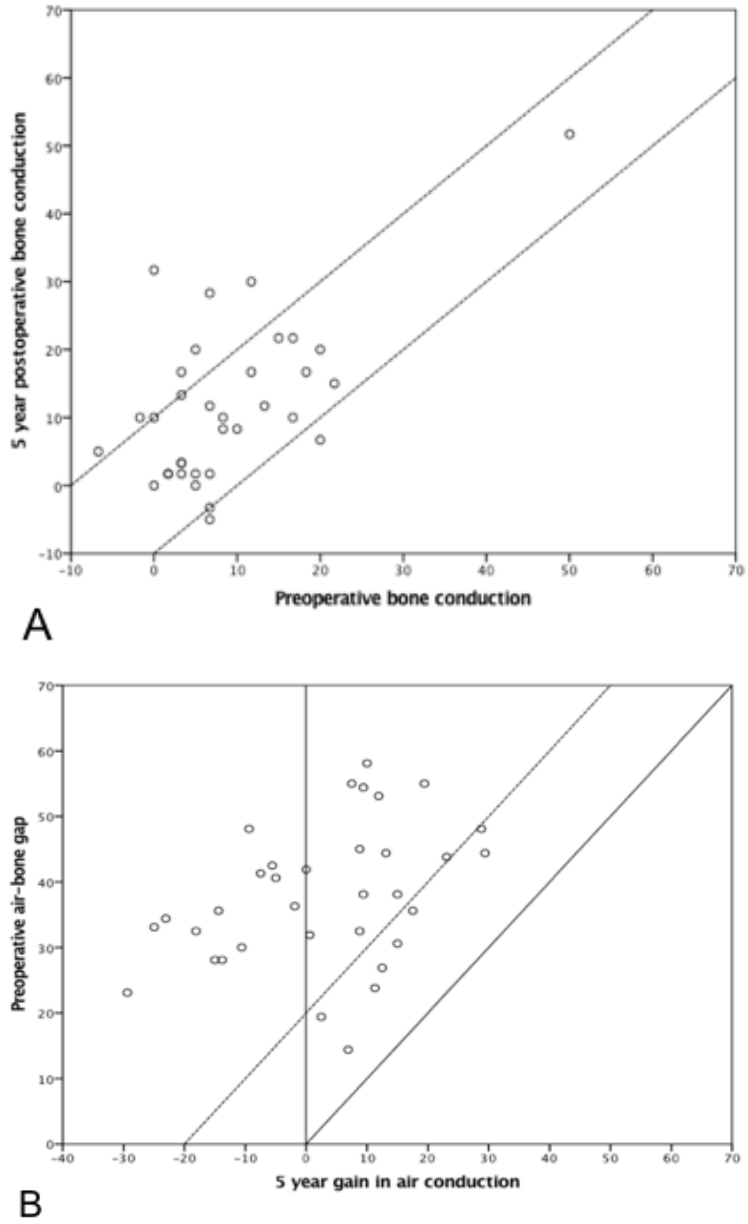

Figure 4. The 5-year postoperative Amsterdam Hearing Evaluation Plots (AHEPs) in 34 ears (n = 34). A, Preoperative bone conduction plotted against 5-year postoperative bone conduction for each operated ear (both in PTA high frequency or Fletcher Index). The two diagonal lines enclose the area in which bone conduction did not change over more than 10 dB, n = 26 (76.5%). The area above the upper dotted line encloses the cases with postoperative cochlear damage > 10 dB, n = 6 (17.6%). The area below the lower dotted line encloses the cases with postoperative "improvement" of the bone conduction, n = 2 (5.9%). B, Postoperative gain at 5-year in air conduction plotted against the preoperative air-bone gap for each operated ear (both in PTA-3 kHz). The solid diagonal line indicates total closure of the gap between preoperative air conduction and bone conduction. Every point below this line is defined as overclosure, n = 0 (0%). A successful functional result regarding air conduction is defined as a positive change in air conduction or a change in air conduction which was enough to close the gap between postoperative air conduction and preoperative bone conduction to 20 dB or less. This is indicated by the dotted diagonal line (at the right from the solid vertical line), n = 8 (23.5%). The solid

vertical line indicates no change in air conduction, n = 1 (2.9%). Every point at the right side from this line and above the dotted diagonal line is defined as an improvement in air conduction between 0 and 20 dB, n = 12 (35.3%). Every point at the left side of the vertical line is defined as a deterioration of air conduction (more than 0 dB), n = 12 (38.2%).

The Air Conduction Status (PTA) at 5-year

For the functional hearing status in AC PTA we categorized this population in three different groups: "normal hearing" (PTA < 30 dBHL) in 29%, "mild to moderate hearing loss" (PTA 30-60 dBHL) in 47%, and "severe to profound hearing loss" (PTA > 60 dBHL) in 24% (Table 1). In the two last groups in total five footplates were fixed.

Table 1. Hearing results: comparison with the literature

	This study	Schilder et al.(8)	Trinidade et al. (14)	Gantz et al (11)
AC status (PTA)				
< 30 dB	29%	--	--	--
30-60 dB	47%	--	--	--
> 60 dB	24%	--	--	--
AC-gain (PTA) Schilder et al.				
Improved				
≥ 15 dB	24%	25%	--	--
5-15 dB	32%	25%	--	--
Maintained				
-5-5 dB	15%	25%	--	--
Deteriorated				
< -5dB	29%	25%	--	--
AC Gain (PTA) Trinidade et al.				
Improved				
≥ 10 dB	35%	--	12.5%	--
Maintained				
-10-10 dB	41%	--	62.5%	--
Deteriorated				
< -10 dB	24%	--	25%	--
ABG-closure Gantz et al.				
Within 20 dB	17.6%	--	--	19%
Within 30 dB	41.1%	--	--	24%

ABG indicates air-bone gap; PTA, pure-tone average; AC, air conduction.

The Air Conduction Gain (PTA) at 5-year

To compare our findings with the literature, the hearing improvement was defined and calculated in two different ways. First, to compare with our formerly published CWU without obliteration population (8), we defined and calculated the hearing levels at PTA as "improved hearing" (>= 15 dBHL) in 23.5%, as "slightly improved hearing" (between 5 and 15 dBHL) in 32.4%, as "maintained hearing" (between 5 and -5 dBHL) in 14.7% and as "deteriorated hearing" (< -5 dBHL) in 29.4% (Table 1).

Table 2. Matrix with squared effect sizes illustrating the variance of the dependent outcome variables explained by the independent factors

	Squared Point Biserial								Squared Eta			Squared Spearman	Squared Pearson	
Gain	Sex	Primary versus Revision	Side	Stapes status	Stapes Mobility	Silastic Use	Meato-Canal Plasty	Staging Surgery	Choles-teatoma Type	Eardrum	Aeration	Mucosal Pathology	Age	Functional Revision
1 yr AC PTA	0.017	0.075	0.163	0.008	0.003	0.025	0.136	0.004	0.225	0.001	0.052	0.006	0.000	0.019
1 yr AC PTA3	0.028	0.082	0.153	0.004	0.000	0.006	0.105	0.023	0.181	0.001	0.028	0.018	0.000	0.014
1 yr AC PTA-HF	0.026	0.100	0.114	0.000	0.007	0.007	0.045	0.063	0.134	0.006	0.005	0.028	0.003	0.000
1 yr BC PTA	0.040	0.017	0.009	0.003	0.009	0.010	0.058	0.029	0.049	0.021	0.080	0.021	0.146	0.014
1 yr BC PTA3	0.027	0.012	0.007	0.005	0.003	0.006	0.030	0.020	0.051	0.017	0.036	0.013	0.116	0.004
1 yr BC PTA-HF	0.011	0.005	0.003	0.013	0.013	0.004	0.007	0.024	0.028	0.001	0.015	0.014	0.051	0.001
5 yr AC PTA	0.090	0.022	0.004	0.010	0.000	0.035	0.009	0.134	0.142	0.013	0.129	0.016	0.006	0.005
5 yr AC PTA3	0.085	0.012	0.021	0.000	0.001	0.056	0.000	0.141	0.167	0.018	0.096	0.029	0.000	0.000
5 yr AC PTA-HF	0.101	0.017	0.017	0.004	0.006	0.076	0.008	0.134	0.188	0.011	0.091	0.086	0.004	0.001
5 yr BC PTA	0.011	0.023	0.030	0.007	0.010	0.000	0.000	0.010	0.058	0.002	0.008	0.009	0.083	0.031
5 yr BC PTA3	0.011	0.015	0.025	0.014	0.020	0.001	0.000	0.008	0.052	0.001	0.011	0.049	0.083	0.030
5 yr BC PTA-HF	0.011	0.013	0.013	0.029	0.060	0.008	0.006	0.010	0.063	0.001	0.011	0.069	0.061	0.040

AC, Indicates air conduction; BC, Bone conduction; PTA-HF, pure-tone average high frequency.

Secondly, to compare with a CWD with obliteration population in the literature (14), we defined and calculated the hearing levels at PTA as "improved hearing" (>= 10 dBHL) in 35%, as "maintained hearing" (between 10 and -10 dBHL) in 41% and as "deteriorated hearing" (< -10 dBHL) in 24% (Table 1).

The Postoperative Air-bone Gap at 5-year

The postoperative ABG (postoperative AC PTA-preoperative BC PTA) was calculated to compare with other obliteration populations in the literature (11). Closure of the ABG <= 20 dBHL was obtained in 17.6% and <= 30 dBHL in 41.1% (Table 1).

Functional Outcome Determining Factors

In this population 6 ears (18%) had a stapes fixation, in 22 cases (65%) the stapes supra structure was absent, in 32 ears (94%) the malleus was absent, destroyed or could not be surgically preserved and in only 2 cases (6%) the malleus could be partially preserved. In none of the cases the incus was surgically preserved. Table 2 lists the findings related to the degree with which the 12 dependent outcome measures (air or bone conduction gain in PTA, PTA 3 kHz, and PTA-HF after 1 and 5 yrs) are determined by the 14 independent factors. Factors explaining more than 10% of one or more dependent variables' variance (i.e., factors with R^2 = 0.100, arbitrarily chosen threshold) were the following. With R^2 equalling 0.225, 0.188, 0.181, 0.167, 0.142, and 0.134 for all air conduction gains at both 1 and 5 years, cholesteatoma type, more than the other factors, seems to explain most of the audiometric gain variance. The variables side, meatocanalplasty, staging surgery, age, aeration, sex, and primary versus revision surgery seem to contribute to a lesser degree to the variance.

The Re-operative Rate

The number of operations to reach the preoperative goals of full eradication of the pathology, safety, hygiene, and function at 5-year follow up were as follows: 6 preliminary meatocanalplasties, 34 CWU-BOTs (several combined with meatocanal-plasties), 19 mostly combined revision operations (meatocanalplasties, myringoplasties for perforations and retraction, tympanoplasty for residual or recurrent cholesteatoma disease and functional improvement). In total 59 operations were performed to reach the presented eradication, safety, hygienic level, and functional outcome with an operation rate of 1.7 at 5-year follow up.

Discussion

We present our 5-year follow up hearing results of the single-staged CWU-BOT with TOA reconstruction in a pediatric cholesteatoma patient population. We only included cases in which the incudo-mallear complex was destroyed by the pathology. Cholesteatoma cases with a (nearly) intact ossicular chain and good preoperative hearing are not suitable for epitympanic bony obliteration and were therefore excluded from this series. The pediatric cholesteatoma patients are a subgroup and form a special challenge. Most authors have reported inferior outcomes in children compared with the adult cholesteatoma patient population regarding residual and recurrent disease and hearing outcome (3-9). Various studies regarding CWU techniques in children without obliteration (3-9) reported inferior results concerning residual and recurrent rate compared with the obliteration techniques (10-16). If we compare the hearing gain between our former CWU without obliteration population and the CWU-BOT group in this study (Table 1), there seems to be no significant difference. However, the former CWU without obliteration group included also the ears with a very small attic cholesteatoma with an intact ossicular chain. Moreover, the former total group had a higher reoperative rate with extra opportunities to improve the final hearing level (8). We have the impression that all the reinterventions together (a few pure functional and some combined with functional revision) did influence the hearing result positively between 1 and 5 year, however not significantly (Fig. 1). Most of the performed reinterventions were necessary to fulfil the safety and hygienic goals and this at different points in time. In our opinion the somewhat disappointing hearing outcomes in this study are biased by at least five important possible negative influencing factors. A first possible negative factor is the status of the remaining ossicular chain: in 18% of the ears the stapes footplate was fixed (five cases detected during the one-stage CWU-BOT; one case detected during revision surgery); in 65% of the ears the stapes supra structure was absent; in 94% of the ears the malleus was absent or could not be preserved; and in every ear the incus was absent or could not be surgically preserved. Different authors published about decreased hearing outcome in these situations (27,28). A second possible negative influencing factor is the poor possible gain in hearing by ossicular chain reconstruction due to an abnormal good preoperative hearing with a destroyed stapes supra structure (65%) also explained as "cholesteatoma hearing." A third possible bias in this study is the exclusion of small cholesteatoma cases. From the literature and from personal experience we know that the small epitympanic cases with preservation of an intact ossicular chain after cholesteatoma dissection have a near normal hearing level pre- and postoperatively with ABGs <= 15 dBHL pre- and postoperatively after closed tympanoplasty techniques (22). In patients with minor damage at the site of the processus longus of the incus we are nowadays able to

reconstruct easily and successfully the chain with hydroxyapatite cement (29). In these types of small cholesteatoma cases, we do not disrupt the ossicular chain in the epitympanic space and therefore we do not obliterate the epitympanic space. In our clinic, these situations represent between 10 and 15% of the pediatric cholesteatoma cases. A forth possible bias in this study is the high number of referred revision cases (50%) which might negatively influence the results. A fifth possible negative influence is an underlying cleft palate (3%). For comparative goals only a few studies that report on hearing outcome in obliteration tympanoplasty in children can be considered. These studies, with significant lost in follow up rates concerning hearing, only report on short-term postoperative hearing results (11,14). Based on our 5-year results, we can conclude that our series of CWU-BOT for extensive cholesteatoma in children has at least comparable results with other obliterating techniques in children (Table 1). Given all the negative predictive factors in our series this is better than we could hope for. We expected a different hearing outcome between the two ossicular reconstruction types (i.e., the situation with or without a mobile stapes supra structure), but no significant difference could be found. We cannot explain why the effect is not more pronounced if the supra structure was present. Maybe, there is a relative more pronounced positive effect of the rotation of the implanted malleus handle above the oval window niche with an ideal longitudinal columellar reconstruction in cases with an absent stapes supra structure? There is still a challenge to explain this with analysis of better samples. An interesting finding in the 5-year follow up of bone conduction thresholds is the slight deterioration of these levels in six cases (17.6%), as compared with the 1-year follow up BC levels (3%). It is not clear what caused this deterioration. Possibly, there is an influence of the still unstable mucosal state on the middle ear. Another possibility is the replacement of a triossicular structure of the chain with a columellar reconstruction, thus taking away the protective function of the normal chain. The 5-year results of this long-term monitored cohort of pediatric patients operated with the single-stage CWU-BOT with TOA reconstruction show that this is a reliable and safe technique resulting in a stable hygienic condition of the ear. The mastoid and epitympanic bony obliteration technique is a valuable addition to the combined approach tympanoplasty technique. It reduces the residual and recurrence rates as well as the number of operations needed to reach the safety, hygienic and functional goals we set ourselves. If we compare the children of our former published positive biased CWU without BOT data (also including small attical cholesteatomas with intact ossicular chains) with this negative biased study of CWU with BOT (for exclusively extensive cholesteatomas with poor ossicular chain status), the hearing results are still somewhat better in this study with obliteration. Nevertheless, better hearing outcomes in this group of children are still necessary. This remains a challenge. Some authors state that unilateral hearing loss is negatively

influencing the development of children and adolescents, and prevention of possible irreversible lifelong developmental damage by restoring the binaural situation is urgent and mandatory in every single pediatric and adolescent case (20). If the functional result remains insufficient after surgery, the goal is to restore the binaural situation for optimal summation and localization. A conventional hearing aid (if necessary with an ear canal occlusion mould) can be safely worn in these intact and dry external ear canals. If conventional hearing aids are not able to overcome the air-bone gap, we should consider a bone-anchored hearing solution in every pediatric and adolescent ear. However, in daily practice our goal of binaural restoration by any type of hearing solution (including functional revision surgery) is not shared by a substantial part of our unilateral hearing impaired patients, even after intensive counselling of its possible negative effects. Although as chronic ear surgeons we always hope to develop new techniques to improve hearing, completely eroded ossicular chains and unaerated middle ears are part of the chronical middle ear reality. It will always be a huge challenge to surgically rehabilitate these ears to the normal hearing situation. Since we do not know what future developments will bring, we believe that the preservation and reconstruction of a normal external auditory canal and middle ear space with its normal anatomical relations is necessary. This keeps open all the possibilities to improve the hearing in the future with new techniques.

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Chapter 3

Bony Obliteration in Canal Wall Up Tympanoplasty with Allograft and Autograft for Cholesteatoma

Chapter 3.1

The Bony Obliteration Tympanoplasty in Cholesteatoma: Safety, Hygiene and Hearing Outcome: Early Results of Allograft and Autograft Tympanic Membrane Reconstruction

van Waegeningh H*, van Dinther JJS*, Vanspauwen R, Zarowski A, Offeciers E.

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*both first authors contributed equally

Abstract

Objective: The objective of this study was to evaluate early results on hygiene, safety and functional outcome in a population undergoing surgery by a single surgeon for extensive cholesteatoma. A canal wall up technique with bony obliteration (CWU-BOT) of the mastoid and epitympanic space was used. This study reports on the functional outcome and safety of the CWU-BOT technique and compares different techniques of tympanic membrane reconstruction, viz. allografts and autografts.

Study design: A retrospective cohort study was performed in a tertiary referral centre.

Patients: Patients with acquired cholesteatoma treated with primary or revision CWU surgery with bony obliteration of the epitympanum and mastoid were identified retrospectively. A consecutive series of 61 ears in 60 patients operated from 2009 to 2014 by a single surgeon were evaluated.

Intervention: Obliteration was performed by the use of cortical bone-chips and bone pâté. Patients were followed up with micro-otoscopy and MRI with diffusion weighted imaging (DWI) at least 3 years postoperatively. In 59 cases reconstruction of the ossicular chain was performed using a remodelled autologous or allogenic incus or malleus.

Main outcome measures: The following outcome measures were analyzed: residual rate, recurrence rate, short-term hearing outcome within the first postoperative weeks and mid-term hearing outcome at least 3 months postoperatively and prior to any revision tympanoplasty. The effect of type of tympanic membrane reconstruction on hearing outcome (*AHEP plot, AC status, AC gain, ABG closure)* and risk of residual or recurrent disease were analyzed.

Results: Sixty-one ears in sixty patients were treated with CWU surgery combined with obliteration of the epitympanum and mastoid. 44 Ears (72%) were primary cholesteatoma cases, the other 17 cases (28%) were referred to our center for revision surgery. The mean postoperative follow up was 45 months (SD 18.08) and mean follow up until the last non-EP DW MRI was 42 months (SD 17.72). Recurrent disease was present in 3% of all operated ears, no residual disease was present. An AC gain was seen in 75% of all ears undergoing ossicular reconstruction and 55% had a clinically relevant improved AC gain according to Schilder et al. All ears became waterproof and free of otorrhea and all external ear canals were patent and self-cleaning with an operation rate of 1.24 operations per ear. The use of a tympano-ossicular allograft in ears with an intact stapedial superstructure and normal mobile footplate showed a significant positive effect (p=0,009) on ABG change when compared to the use of the composite cartilage with perichondrium autograft.

Conclusion: Reproducible safety, hygiene and hearing results with limited recurrence and residual disease can be obtained by different surgeons performing the BOT-CWU for extensive cholesteatoma while using a variety of grafts for tympano-ossicular reconstruction. The tympano-ossicular allograft nevertheless shows superior hearing results when a mobile intact stapes is present.

Introduction

Both canal wall up (CWU) tympanoplasty combined with obliteration of the epitympanum and mastoid, and canal wall down (CWD) tympanoplasty with or without reconstruction of the posterior canal wall significantly lower the residual and recurrence rates in cholesteatoma surgery [1-7]. Since CWU surgery keeps the original posterior canal wall intact, it ideally gives the patient a carefree, dry, self-cleaning and water tolerant ear, if needed allowing the ear to be fitted comfortably with a conventional hearing aid. CWU surgery with obliteration of the epitympanum and mastoid shows an excellent hygienic outcome and low re-operative rates [2-9]. It is safe in terms of preservation of bone conduction levels even in the presence of labyrinthine fistulas [10] and eliminates the risk of postoperative meningoencephaloceles in cases of pre-existing or iatrogenic tegmen defects. Considering these factors, a canal wall up bony obliteration tympanoplasty (CWU-BOT) technique is systematically used at our institute in cases presenting with extensive cholesteatoma [2, 5, 6, 8, 9]. In cholesteatoma surgery preservation or improvement of air conduction levels might not be the first priority. However, when an intact ossicular chain is present or when an incudostapedial connection can be easily restored with hydroxyapatite cement, and when the ossicles can be securely cleaned of cholesteatoma, we often prefer to only partially obliterate and leave the attic space and the incudomallear block intact, or opt for a more conventional technique [11]. During surgery the CWU-BOT technique leaves the bony canal wall intact while the mastoid and epitympanic space are sealed off with cortical bone chips and obliterated with bone pâté (Figure 1). For tympanic membrane reconstruction we use either a tympano-ossicular allograft, autologous fascia or a composite cartilage with perichondrium autograft (Figure 2). A remodelled allogenic or autologous incus or malleus is used for ossicular reconstruction. For the detection of recurrent disease CWU-BOT ears are followed up yearly by micro-otoscopy for at least 10 years. At one, three and five year postoperatively non-echo-planar diffusion weighted magnetic resonance imaging (non-EP DW MRI) is used for the detection of residual cholesteatoma [2, 5, 6, 8]. This imaging sequence makes routine exploratory second-look surgery redundant. As a downside this entails a loss of a second opportunity for a functional ossicular reconstruction [12-14].

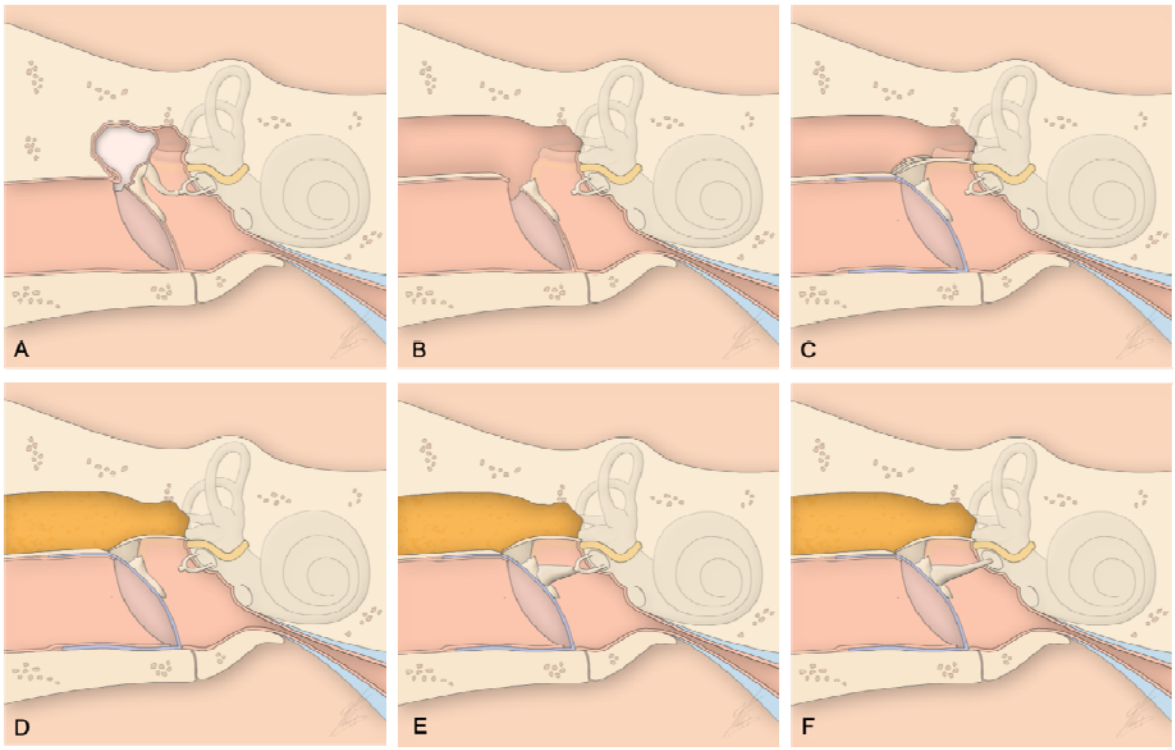

Figure 1. Illustrating the sequential steps as performed in the BOT-CWU technique.
A Cholesteatoma affecting the ossicular chain prior to any intervention ; **B** Situation after posterior tympanotomy, attico-antrotomy, anterior epitympanotomy and partial ossicular removal ; **C** Situation after placement of a tympano-ossicular allograft and bone chips to seal of the epitympanic space and posterior tympanotomy ; **D** Situation after obliteration of the cavity with bone pâté impregnated with Rifampicin ; **E** Situation after interposition of a remodelled allogenic incus with an intact stapedial superstructure ; **F** Situation after interposition of a remodelled allogenic incus with a destroyed stapedial superstructure.

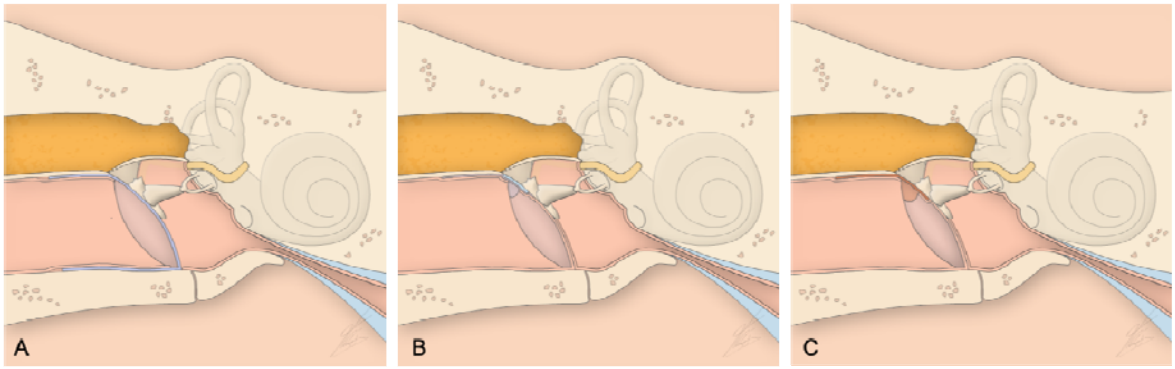

Figure 2. Illustrating the different types of tympanic membrane reconstruction.
A The tympano-ossicular allograft ; **B** A composite cartilage with perichondrium autograft; **C** An autologous fascia autograft.

Therefore, we always try to reconstruct the chain during the primary surgery. However, if needed and wished for by the patients, functional revision surgery can be done as a second stage elective procedure. Second stage functional reconstruction is potentially more successful compared to first stage functional reconstruction as it is usually performed in a healed tympanic cavity and lacks the negatively influencing factors seen in chronically diseased ears. The CWU-BOT technique also improves the safety and hygienic situation by which re-operative rates drop even further [2, 8]. Getting rid of routine exploratory or functional second stage interventions requires the need for a thorough evaluation of the first stage hearing outcome in the CWU-BOT technique.

Previous reports of the CWU-BOT performed in our institute by the senior author (EO) show excellent systematic results. The current study was performed to evaluate the safety and effectiveness of the CWU-BOT performed by another surgeon of our team (JVD). It includes his learning curve and compares allograft versus autograft tympanic membrane reconstruction techniques. All the CWU-BOT´s performed for cholesteatoma from December 2009 to December 2014 were retrospectively evaluated for residual and recurrent disease, hygiene and hearing outcome. Re-operative rates were calculated. Hearing outcome was then categorized based on ossicular status.

Materials and methods

Patients

A retrospective cohort study was performed in a tertiary referral center and was approved by the Institutional Review Board. Patients with acquired extensive cholesteatoma treated with primary or revision CWU surgery with complete obliteration of the epitympanum and mastoid were identified retrospectively. A consecutive series of 61 ears in 60 patients operated on from 2009 to 2014 were evaluated. The following outcome measures were analyzed: residual rate, recurrence rate, hygiene and functional outcome prior to any functional revision surgery. Recurrent disease was defined as expanding keratin accumulation inside a newly formed non-self-cleaning retraction pocket detected at routine yearly micro-otoscopy follow up. Residual disease was defined as isolated epidermal cysts or collections in the mastoid or tympanic cavity left behind during previous surgery as detected at non-EP DW MRI performed one, three or five years postoperatively. Hearing outcome was evaluated using pure-tone audiometry including air conduction (AC), bone conduction (BC), air-bone gap (ABG) and AAOHNS pure-tone averages (PTA) at 0.5, 1, 2 and 3kHz. Hearing levels were measured within 2 months preoperatively and at least 3 months postoperatively and before any revision tympanoplasty was performed. Both successful ABG closure within 20dB [4] as well as

successful PTA AC gain according to Schilder et al. [15] were calculated and the Amsterdam Hearing Evaluation Plot (AHEP) [16] was plotted.

Ossicular status

A detailed status of all the ossicular chain elements was consistently reported in all surgical reports, with exception of the status of the malleus head in a few cases. In those cases, enough information about the status of the malleus head, i.e. destruction, could be obtained on preoperative high-resolution cone beam CT scans taken shortly before surgery.

Surgical technique

Surgery was done under general anaesthesia with facial nerve monitoring. A question mark-shaped retro-auricular incision was performed followed by the development of separate anteriorly based musculoperiosteal flap. Complete mastoidectomy and epitympanotomy were followed by a posterior tympanotomy to completely visualise the cholesteatoma in the middle ear and/or facial recess. The cholesteatoma matrix and keratin, inflamed soft tissue, diseased bone and unusable ossicular remnants were removed. Obliteration was performed using autologous bone pâté after completely having sealed off the epitympanum, posterior tympanotomy and mastoid cavity with meticulously remodelled cortical bone chips thus separating them completely from the tympanic cavity. [2,5,6] The tympanic membrane reconstruction was performed using a tympano-ossicular allograft, a composite cartilage with perichondrium autograft or autologous fascia. An autologous fascia tympanic membrane reconstruction was chosen in cases of attic retractions in which the scutum and pars tensa were almost completely intact. A cartilage with perichondrium autograft was used if the scutum was severely affected and if the pars tensa was at least partially affected. A tympano-ossicular allograft (tympanic membrane + malleus handle) was used in cases of severe malleus and tympanic membrane destruction. The tympano-ossicular allograft cuff was rotated in such a way that the implanted malleus handle was positioned perpendicularly above the oval window niche, which allows a more favourable energy conduction. In all ears the reconstruction of the ossicular chain was performed by remodelling and interposition of an autologous or allogenic incus or malleus. Perioperative prophylactic antibiotics were given intravenously and oral antibiotics (Cefuroxim 500mg 3 times daily) were given during the first postoperative week. [6]

Statistical Analysis

The independent sample *t*-test, two tailed Fisher's exact test, Mann-Whitney U test and Kruskal-Wallis H test were used for statistical analysis. $P<0.05$ was considered to indicate statistically significant differences. Statistical analysis was conducted using SPSS 24.0.

Results

Sixty-one ears in sixty patients were treated with CWU surgery combined with obliteration of the epitympanum and mastoid: 29 right (48%) and 32 left ears (52%), 29 male (48%) and 32 female (52%) ears. Forty-four ears (72%) were primary cholesteatoma cases, the other 17 cases (28%) were referred to our center for revision surgery. All these primary cases had extensive cholesteatomas with substantial ossicular destruction, the ossicular connection in the epitympanic space was severely affected in all primary and revision cases and therefore a CWU-BOT with full obliteration was performed. The mean postoperative micro-otoscopic follow up was 45 months (SD 18.08) and the mean follow up until the last non-EP DW MRI was 42 months (SD 17.72). No postoperative facial nerve dysfunction, dizziness or significant deterioration of bone conduction was found in this cohort.

Residual disease

Of all sixty-one patients one patient was lost in follow up and three patients returned to their initial referring ENT-specialists and did not receive adequate non-EP DW MRI follow up at 3 years. In the remaining patients no residual disease (0%) was detected by non-EP DW MRI during a mean imaging follow up of 42 months (SD 17.72).

Recurrent disease

In two (3,27%) of all operated ears cholesteatoma recurrence occurred during a mean postoperative micro-otoscopic follow up of 45 months (SD 18.08). In two patients, otoscopic follow up revealed the presence of a self-cleaning mesotympanic tympanic membrane retraction. In one patient the retraction progressed towards the sinus tympani one year postoperatively and was considered recurrent disease. Revision surgery revealed a retraction progressing towards the sinus tympani between the posterior canal wall and the bone chip reconstruction. During revision surgery the retraction pocket was progressively dissected by an endaural approach and after revision mastoidectomy and posterior tympanotomy a re-closure of the epitympanum was performed by the use of bone pâté. The canal wall was reconstructed by the use of bone chips and bone pâté and reinforced with hydroxyapatite cement (Mimix®). Similarly, in a second patient a

retraction between the posterior canal wall and the bone chip reconstruction had developed 3 years postoperatively and was considered recurrent disease. Revision surgery was performed endaurally and the canal wall defect was reconstructed using hydroxyapatite cement (Mimix®). A cartilage tympanoplasty was performed. During subsequent follow up, in both cases no new recurrence developed at 3 years after revision.

Hearing outcome

In 2 out of 61 cases no ossicular reconstruction was performed. In one of those cases the cholesteatoma showed an extensive supra-labyrinthine spread involving the facial nerve into the internal acoustic meatus and the apex of the temporal bone. In this case an additional middle fossa approach was chosen and because of a preexisting 3rd and 4th window it was decided not to undertake any ossicular reconstruction. In the second case a tympano-ossicular allograft was used without any ossicular reconstruction because of a hypermobile footplate and a perilymphatic fistula which occurred while removing cholesteatoma matrix from the footplate.

In all other 59 cases (97%) ossicular reconstruction was performed using a remodelled and autologous or allogeneic incus or malleus. Of those cases, four received incomplete or inadequate audiological mid-term follow up. One of those patient was lost in follow up and another returned to the initial referring ENT-specialist and did not receive adequate PTA audiometry and non-EP DW MRI. Two of the cases, of which one moved abroad, returned for a non-EP DW MRI scan 3 year postoperatively but did not show up for audiometry.

The median preoperative PTA AC of the 55 remaining cases was 51 dBHL with a preoperative PTA ABG of 31 dBHL. Postoperative hearing levels were measured at least 3 months postoperatively or on the latest evaluation date prior to any subsequent tympanoplasty (mean follow up of 26 months) and revealed a postoperative PTA AC of 45 dBHL with a PTA ABG of 23 dBHL. The median preoperative PTA BC of the 55 remaining cases was 20dBHL, the median postoperative PTA BC taken at least 3 months postoperatively and prior to any subsequent tympanoplasty was 22dBHL. Preoperative BC was considered as being similar to the postoperative BC unless the postoperative BC showed to be worse compared to preoperatively. Twenty eight ears (51%) reached an ABG closure within 20dB [4], 41 ears (75%) showed an AC gain of which 30 ears (55%) had an improved AC gain according to Schilder et al. [15] (Figure 3). Final hearing results after second or further stage ossiculoplasty, because of insufficient first stage postoperative ABG closure, were not evaluated in this study. Ten secondary functional revisions (16%) were performed but many potentially good candidates for functional revision waived

revision ossiculoplasty because they preferred being fitted with a hearing aid or because they were satisfied with their postoperative situation, an ear free of care.

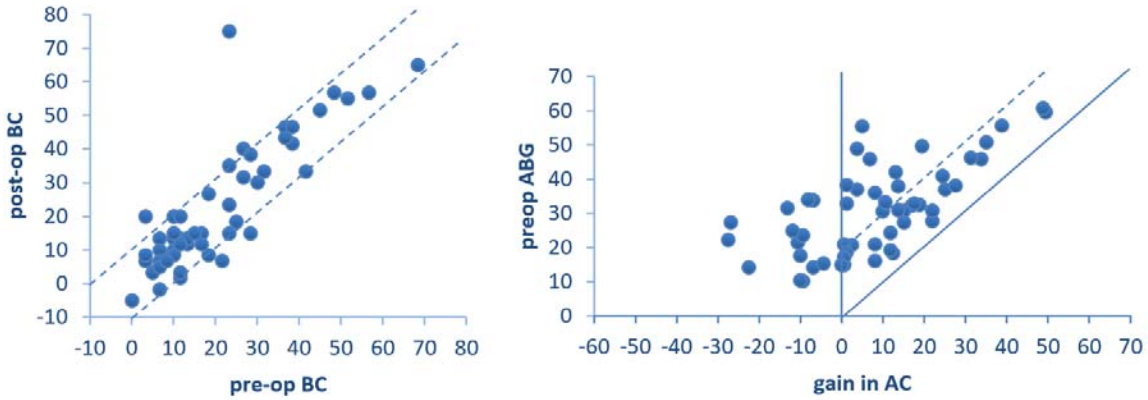

Figure 3. The Postoperative Amsterdam Hearing Evaluation Plot (AHEP)
AHEP's in 55 ears after CWU with BOT and malleus/incus interposition. The left graph shows the preoperative bone conduction plotted against postoperative bone conduction for each operated ear (both in PTA at 0.5 , 1 , 2 and 3 kHz). The two diagonal lines enclose the area in which bone conduction did not change more than 10 dB, n=47 (85%). The right graph shows the postoperative gain in air conduction plotted against the preoperative air-bone gap for each operated ear (both in PTA at 0.5 , 1 , 2 and 3 kHz). The solid diagonal line indicates total closure of the gap between preoperative air conduction and bone conduction. Every point below this line is defined as overclosure, n=0 (0%). A successful functional result regarding air conduction is defined as a positive change in air conduction or a change in air conduction which was enough to close the gap between postoperative air conduction and preoperative bone conduction to 20 dB or less n=28 (51%). This is indicated by the dotted diagonal line (to the right of the solid vertical line). The solid vertical line indicates no change in air conduction. Every point to the right of this line is defined as an improvement in air conduction, n=41 (75%). Every point to the left of the vertical line is defined as a deterioration of air conduction (more than 0 dB), n=13 (24%).

No significant effect on hearing outcome was found when comparing all ears in which a tympano-ossicular allograft, a composite cartilage with perichondrium autograft or a fascia autograft was used for tympanic membrane reconstruction. Although no significant effect was found Kruskal-Wallis H testing did show a trend towards significance (p=0,075) on ABG change when comparing all three types of tympanic membrane reconstructions. Mann-Whitney U testing showed a trend (p=0,06) towards a more pronounced positive effect on ABG change in the tympano-ossicular allograft group compared to the composite cartilage with perichondrium autograft group. Mann-Whitney U test showed a favourable effect on ABG change in the fascia group when comparing the ears with fascia autograft to the ears with a composite cartilage with perichondrium autograft (p=0,041). When evaluating all ears with an intact stapedial superstructure and normal mobile footplate (Figure 4-7) Kruskal-Wallis H testing did show a clear significant effect (p=0,02) on ABG change when comparing all three types of tympanic membrane reconstructions.

In these ears Mann-Whitney U testing showed a significant effect in favour of the tympano-ossicular allograft on postoperative ABG (p=0,043) and a highly significant effect on ABG change (p=0,009) when comparing the ears with a tympano-ossicular allograft to the composite cartilage with perichondrium autografts.

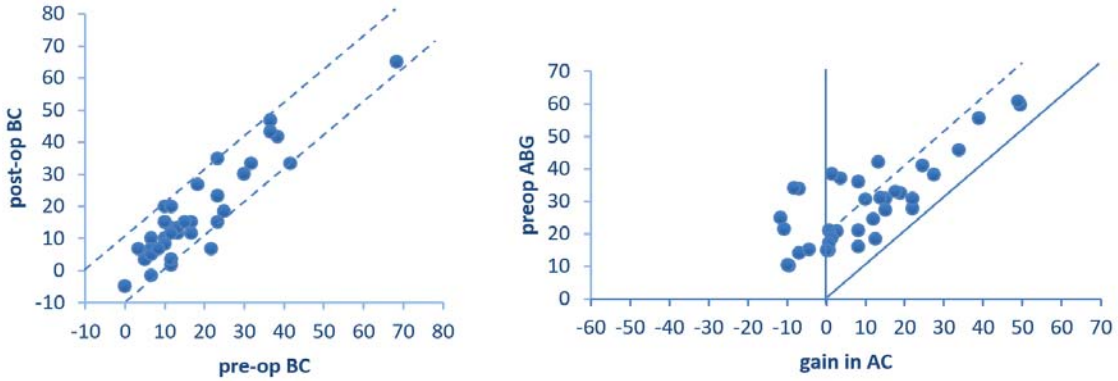

Figure 4. The Postoperative Amsterdam Hearing Evaluation Plots in all ears with a mobile footplate and intact superstructure.

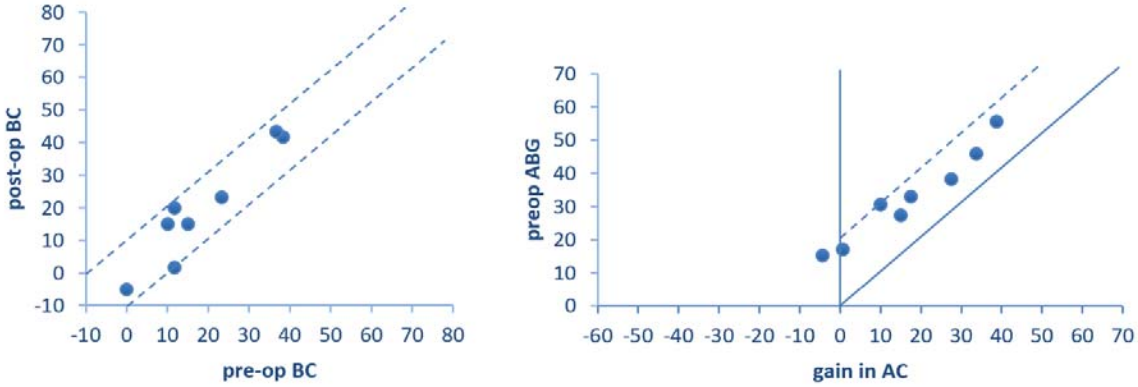

Figure 5. The Postoperative Amsterdam Hearing Evaluation Plots in all ears with a tympano-ossicular allograft tympanic membrane reconstruction and a mobile footplate and intact superstructure.

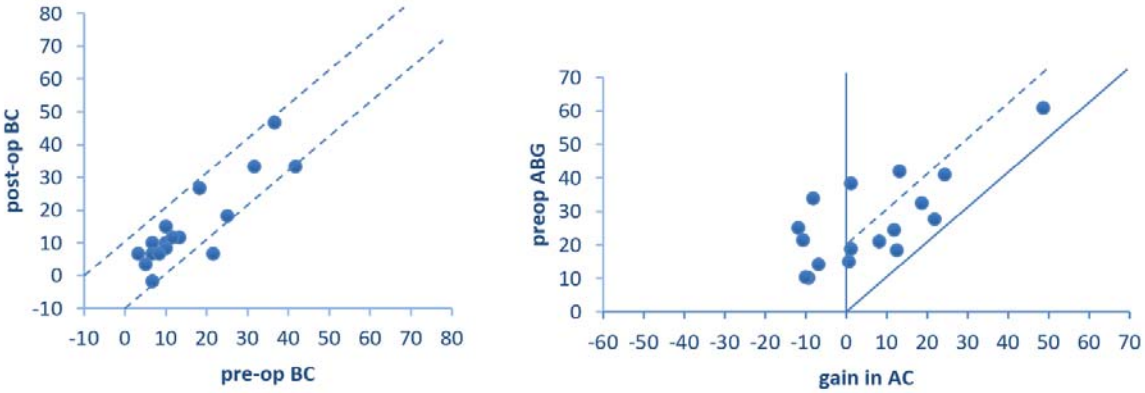

Figure 6. The Postoperative Amsterdam Hearing Evaluation Plots in all ears with a composite cartilage with perichondrium autograft tympanic membrane reconstruction and a mobile footplate and intact superstructure.

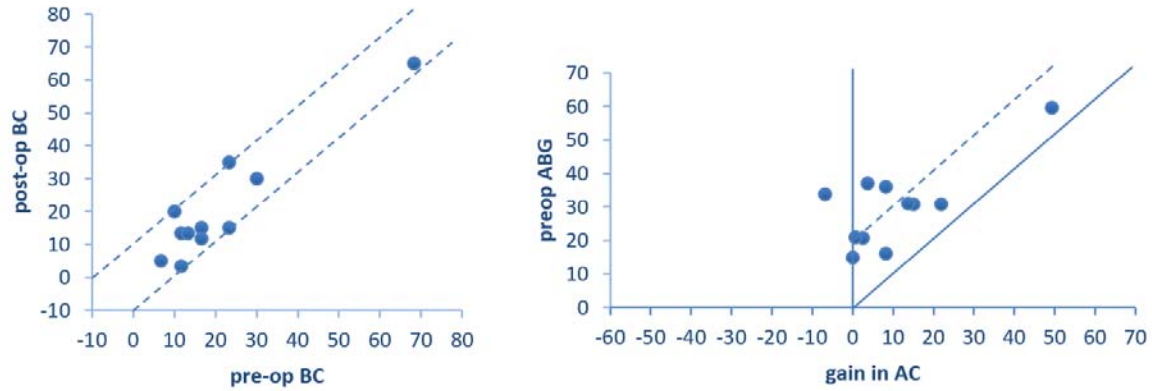

Figure 7. The Postoperative Amsterdam Hearing Evaluation Plots in all ears with a temporalis fascia autograft tympanic membrane reconstruction and a mobile footplate and intact super-structure.

Long-term hygiene and safety results

A safe, dry, trouble-free graft, and self-cleaning EAC was achieved in all ears at the latest micro-otoscopic evaluation. Two patients developed a tympanic reperforation, which needed no further surgery because of the limited size of the perforation and because these ears eventually became dry and free of care and these patients chose not to undergo further surgery. Myringitis of the tympanic graft was temporarily present in one patient, a minor lateralization of the allograft tympanic membrane was observed in two patients and a minimal blunting of the reconstructed tympanic membrane was observed in one patient. Five patients showed a slight progressive postoperative narrowing of the external auditory canal and received a M- or MO-meatocanalplasty [17,18] after which these ears became free of care.

Re-operative rate

The number of operations to reach the eradication, safety, and hygienic goals as reported were as follows: two preliminary meatocanalplasties, 61 CWU-BOTs, thirteen revision operations (two revision tympanoplasties for cholesteatoma disease, five revisions for shallow stable self-cleaning retractions initially only followed-up clinically but eventually reinforced surgically during functional revision, one revision for an ear canal irregularity, five second stage meatocanalplasties). In total 76 operations were performed to reach the presented eradication, safety and hygienic level, with an operation rate per ear of 1.24 at 3-year follow up (1.31 if all the functional revisions are included).

Discussion

While the first report of mastoid obliteration [19] dates from the beginning of the nineteenth century, only during the last two decades mastoid obliteration is increasingly used as a standard of care in the treatment of extensive cholesteatoma.
The success of the bony obliteration of the mastoid and paratympaninc spaces is explained by: the physical pressure models [20]; the inability of growth of residual disease in an obliterated cavity [21]; the relative inability of growth of recurrent disease in a sealed of epitympanum with removed malleus neck, head and incus body remnants [22]. Various obliteration techniques have been described [23-28]. The advantage of the BOT is the presence of osteocytes and osteoblasts in the bone pâté needed for osseointegration and bone formation, whereas bioactive materials need time to facilitate ingrowth of osteoblasts [29] which might not always happen. Bone chips combined with bone pâté offer a very predictable and solid construction to seal the attic and are both abundant in availability. Volume-wise the material remains stable as opposed to atrophying subcutaneous tissue and muscle flaps and certain bioactive materials which have shown expansion and seroma formation [30,31]. The rate of postoperative infections in BOT can be considered very low as long as the bone pâté is impregnated with Rifampicin and as long as a peri-operative IV prophylactic antibiotic is given combined with postoperative antibiotics [6,32].

In this study we present the 3-year follow up results of the single-staged CWU-BOT in cholesteatoma, performed by a single surgeon during his learning curve, i.e. the first four years of fulltime, mainly otological practice. Only extensive cholesteatoma cases were included, cases in which the ossicular chain could not be preserved. If the ossicles could be preserved or reconstructed with hydroxy-apatite cement, patients were not considered candidates for complete epitympanic bony obliteration. In such cases a partial obliteration technique or even more conservative surgical approaches were performed because they produce better hearing results [11]. Postoperative hearing outcome was evaluated prior to any revision tympanoplasty. The final hearing outcomes after subsequent functional tympanoplasties were not evaluated in this study. Aforementioned selection criteria result in a negative selection bias concerning hearing outcome compared to other reports on cholesteatoma surgery.
The residual or recurrent disease levels and the safety and hygiene results show comparable results to other experienced surgeons at our department including the surgeon who was first to develop and implement the CWU-BOT technique. [6] This shows the potential of the CWU-BOT as being a very safe technique with predictable outcome on residual and recurrent disease. The limited recurrence level (3,27%) and the absence

of residual disease at 3-years after surgery are among the best results published in literature. Some of the patients included in this study have now been followed-up clinically at our institute for more than five years and had their 5-year postoperative MRI. None of these patients currently show any tendency of change in the reported outcomes.

The drop in the re-operative rate and decreased number of needed second looks as a consequence of using this technique required a thorough assessment of one stage hearing outcome of the BOT-CWU. In all cases reported in this study the incudomallear block was taken out because of pathological involvement. Despite the mentioned negative selection bias the hearing outcome in this study can be considered to at least equal the functional outcome in previous reports on cholesteatoma surgery with extensive disease and need for ossicular disarticulation. The incidence of residual and recurrent disease shows remarkably low numbers and is comparable to the low incidence reported by the experienced surgeon who was first to develop and implement the BOT-CWU technique. [6] As opposed to previous reports on the BOT-CWU technique this study includes a variety of grafts used for tympanic membrane reconstruction. No difference in recurrent or residual disease could be found between cases with a tympano-ossicular allograft tympanic membrane reconstruction or more widely used tympanic membrane reconstructions with autologous temporalis fascia or cartilage-perichondrium grafts. One case of recurrence occurred in both the cartilage-perichondrium autograft and the tympano-ossicular allograft group, which were roughly equally sized groups. This would indicate that the low recurrence rate in the BOT-CWU is not necessarily attributed to the use of tympano-ossicular allografts but more likely to the obliteration technique itself.

Although the type of tympanic membrane reconstruction did not show a clearly significant effect on overall hearing outcome, a trend was seen favouring the group in which a tympano-ossicular allograft was used for tympanic membrane reconstruction. A significant positive effect on postoperative ABG and ABG improvement was found in favour of the tympano-ossicular allografts in all ears with a normal mobility of the footplate and intact stapedial superstructure compared to the composite cartilage with perichondrium autografts. This significant effect might be caused by the optimal sound transmission due to the rotation of the malleus handle of the tympano-ossicular allograft perpendicular above the oval window niche.

Another factor might be the rigidity of the composite cartilage with perichondrium autografts causing a potential suboptimal sound transmission. No evidence of such an effect was found in the literature but high-quality data on this characteristic are not available [33]. This study also shows a trend towards a better postoperative ABG in autologous fascia tympanic membrane reconstructions compared to the composite

cartilage with perichondrium grafts, which gives some weight to the argument of graft rigidity.

Future studies might be needed to evaluate the effect on hearing outcome and residual or recurrent disease in more conservative BOT approaches such as partial obliteration with ossicular preservation or ossicular restoration by hydroxy apatite cement.

Overall, this study shows the potential of the BOT-CWU as being a safe technique in different surgeons' hands, including those of a younger otologist. The knowledge that various grafts can be used for tympanic membrane reconstruction with a similar outcome regarding recurrent and residual disease levels might help to popularise this technique. Also, the fact that the natural material to obliterate is abundantly and free of cost available within the surgical field, while offering very stable results might help in this respect.

Conclusion

The chronicity of cholesteatoma ears with their suboptimal mucosal migratory and pressure regulating characteristics and their extensive ossicular destruction will remain a challenge. Rehabilitation to a normal hearing by tympanoplastic reconstruction may not always be possible. Aiming for low recurrence and residual disease levels and creating a normal external auditory canal and a self-cleaning carefree ear fortunately leaves us with many possibilities for auditory rehabilitation by modern hearing technology, surgery or a combination of both. Reproducible safety, hygiene and hearing results with limited recurrence and residual disease can be obtained by various surgeons performing the BOT-CWU for extensive cholesteatoma while using a variety of grafts for tympano-ossicular reconstruction. The tympano-ossicular allograft might nevertheless show superior hearing results when an intact, mobile stapes is present.

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Chapter 4

Bony Obliteration of the Mastoid with Canal Wall Reconstruction for Draining Cavities

Chapter 4.1

Long-Term Results of Troublesome Canal Wall Down Cavity Reconstruction by Mastoid and Epitympanic Bony Obliteration (CWR-BOT) in adults

Vercruysse JP*, van Dinther JJS*, De Foer B, Casselman J, Somers T, Zarowski A, Cremers CW, Offeciers E.

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*both first authors contributed equally

Abstract

Objective: To present the long-term surgical outcome of the bony mastoid and epitympanic obliteration technique with canal wall reconstruction (CWR-BOT) in adults with an unstable cavity after previous canal wall-down surgery for extensive cholesteatoma.

Study Design: Retrospective study. Interventions: Therapeutic. Setting: Tertiary referral center. Patients: Fifty consecutive adult patients undergoing a CWR-BOT between 1998 and 2009.

Main Outcome Measure(s): (A) Recurrence and residual rates of cholesteatoma, (B) postoperative hygienic status of the ear, including postoperative aspect of the tympanic membrane and external ear canal integrity (EAC), (C) functional outcome, and (D) long-term safety issues.

Results: (A) The percentage of ears remaining safe without recurrent or residual disease after CWR-BOT was 96% after a mean follow up time of 101.8 months. Recurrent cholesteatoma occurred in 2% (n = 1) and a residual cholesteatoma was detected in 2% (n = 1) of the patients. (B) A safe dry, and trouble-free graft and selfcleaning EAC was achieved in 94%. (C) The postoperative hearing results showed a gain of 1.7 dB on pure-tone average air-conduction. (D) Nonecho planar diffusion-weighted imaging (non-EP DW magnetic resonance imaging) documented the residual (n = 1) and recurrent cholesteatoma (n = 1). The 1- and 5-year imaging follow up revealed no other recurrent or residual disease.

Conclusion: The CWR-BOT is a safe and very effective option for treatment of problematic unstable canal wall-down mastoid cavities, resulting in dry trouble-free ears.

The primary goal of surgical treatment of chronic otitis media with cholesteatoma is the complete eradication of the disease, whereas secondary goals are the prevention of recurrent disease, the improvement of the hygienic status of the ear, and the preservation or improvement of hearing (1). Many variables influence the long-term outcome of surgery. The more extensive the disease and damage at initial presentation, the poorer the outcome. Another important variable influencing the outcome of surgery for chronic otitis media is the quality of the surgical act, which depends on different factors including the surgeon's personal experience, the adequate choice of the surgical technique and of the material used for the reconstruction. The canal wall down (CWD) mastoidectomy yields lower recurrence rates, but often requires regular cavity cleaning and is associated with recurrent otorrhea because of inflammation/infection, water intolerance, caloric-induced vertigo, and the diminished ability to comfortably wear a

hearing aid. The problem of recurrent inflammation and infection is mainly caused by the loss of the self-cleaning capacity of the ear, which leads to accumulation of epithelial debris and thus necessitates regular cleaning of the mastoid cavity (2,3). One of the goals of the mastoid and epitympanic obliteration technique is to rebuild an external auditory canal (EAC) with normal dimensions. This results in a better self-cleaning capacity of EAC and leads to a better hygienic status of the ear (4-7). This article addresses the long-term outcome of our mastoid and epitympanic obliteration technique with canal wall reconstruction, including the recurrence rate, the residual rate, the functional results, the hygienic status of the ear, and the otoscopic evaluation of the tympanic membrane and the long-term safety issues using nonechoplanar diffusion-weighted magnetic resonance imaging (non-EP DW MRI) (8-12).

Methods

Fifty consecutive patients (> 16 yr) were surgically treated by means of the CWR-BOT after presenting with a troublesome cavity, and were retrospectively evaluated. All surgery was performed at the European Institute for ORL-HNS at the Antwerp St-Augustine Hospital between September 1998 and March 2009. The surgery was performed by the senior author (E.O.). The indication for bony obliteration was the presence of an unstable, problematic cavity after earlier canal wall down surgery, leading to complaints of chronic or recurrent otorrhea because of inflammation/infection, the bothersome need for regular cleaning of the cavity, vestibular intolerance, hearing aid intolerance, and in some patients recurrent cholesteatoma.

Methodology

The following outcome measures were analyzed: cumulative recurrence rate, residual rate, hygienic status, hearing results, and long-term safety issues of the operated ear. The parameters of Bony Obliteration Tympanoplasty database included in the study: age at surgery, sex, side, surgical history, surgical findings, reconstruction method and material, otoscopic, radiological and audiometric follow up details. During the clinical follow up, the postoperative anatomical status of the EAC and tympanic membrane was evaluated by yearly micro-otoscopic control, checking for retraction pockets, canal wall breakdown, bare bone exposure, external meatal stenosis, or recurrent cholesteatoma. We defined recurrent cholesteatoma as a new cholesteatoma, developing from an unsafe, non-self-cleaning retraction pocket in the tympanic graft or through the reconstructed bony canal wall, as identified by micro-otoscopy. We defined residual cholesteatoma as keratinizing squamous epithelium left behind during the CWR-BOT surgery, which has regrown into a

cholesteatoma, identified by direct vision during a planned transmeatal second-stage procedure or by non-EP DW MRI follow up. The audiological database included the preoperative and postoperative air conduction, bone conduction, and pure-tone averages. The audiological assessment was conducted every 3 months during the first postoperative year and once yearly in the following postoperative years, in a sound-treated room.

Surgical Technique

The surgery was performed under general hypotensive anesthesia using facial nerve monitoring. A question mark-shaped retro-auricular incision was made, sufficiently wide to facilitate cortical bone and bone pate harvesting, followed by the elevation of a musculoperiosteal flap. Since in radical cavities the mastoid cortex is not (fully) available for bone harvesting, often the temporal squama must be accessed. Cortical bone chips are harvested using a flat broad chisel and put aside. It is essential to harvest enough solid cortical bone. Preferably one or as few solid fragments that allow complete reconstruction of the postero-superior bony canal wall to have less risk of gaps in the reconstruction. A bone pate collector and a cutting burr were used to collect healthy bone pate. The bone pate was mixed with an antibiotic solution (rifamycin solution) forming a semisolid paste. During the subsequent dissection of the radical cavity, the epithelial lining and all pathological soft tissue, cholesteatoma, diseased ossicular remnants, and unhealthy bone were removed and the remaining bony walls of the mastoid and attic space were adequately checked and drilled clean (Fig. 1, A and E).

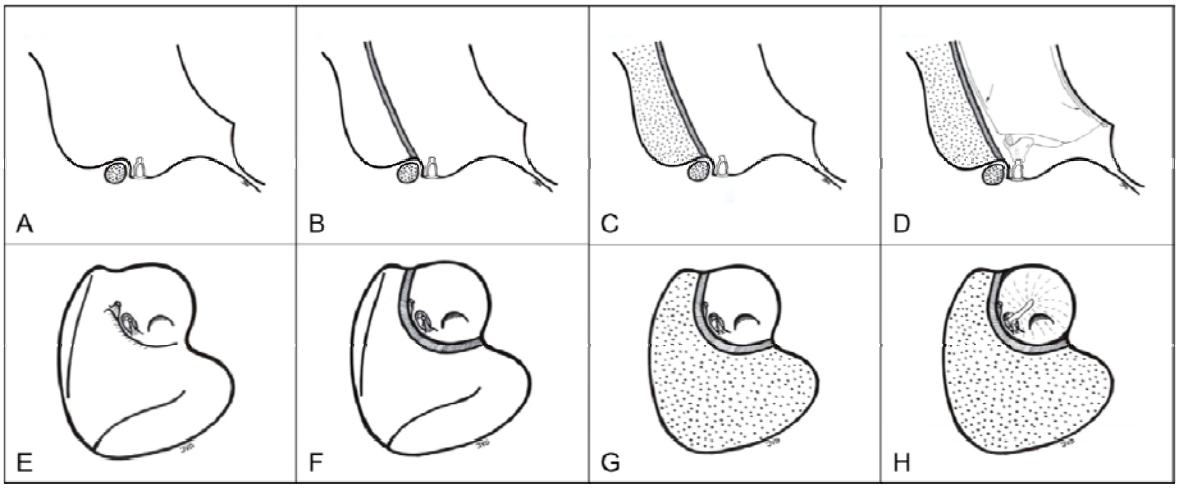

Figure 1. Surgical principle of the CWR-BOT with intact stapes superstructure. A, E, All the epithelial lining of the radical cavity and all pathological soft tissue, cholesteatoma, diseased ossicular remnants, and unhealthy bone were removed. B, E, A new, normally sized external auditory canal is built up by means of the cortical bone chips, from the cortical level down to the facial nerve canal. C, F, Paratympanic space obliteration with bone pate. D, G, Counter clockwise tympano-ossicular graft rotation with malleus handle above oval window.

It is of extreme importance to carefully dissect the posterior margin of the cavity's external meatus. The skin is often sharply folding back posteriorly toward the cavity. This fold must be eliminated by sharp dissection, to create a smooth skin surface of the lateral posterior part of the new meatus. If this is neglected or not well executed, a new retraction pocket can develop in the lateral posterior part of the EAC. To create a new, normally sized EAC, a complete bony partition between the tympanic cavity and EAC on the one hand and the paratympanic space on the other hand was then built up by means of the cortical bone chips, from the cortical level down to the facial nerve canal (Fig. 1, B and F). Bony irregularities on the EAC side can be smoothened out with a diamond burr, and minor gaps can be filled up with hydroxyapatite bone cement (OtoMimix). The paratympanic space was then completely filled with bone pate, up to the level of the mastoid cortex (Fig. 1, C and G). The new canal wall was covered with a vascularized autologous deep temporoparietal fascial flap (13), or lacking that, a free graft of autologous temporal fascia. When the external meatus of the EAC was too narrow, an M-meatoplasty according to Mirck (14) or an antero-superior oblique extended meatocanalplasty according to Offeciers (15) was performed to optimize the size of the external meatus. The middle ear reconstruction was performed using a tympano-ossicular allograft. The malleus head was removed with a malleus nipper at the level of the lateral process of the malleus. The allograft TM (with malleus handle) was rotated clockwise (left ear) or counterclockwise (right ear) to place the malleus handle in an advantageous position, perpendicularly centered above the oval window (Fig. 1, D and H). This allows for the most effective columellar energy transduction between the implanted malleus handle and the stapes or stapes footplate. The ossicular reconstruction was done by placing a remodeled allograft incus or malleus between the malleus handle and the stapes head or footplate. Peroperative intravenous antibiotics (cefazoline) were continued for 24 hours.

Surgical Staging and Imaging Follow up

Before the non-EP DW MRI sequence became available, patients were often surgically staged for safety reasons. Second-look surgery was performed in 64% of the patients (n = 32), after a mean time delay of 13.7 months, using a transmeatal or retroauricular approach. The decision to perform a second stage or not was taken by the surgeon during the first-stage surgery. Functional revision surgery was considered an elective procedure, not a planned, compulsory second-stage procedure. However, all patients were regularly followed up by yearly micro-otoscopy. Before 2006, we mainly relied on high-resolution computed tomography (HRCT) and echoplanar diffusion-weighted images (EP DW MRI) for the follow up of obliterated mastoids. Since the availability of an MRI protocol

including the non-EP DW MRI sequence, all patients were followed using this protocol, 1 and 5 years after primary surgery.

Results

Fifty adult patients were surgically treated by CWR-BOT. Thirty-four (68%) were men and 16 (32%) were women. The left-right ear ratio was 24/26. The average age was 44.71 years (range, 16.3-68.1 yr). All patients had before the CWR-BOT at least one to nine surgical procedures with (mean of 2.5 surgical procedures). The mean postoperative follow up period was 100.3 months (range, 29.36-165.96 mo). Seventeen patients (34%) had a follow up of 10 years or more. Six patients were followed for more than 12 years (Table 1).

Table 1. Patient demographics

Mean age (yr)	44.71 yr (range, 16.3-68.1 yr)
Sex (M/F)	34/16
Side (R/L)	24/26
Average previous surgical acts	2.5 (range, 1-9)
Average postoperative follow up (mo)	101.86 (range, 29-166 mo)
Follow up > 10 yr	17 (34%)
Follow up > 12 yr	6 (12%)

Forty-nine of the 50 ears (98%) remained without recurrent disease and 49 ears (98%) were free of residual disease. The standard long-term recurrent and residual rate in this series of CWR-BOT are respectively 2% and 2%.

Primary Surgery

The indications for CWR-BOT are outlined in Table 2. During primary surgery, a reconstruction of the ossicular chain was done in 88% (n = 44). The stapes superstructure was absent in 68% (n = 34) because of previous destruction by a primary or recurrent cholesteatoma. All ossicular reconstructions were performed using remodeled incus (n = 27) or malleus allografts (n = 17). In three patients the reconstruction of the ossicular chain was postponed to the planned second-look stage (n = 2) because of the presence of extensive, invasive cholesteatoma.

In three patients it was not performed because of stapes fixation (n = 2) or sensorineural hearing loss(SNHL; n = 1). This last patient was urgently operated on because of a progressive facial paralysis and profound SNHL on the affected side, ear because of an extensive cavity infection. The CWR-BOT was successfully performed, resulting in a dry trouble-free ear and recovery of the facial nerve function. The SNHL remained

unchanged. In this CWR-BOT series no major complications (facial nerve palsy or paresis, SNHL) occurred.

Table 2. Surgical indications (n = 50)

Recurrent infections	50
Excessive recurrent cleaning	32
Vestibular/caloric intolerance	2
Hearing device intolerance	20
Cholesteatoma (residual/recurrent)	4

Second Stage and Residual Disease

The decision to perform a planned second-look stage was made by the surgeon during the primary surgery in 64% (n = 32). In the later patients, since 2006, imaging follow up using the non-EP DW MRI protocol was performed at 1 and 5 years after the first stage. This revealed the presence of one residual cholesteatoma after primary CWR-BOT surgery. The residual cholesteatoma was located in the epitympanum eroding the reconstructed tympano-attical barrier resulting in a lysis of the bony obliterated epitympanic space. A meticulous removal of the residual cholesteatoma was subsequently performed, followed by reobliteration of the epitympanic cavity with bone pate and cortical bone. At latest MRI follow up no other residual or recurrent cholesteatoma was detected in the middle ear cavity or within the bony obliteration. Functional revision was performed in 38% (n = 19) as an elective second-stage transmeatal or retroauricular procedure (n = 19). During these procedures, minor TM defects and EAC irregularities were surgically corrected, including a self-cleaning retraction pocket in the TM (n = 3), a TM reperforation (n = 2), a minor canal wall depression (n = 9), bare bone exposure (n = 4), and external meatal narrowing (n = 1). The self-cleaning retraction pockets and perforations were corrected with cartilage reinforcement. Minor canal wall depression in the EAC, which possibly could result in a later canal wall lysis and/or breakdown, was corrected during this elective second-stage surgery by means of sculpted cortical bone ships and bone pate. Bare bone exposure in the reconstructed canal wall was covered with split skin dermal grafts. The meatal stenosis was corrected using a meatocanalplasty.

Retraction/Recurrent Disease

In four patients, the otoscopic follow up revealed the presence of a self-cleaning mesotympanic retraction of the TM. One patient progressively became a recurrent cholesteatoma in the 9th year of otoscopic follow up. In this patient, revision surgery revealed partial resorption and lysis of the medial superior reconstructed canal wall and of the tympanoattical barrier with extension of the cholesteatoma into the attic.

Reclosure of the epitympanum and reconstruction of the canal wall by means of bone chips and bone pate, in combination with cartilage tympanoplasty, was performed. During subsequent follow ups, no new recurrence developed.

Hearing Results

The median preoperative pure-tone average air-conduction was 61.7 dBHL with a preoperative PTA-ABG of 36.7dBHL. Postoperative hearing results were assessed after 1 year and on the latest evaluation date (average follow up: 100.3 mo) and revealed respectively a postoperative pure-tone average air-conduction of 55 dBHL and 60 dBHL. No statistically significant difference was found between preoperative and postoperative bone conduction ($p > 0.05$; *t* test). A primary ossicular reconstruction was performed in 88% (n = 44) of all patients during the primary CWR-BOT. In six patients a functional correction was postponed because of extensive cholesteatoma in three patients and abandoned in three patients because of the presence of a fixed footplate (n = 2) and a severe SNHL (n = 1). In 59.3% (n = 19) of the patients undergoing an elective second stage (n = 32), a functional correction was attempted using a remodeled malleus or incus allograft for chain reconstruction. In several patients, a conductive hearing loss persisted because of the lack of middle ear aeration or a fixed footplate. In many of the patients in the series there was a quite important sensorineural component of the hearing loss pre-existing to the primary CWR-BOT. Seventeen patients (34%) were fitted with a conventional hearing aid (n = 14) or bone-anchored hearing aid (n = 3), because of unsatisfactory hearing levels at the affected side.

Long-term and Safety Results

A safe dry, trouble-free graft, and self-cleaning EAC was achieved in 94% (n = 47) at the latest micro-otoscopic evaluation. Three patients developed a tympanic reperforation, which needed no further surgery. All perforations observed during otoscopic follow up were dry perforations of which two were very small dry perforations. Myringitis of the tympanic graft was temporarily present in two patients. A minor lateralization of the graft was observed in six patients. One patient required occasional ear canal cleaning. At the latest micro-otoscopic follow up, four patients had a minor external auditory canal wall depression, not accumulating keratin, thus not necessitating a further treatment. Imaging follow up by non-EP DW MRI performed after a follow up of 5 years or even longer in some patients after the primary surgery (since the availability of the non-EP DW MRI sequence) was available in 76% (n = 38). Before 2006 HRCT and/or EP DW was performed in 14% (n = 7). In the remaining five patients, the MRI control was deemed redundant because of an earlier executed planned second-look control without pathological findings. In summary, in this early series of 50 CWR-BOT, the long-term combined safety control by means of planned second-look surgery and late non-EP DW MRI showed one of residual

cholesteatoma (2%) and one recurrent cholesteatoma (2%). Because our current imaging protocol for cholesteatoma surgery follow up has been strictly validated (8-12), we no longer apply routine planned second-look surgery.

Discussion

Unstable and problematic cavities after CWD mastoidectomy are a major indication for performing an obliteration of the mastoid and epitympanum. The decision to perform revision surgery with bony obliteration is usually based on one or more of the following complaints; persistent or periodic discharge that is difficult to control with regular cleaning and eardrops, the need for frequent micro-otoscopic cleaning, water intolerance, caloric induced vertigo, and the difficulty to wear a hearing aid (2,3). The problems are mainly caused by the loss of the self-cleaning capacity of the ear. The self-cleaning capacity of the migratory skin in the medial part of the EAC has its limitations, and cannot cope with the extended surface area of skin in most cavities. When performing CWR-BOT we aim to rebuild a normally sized EAC, which restores the EAC anatomy and its self-cleaning capacity, thus solving the hygienic problems. The CWR-BOT can also be applied successfully in therapy-resistant COM without cholesteatoma, more specifically when the ear's bone conduction levels offer potential for unaided or aided hearing after reconstruction. Since the first description of mastoid obliteration surgery more than one century ago (16), various surgical techniques have been developed, using a variety of obliteration material and can be divided into two distinct subgroups: free graft obliteration (autologous or synthetic) and soft tissue flap obliteration (17). When performing soft tissue flap obliteration, vascularized soft tissue flaps are mobilized and rotated into the empty mastoid cavity (18,19). In free graft obliterations, various materials including soft tissues (20), bone (21), cartilage (22), or synthetic biomaterials (23-25) are used to fill the empty mastoid and epitympanic space. The main surgical principle is the intention to decrease the mastoid size and to normalize the size of the EAC. The ideal obliteration material should stimulate the formation of new bone at the surgical site, become incorporated as an inert filler without additional stimulation of an inflammatory response, should not have unwanted systemic or local effects, should be easy to handle, and should be relatively inexpensive. Bone pate fulfills all the requirements (21). Perkins (26) first demonstrated the value of bone pate for the reconstruction of cavities. An adequate application of healthy cortical bone pate mimics the natural osteo-induction and osteoneogenesis of bone. Several authors abandoned the use of bone pate for mastoid obliteration because of the high rate of postoperative infection (16%) and the high incidence of chronic resorption of bone pate resulting in

local retraction pockets and canal wall defects, leading to long-term failure rates of 52% (17,21,27). The CWR-BOT procedure applied in our department differs from the above-mentioned earlier reports in two very crucial aspects. The administration of intravenous per- and postoperative antibiotics and the impregnation of the bone pate with an antibiotic solution lead to a marked reduction in the rate of postoperative infections, as was also previously reported (28). Moreover, in our CWR-BOT technique, the bone pate is strictly separated from the canal skin over the full length of the EAC by sculpted solid cortical bone, used for the meticulous reconstruction of the canal wall and the tympano-attical barrier. This is an extremely important condition for long-term stability of the new EAC in the reconstruction of unstable cavities. In our experience autogenous solid cortical bone chips are the most ideal material for reconstruction of the external ear canal. They integrate well with the original bone margins, which is a definite advantage over the use of cartilage to reconstruct the canal wall. Moreover, cortical bone is abundantly available in comparison with cartilage. A histopathological evaluation concluded that bone chips and bone pate, used for obliteration, retain their original volume and consistency, whereas subcutaneous tissue and muscle tend to atrophy (29). During the postoperative healing, the migration of squamous epithelium starts at the margins of the meatal or tympanic membrane skin remnants. This process can be hampered by infection, by areas of bare bone and by ischemia and necrosis of the underlying soft tissue flap. If the EAC does not epithelialize completely, it will lead to inflammation and granulation. With time, this will either cause scar tissue formation and secondary stenosis of the EAC, or breakdown of the underlying soft tissue, the reconstructed canal wall bone, and the underlying bone pate. This process can cause intermittent or persistent ear discharge. Postoperative inflammation or infection can cause perforation of the tympanic membrane graft and extrusion of the columellar reconstruction. The combined creation of a normally sized external meatus and a solid bony ear canal provides the ideal basis for a stable hygienic condition of the ear, as reported in this study.

Hearing Results

One of the goals of chronic ear surgery is the improvement or at least the preservation of the preoperative hearing level. The long-term functional outcome depends on the following variables: the extent and severity of the pathology; the quality of the surgical act; the applied technique and the nature of the reconstructive materials; the quality of the healing process; the postoperative biological behavior of the ear. There is an inverse relation between the preoperative extent of the ossicular damage and the postoperative long-term functional gain. It stands to reason that greater ossicular damage and a higher number of previous surgical interventions often reflect a worse biological behavior of the ear, which makes it less probable for the biology to normalize during the postoperative

period. The preconditions for a good middle ear function, such as normal gas exchange and middle ear aeration as well as the presence of normal mucosa with efficient mucociliary clearance, are often not present. As a consequence, in these patients the functional result will be disappointing to surgeon and patient alike, however well the middle ear is reconstructed. As a result of these preconditions, it is not surprising that a number of patients reported in this study have a persistent air-bone gap despite adequate ossicular chain reconstruction. Although the average long-term improvement (101.8 mo after previous surgery) in hearing was small in many patients, also some patients experienced a major improvement. When the postoperative hearing was unsatisfactory after primary surgery on the affected side a conventional hearing aid was fitted.

The decision making for using the CWR-BOT or an alternative surgical technique, such as a subtotal petrosectomy, is mainly based on the preoperative hearing level. If the preoperative hearing of the patient is a severe or profound hearing loss, we prefer the technique of tympanomastoid exenteration with blind sac closure of the EAC over the CWR-BOT technique, to eradicate the pathology and solve the hygienic problems (30). A subtotal petrosectomy with blind sac closure of the EAC accounts for approximately 3% of our COM patients. In the absence of residual disease as documented by non-EP DW MRI after primary surgery, a bone anchored hearing aid, an active middle ear implant, or a cochlear implantation can be safely performed. In case a nonsurgical hearing revalidation is needed in the presence of an open external ear canal, a conventional air conduction hearing aid remains the first option. If the air-bone gap exceeds 35 dB, a passive semi-implantable Bone Anchored Hearing Device (BAHD) (Baha by Cochlear or Ponto by Oticon) and a semi-implantable active bone conduction device like the Bonebridge (Medel) might be expected to outperform the conventional air conduction hearing aid option. If the sensorineural component in such a mixed hearing loss is in between 40 and 60 dB, the bodyworn variant of the BAHD might be taken into consideration as a good option. So when a subtotal petrosectomy with blind sac closure has been performed the options for hearing revalidation are mainly determined by the present sensorineural hearing level. The Vibrant Soundbridge option (Medel) should only be applied if the sensorineural component is 20 dB or even better. If the sensorineural component exceeds 60 to 70 dB cochlear implantation is the only option (31). After performing a subtotal petrosectomy in patients of a profound conductive hearing loss (air bone gap >30-35 dB), a bone-anchored hearing aid (BAHA) can be implanted or a middle ear implantable hearing aid if bone conduction levels are worse than 40 dB but better than 70 dB (31). The subtotal petrosectomy technique is also used in deaf ears or profound SNHL with COM needing a cochlear implant, as a preparatory stage 3 to 6 months before cochlear implantation.

Long-term Safety Issues

Adequate imaging follow up of obliterated mastoids is necessary to prevent late complications caused by residual cholesteatoma left behind in the bony obliterated mastoid. Previous studies published in the literature advocated the combination HRCT and diffusion-weighted MR imaging in the follow up of cholesteatoma after mastoid obliteration (32). The application of non-EP DW MRI monitoring has become a standard evaluation protocol in our department at 1 and 5 years postoperatively. In case of doubt we repeat the examination after 1 year (8-12). Clinical monitoring by micro-otoscopy and audiometry remains mandatory to exclude recurrent disease. Therefore, we advise yearly otoscopy for at least 10 years, and 3-yearly micro-otoscopic and audiometric follow up later on.

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Chapter 5

Quality of Life Questionnaires for COM in the Dutch Language

Chapter 5.1

Validity and Test-Retest Reliability of the Dutch Version of the Chronic Otitis Media Questionnaire 12 (COMQ-12)

van Dinther JJS, Droessaert V, Camp S, Vanspauwen R, Maryn Y, Zarowski A, Somers T, Offeciers E

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Abstract

Objective: To test the validity and test–retest reliability of the Dutch translation of the Chronic Otitis Media Questionnaire 12 (COMQ-12).
Materials and methods: Thirty-five healthy individuals with no history of chronic otitis media (COM) received the questionnaire as well as a group of 35 patients with complaints of COM. The healthy participants had to complete the questionnaire twice (control group 1 and control group 2) to estimate the test–retest reliability, and their scores were compared with those of the patients (group 3) to test the validity.
Results: The overall COMQ-12 score in control group 1 ranged from 0 to 11, in control group 2 from 0 to 6, and in group 3 from 7 to 46. The mean score in control group 1 was 1.43 [standard deviation (SD) 2.30], 1.34 in control group 2 (SD 2.06), and 27.80 in group 3 (SD 10.51). A comparison of the absolute COMQ-12 scores of the two control groups and the patient group showed a significantly higher COMQ-12 score in patients with COM than in controls. The diagnostic accuracy was investigated, and a COMQ-12 cut-off score of 8 was found to have a near-perfect sensitivity and specificity in distinguishing between the presence and absence of COM. The single-measures intraclass correlation coefficient for absolute agreement (ICCAA) was 0.859 (with a 95% confidence interval from 0.738 to 0.926). This clearly exceeded the ICC threshold for acceptable reliability (ICC≥0.75) and therefore confirmed that there was reasonable test–retest reliability when applying the questionnaire to control subjects.
Conclusion: The Dutch version of the COMQ-12 has good validity, diagnostic accuracy, and test–retest reliability.

Introduction

Chronic otitis media (COM) remains a common disease that has a serious health impact on up to 2% of the population [1]. In the assessment of healthcare, patient-based measuring instruments regarding the quality of life and perceived handicap have become increasingly important. Combining three COM-related quality of life questionnaires—the Chronic Ear Survey [1], the Chronic Otitis Media Outcome Test 15 (COMOT-15) [2], and the Chronic Otitis Media 5 (COM-5) [3] —the Chronic Otitis Media Questionnaire 12 (COMQ-12) is a disease-specific tool that was recently developed by Phillips et al. [4] to meet that purpose. The COMQ-12 consists of 12 questions grouped in four categories regarding the severity of symptoms, impact on lifestyle and work, impact on the health service, and general impact on the patient. Each question needs to be scored on a six-point ordinal scale from 0 (i.e., no impact) to 5 (i.e., most severe impact), depending on

the level of inconvenience or frequency of symptoms. Initial validation has been completed, and this provides a useful clinical tool for the assessment of active COM [4]{Formatting Citation}. In 70 subjects without active chronic middle-ear disease, the overall mean score was 2, the modal score was 0 in 39% of participants, and the majority of participants had a total COMQ-12 score of 5 or less [5].

The purpose of the present study was to culturally adapt the COMQ-12 to Flemish Dutch and to obtain measures of the validity and test–retest reliability of this Dutch translation of the original COMQ-12. The scores of controls were compared with those of patients to test the validity. The diagnostic accuracy or the ability of COMQ-12 to discriminate between normal subjects and subjects with chronic middle-ear pathology was investigated. Finally, the test–retest difference between two repeated administrations was assessed.

Materials and methods

Firstly, the original COMQ-12 that was developed by Phillips et al. [4] was translated by the first three authors. The translation was sent to a native English-speaking person who has lived in Flanders for more than 40 years and speaks fluent Dutch. Secondly, this person translated the Dutch version back into English. Both the original and retranslated English versions of the COMQ-12 were then compared by the first three authors. There were no substantial differences between these two English versions; therefore, it was decided to adopt the Dutch version for further scientific and clinical use (Appendix A). As in the original COMQ-12, controls as well as patients were asked to rate the severity or frequency of their symptoms on a six-point equal-appearing interval scale from 0 (i.e., “this doesn’t bother me at all or less frequently than once every 6 months”) to 5 (i.e., “the worst thing that has ever affected my life or most days in the week”).

Study Population

In total, 70 individuals were asked to complete a Dutch version of the COMQ-12. The control group consisted of 26 women with a mean age of 41.6 years [standard deviation (SD)=10.8; range=24–65] and nine men with a mean age of 40.9 years (SD=11.3; range=24–67) without a history of COM. These were healthy volunteers who were selected randomly from hospital staff (i.e., medical doctors, nurses, and administrative staff members) and among relatives and friends of the authors.

In addition to completing the COMQ-12, control subjects were also asked for their age and the presence of ear-related problems such as acute ear infections or previous ear surgery. One separate episode of infection was accepted; only a history that was

consistent with COM led to exclusion. The dataset from the first completion (i.e., test) by the control subjects was called “control group 1.” The dataset from their second completion of the COMQ-12 questionnaire (i.e., retest) was referred to as “control group 2.”

The study group comprised 19 female subjects with a mean age of 36.2 years (SD=19.8; range=8–78) and 16 male subjects with a mean age of 41.7 years (SD=20.2; range=7–68) with COM. They visited our clinic in July 2015 with complaints of COM. The dataset from their completion of COMQ-12 was called ”group 3.”

All data were analyzed anonymously.

Statistics

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) Statistics version 20 (IBM; Armonk, NY, USA). For each analysis, a significance level of 5% was adopted. Various tests were used.

Firstly, the normality of the data distribution was investigated with the one-sample Kolmogorov–Smirnov test.

Secondly, the absolute scores of healthy participants and patients were analyzed with the non-parametric Mann–Whitney U-test to assess the validity of the questionnaire.

Thirdly, to examine the diagnostic value of COMQ-12, several estimates of diagnostic precision were calculated: sensitivity, specificity, and the area under a receiver operating characteristics curve (i.e., AROC). The AROC statistic is interpreted as a score between 1.0 (for perfect discrimination between cases and non-cases) and 0.5 (for chance-level diagnostic accuracy). To facilitate the clinical interpretation of COMQ-12 scores, a threshold score for distinguishing normal from abnormal subjects was derived from the ROC curve.

Fourthly, to assess test–retest reliability, the single-measures type A intraclass correlation coefficient using an absolute agreement definition (i.e., ICCAA) was calculated. Similar to other reliability coefficients, the ICC ranges from 0.00 (i.e., total absence of reliability) to 1.00 (i.e., perfect reliability). Although there are no standard criteria for the interpretation of ICC, a general guideline suggests that values of above 0.75 indicate good to excellent reliability, and values below 0.75 correspond to poor to moderate reliability [6].

Ethics committee approval was received for this study from the ethics committee of the Sint-Augustinus Hospital, GZA Antwerp.

Results

Study Population

In the control group of 35 healthy individuals, one participant reported a history of ear disease. This participant had undergone an ossiculoplasty for traumatic luxation of the incus. The overall COMQ-12 score in control group 1 ranged from 0 to 11, with a mean score of 1.43 (SD=2.30). In control group 2, the overall COMQ-12 scores ranged from 0 to 6, with a mean of 1.34 (SD=2.06). The COMQ-12 scores of the individual who reported an ear problem were 3 (test) and 6 (retest). The median COMQ-12 score overall was 0 in control groups 1 and 2, and the modal (or most prevalent) score was 0 in 18 participants (51.4%) in control group 1 and 21 participants (60%) in control group 2 (see Table 1). The distribution of control group 1 data was not normal (Kolmogorov–Smirnov Z=1.584; p=0.013). The distribution of control group 2 data was not normal (Kolmogorov–Smirnov Z=2.029; p=0.001).

The overall COMQ-12 scores in the patient group (group 3) ranged from 7 to 46, with a mean score of 27.80 (SD=10.51). The median overall COMQ-12 score was 28 (Table 1).

The distribution of group 3 data was normal (Kolmogorov–Smirnov Z=0.085; p=0.200). Non-parametric statistical methods were chosen based on the abnormal distribution of the data of the control subjects.

Table 1. Descriptive statistics

	Number (n)	Min	Max	Range	Mean	SD	SE
Control Group 1	35	0	11	11	1.43	2.30	0.39
Control group 2	35	0	6	6	1.34	2.06	0.35
Patient group	35	7	46	39	27.80	10.51	1.79

Validity

A comparison of the absolute COMQ-12 scores of the two control groups (control group 1 and group 2) with that of the patient group using the Mann–Whitney U-test showed that the COMQ-12 score was significantly higher in patients with COM than in control subjects (U=2.00; p=0.000).

To determine the diagnostic accuracy of COMQ-12 and its ability to distinguish normal from COM subjects, an ROC curve was constructed (Figure 1). The value of AROC, with COMQ-12 scores as the test variable and the group (i.e., control group 1 versus group 3) as the state variable, was 0.998, which revealed very high discriminatory power to distinguish subjects with normal middle ears from those with chronically abnormal middle ears (with statistical significance at $p<0.001$). The ROC curve was also used to identify which cutoff point achieved the best balance between sensitivity and specificity and would provide optimal discrimination between experimental and control groups. In this

regard, a COMQ-12 cutoff score of 8 produced estimates of sensitivity and specificity of 1.00 and 0.97, respectively. Therefore, using this threshold, 100% of patients were correctly classified as having COM, whereas 97% of non-cases were correctly categorized as normal.

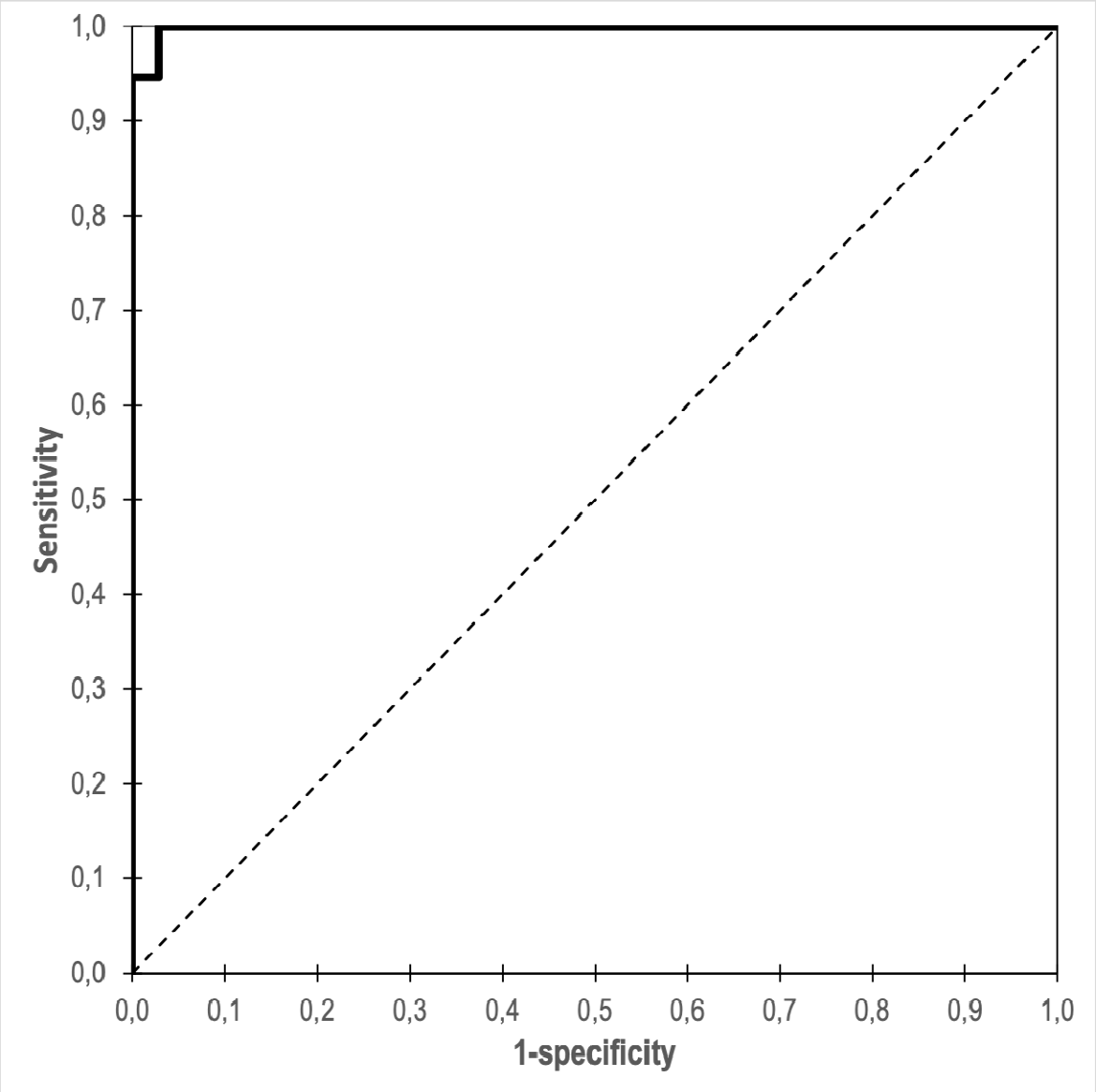

Figure 1. ROC curve. The ability of COMQ-12 to discriminate between normal and chronic middle-ear infection is represented by AROC. To facilitate the clinical interpretation of COMQ-12 scores, a threshold score of 8 for distinguishing normal from abnormal subjects was derived from the ROC curve.

Test–Retest Reliability

The single-measures ICCAA was 0.859 (with a 95% confidence interval from 0.738 to 0.926), which clearly exceeds the ICC threshold of 0.75 and confirmed that there was acceptable test–retest reliability with the control subjects.

Discussion

The measurement of patient-based perception of the quality of life and handicaps has become very important in healthcare. The COMQ12 is a patient-related outcomes questionnaire that is constructed to obtain information about the symptoms that are most important for the patient. It allows the clinician to get an idea of the expectations of patients regarding therapy and to choose an adequate management strategy that is consistent with these expectations [7]. We translated the original COMQ-12 into Dutch and tested it for validity, diagnostic accuracy, and test–retest reliability.

The scores for normal subjects, which varied from 0 to 11 and from 0 to 6 with mean scores of 1.43 and 1.34 as well as modal scores of 0 in 51.4% and 60% of the control participants for completion and recompletion, respectively, are comparable to the values for normal subjects calculated by Phillips et al. [5]

A cutoff value of 8 was determined to distinguish between the absence and presence of COM, although in the control group one 44-year-old patient had a COMQ-12 score of 11 (test) and 6 (retest) in the absence of COM. This can be explained by a high score for the questions regarding hearing, which can be diminished in the absence of COM. Also, two patients reported COMQ-12 scores of 7 and 9. One had COM for years and had undergone several operations for this problem. Because the COMQ-12 is a patient-based measurement, the subjective inconvenience is assessed, and this patient was probably able to cope very well with his COM. The other patient had a small attical cholesteatoma in the absence of otorrhea and with good hearing, which was discovered because of a sensation of ear fullness and tinnitus.

The Dutch version of the COMQ-12 has good reproducibility and high diagnostic accuracy for detecting COM and can be used in clinical evaluation studies to assess the impact of surgery on patients' complaints.

Ethics Committee Approval:

Ethics committee approval was received for this study from the ethics committee of Sint-Augustinus Hospital, GZA Antwerp.

Informed Consent:

Informed consent was obtained from patients who participated in this study.

Peer-review:

Externally peer-reviewed.

Author Contributions:

All authors contributed equally to this study.

Conflict of Interest:

No conflict of interest was declared by the authors.

Financial Disclosure:

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Appendix A

Chronic Otitis Media Questionnaire–12 (COMQ-12):
Deze vragen zijn om te achterhalen hoe erg uw oorproblemen u beïnvloeden. Geen enkele machine kan dit voor u doen: enkel u kan ons dit vertellen. Wij verwachten dat de resultaten van deze vragenlijst ons helpen te begrijpen welke van uw oor symptomen het meest belangrijk voor u zijn. Deze wetenschap zal ons helpen om de wijzen waarop patiënten met oorproblemen worden verzorgd te verbeteren.

Beantwoord alstublieft onderstaande vragen door zorgvuldig elke gestelde vraag te overwegen en vervolgens het geschikte cijfer te omcirkelen. De cijfers verwijzen elk naar een bepaalde beschrijving. Er zijn geen juiste of foute antwoorden, maar probeert u alstublieft goed na te denken over elke vraag voordat u het geschikte cijfer omcirkelt. Overweeg alstublieft elk probleem zoals het in de voorbije 6 maanden geweest is.

VOORBEELD:
Duid voor de volgende vraag alstublieft aan hoe vaak u deze activiteit uitvoert, gebruik makende van de onderstaande schaal en door het geschikte cijfer te omcirkelen:

0 Nooit
1 Minstens éénmaal per drie maanden
2 Minstens éénmaal per maand
3 Minstens éénmaal per week
4 De meeste dagen in de week
5 Heel de tijd

Hoe vaak eet u toast voor ontbijt? 0 1 2 3 *4* 5
Een persoon die zodanig antwoordt, geeft aan dat hij/zij gewoonlijk toast eet als ontbijt doch niet altijd.

Als u enig probleem ondervindt bij het beantwoorden van de vragen, vraag dan hulp aan een lid van de klinische staf. Dank U.

Duid voor de volgende vragen alstublieft aan hoe ernstig de verscheiden beschreven elementen u beïnvloeden, gebruik makende van de onderstaande schaal door het geschikte cijfer te omcirkelen.
0 Stoort me helemaal niet
1 Een beperkt ongemak
2 Een matig ongemak
3 Een groot ongemak maar ik kan er mee omgaan
4 Een groot ongemak en ik vind het zwaar om ermee om te gaan
5 Het ergste dat mijn leven ooit heeft getroffen

Symptoom ernst:

1. Lopend oor of drainage van het oor	0 1 2 3 4 5
2. Een 'slecht ruikend oor' hebben	0 1 2 3 4 5
3. Gehoorproblemen thuis, bv vereisend dat het volume van de TV of radio wordt opgedreven	0 1 2 3 4 5
4. Gehoorproblemen wanneer men spreekt met mensen in groepen of in lawaaierige omgevingen	0 1 2 3 4 5
5. Discomfort in en/of rondom het oor	0 1 2 3 4 5
6. Duizeligheid of gevoel van "instabiliteit"	0 1 2 3 4 5
7. Tinnitus of lawaai in het oor	0 1 2 3 4 5

Duidt u voor de volgende vragen alstublieft aan <u>hoe vaak</u> de verscheiden beschreven elementen u beïnvloeden, door gebruik te maken van de onderstaande schaal en door het geschikte cijfer te omcirkelen.
0 Minder frequent dan eenmaal per 6 maanden
1 Minstens eenmaal per 6 maanden
2 Minstens eenmaal per 3 maanden
3 Minstens eenmaal per maand
4 Minstens eenmaal per week
5 De meeste dagen in de week

Levensstijl en werk impact:

Hoe vaak bent u NIET in staat geweest om:

8. Uw normale dagelijkse activiteiten thuis/op het werk uit te voeren	0 1 2 3 4 5
9. U te wassen, te douchen of te baden zoals u zou willen bv. Hoe vaak bent u angstig geweest dat deze activiteiten een oorontsteking veroorzaken?	0 1 2 3 4 5

Gezondheidszorg impact

10. Hoe vaak bent u langsgegaan bij uw huisarts omwille van uw oorproblemen?	0 1 2 3 4 5
11. Hoe vaak bent u genoodzaakt medicijnen in te nemen (inclusief oordruppels) voor uw oorprobleem?	0 1 2 3 4 5

Voor de volgende vraag, duid alstublieft aan hoe erg de dingen zijn, schaal van '0' tot '5'. '0' betekent helemaal niet erg, '5' betekent het ergste dat u zich ooit kan inbeelden:

Algemeen:

12. In welke mate halen uw oorproblemen u 'onderuit'?	0 1 2 3 4 5

Controleert u alstublieft dat u een antwoord heeft geformuleerd op elke vraag en vraag om hulp indien u dit moeilijk vindt.

Heel erg bedankt om deel te nemen.

Chapter 5.2

Health-Related Quality of Life after Bony Obliteration Tympanoplasty for COM with Cholesteatoma using the COMQ-12 – a Disease Specific PROM

Baetens W*, van Dinther JJS*, Vanspauwen R, Maryn Y, Zarowski A, Offeciers E

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*both first authors contributed equally

Abstract

Objective: In this study we investigate the effect of canal wall up with bony obliteration tympanoplasty (CWU-BOT) on the health-related quality of life (HRQOL) in patients with chronic otitis media with cholesteatoma by using the chronic otitis media questionnaire 12 (COMQ-12).
Materials and methods: A retrospective analysis of the COMQ-12 of 26 patients who completed the COMQ-12 before and after a CWU-BOT with eradication of cholesteatoma followed by obliteration of the mastoid and paratympanic space with bone chips and bone pâté and reconstruction of the tympanic membrane and ossicular chain.
Results: All patients were operated upon between 2014 and 2017 all in our institute. The median score of the 12 questions was calculated pre and postoperatively and compared. A large effect is seen in the total score and the questions about running ear, discharge and visits to the general practitioner. A medium positive size effect is seen in the questions about hearing in noisy surroundings, discomfort, dizziness, tinnitus, medication use and the mental aspect of the patient. In the questions about the hearing at home and quality of life and impact on work, we note a small positive size effect. In 50% patients the HRQOL became normal, the remaining 50% improved to a level very close to normal.
Conclusion: CWU-BOT shows a clear decrease in the severity of the symptoms, life and work impact and health care after surgery.

Introduction

Chronical ear disease affects 2% of the population and is and is associated with material morbidity [1]. Patient reported symptom appraisal is needed to asses disease severity and to appreciate the results of both surgical and nonsurgical interventions [2]. Chronical ear disease including chronical otitis media (COM) is negatively influencing the quality of life (QOL) of patients [1, 3]. In this study we investigate the effect of canal wall up with bony obliteration tympanoplasty (CWU-BOT) [4] on the QOL in patients with COM with cholesteatoma.
The chronic otitis media questionnaire 12 (COMQ-12) is developed by Phillips and published in 2014 [5]. This 12-item questionnaire is mixed generic and disease specific. It investigates the symptom severity, life and work impact and health impact of COM over the past 6 months. Sufficient consistency and initial validity has been obtained to justify the clinical use of the reduced item set which derived from 3 other questionnaires: the Chronic Ear Survey (CES) [1], the Chronic Otitis Media Outcome Test 15 (COMOT-15) [6] and the Chronic Otitis Media 5 (COM-5) [7] after a literature review [5].

In 2015 a Dutch COMQ-12 version [Appendix A] was validated and a cut off value was calculated to distinguish between a normal and abnormal health related quality of life (HRQOL) in COM using a series of healthy volunteers as well as series of patients with COM [8]. In 2017 Philips developed a second questionnaire to overcome the lack of responsiveness, the chronic otitis media benefit inventory (COMBI) which is a dynamic single shot postoperative tool for the same type of patients [9]. Up to now no other publication repeated the COMQ-12 patient reported outcome measure (PROM) before and after surgery for COM with cholesteatoma in the same population.

Our goal was to assess the HRQOL by measuring the patient reported health and impact on work and social life following CWU-BOT with obliteration of the mastoid and paratympanic spaces for COM with cholesteatoma using a disease specific patient related outcome measure (PROM) questionnaire.

Methods

In our institute COM patients planned for tympanoplasty routinely complete the COMQ-12 before surgery and at different points in time after surgery. A retrospective analysis of a first cohort of consecutive cases of CWU-BOT with eradication of cholesteatoma followed by obliteration of the mastoid and paratympanic space with bone chips and bone pâté and reconstruction of the tympanic membrane and ossicular chain was planned.

Power calculation was carried out with the Raosoft sample size calculator. We accepted a margin of error of 5% and confidence intervals of 95%. As a result of the choices and assumptions, the minimum number of subjects to investigate was 25.

Statistical analysis was carried out with the Statistical Package for the Social Sciences (SPSS) Statistic version 23 (IBM; Armonk, NY, USA). The Wilcoxon Signed Rank test with Bonferroni correction was applied in order to compare the preoperative and postoperative outcome. A p level of less than 0.004 was considered statistically significant. The benchmarks we used to determinate the size effect can be found in Cohen (1988) and Rosnow (1996) [10, 11] .

All data were analysed anonymously. Ethics committee approval was received for this study from the medical ethics committee of the GZA Ziekenhuizen Antwerp (180806RETRO).

Results

The study population consisted of 26 patients (13 males, 13 females; average age ± standard deviation = 35,7 ± 20,6 years; age range = (7,5 years – 77 years)) operated upon between 2014 and 2017 all in our institute. The mean interval between surgery and completing the questionnaire post-operatively was 2,35 ± 0,64 years [Table 1].
The median score of the 12 questions was calculated pre and postoperatively and compared. A significant decrease in the scores of all questions was achieved, except for question 3, 4, 7, 8 and 9 [Table 2]. These questions are evaluating the hearing situation including the presence of tinnitus or the ability to complete daily activities mostly related to water contact.

Table 1. Demographics

	N	Mean	Median	Std deviation	Range
Age at surgery (years)	26	35,71	28,69	20,58	7,49-77,00
Completion interval (months)	26	2,28	2,44	0,65	0,69-3,95

Table 2. COMQ-12 results.

	Preoperative scores					Postoperative scores				
	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max
Question 1	2,19	2,5	1,50	0	5	0,19	0	0,49	0	2
Question 2	2,15	3	1,76	0	5	0,08	0	0,39	0	2
Question 3	2,65	2	1,26	0	5	2,00	2	1,94	0	5
Question 4	3,46	4	1,39	0	5	2,37	2,5	2,13	0	5
Question 5	2,27	3	1,48	0	5	0,77	0	1,07	0	3
Question 6	1,11	1	1,14	0	3	0,23	0	0,62	0	3
Question 7	1,89	1,5	1,51	0	5	1,00	0	1,74	0	5
Question 8	0,69	0	1,29	0	5	0,15	0	0,61	0	3
Question 9	1,73	0,5	2,03	0	5	0,69	0	1,46	0	4
Question 10	1,65	2	1,35	0	4	0,12	0	0,43	0	2
Question 11	2,54	2	1,68	0	5	0,73	0	1,22	0	4
Question 12	2,58	3	1,33	0	5	1,04	0	1,34	0	4
Total score	24,92	23	9,48	11	44	9,35	8,5	7,73	0	28

Table 3. Wilcoxon signed rank test

	p-Value	Significant	R	Effect size
Question 1	0,000	Yes	0,56	Large
Question 2	0,000	Yes	0,51	Large
Question 3	0,163	No	0,19	Small
Question 4	0,024	No	0,31	Medium
Question 5	0,000	Yes	0,49	Medium
Question 6	0,002	Yes	0,43	Medium
Question 7	0,010	No	0,36	Medium
Question 8	0,090	No	0,23	Small
Question 9	0,052	No	0,27	Small
Question 10	0,000	Yes	0,53	Large
Question 11	0,000	Yes	0,49	Medium
Question 12	0,001	Yes	0,46	Medium
Total score	0,000	Yes	0,59	Large

Calculating the regression over time, the curve is decreasing in all questions, even in the non-significant questions 3, 4, 7, 8 and 9. Based on the Wilcoxon signed rank test, we calculated the effect size of each question and the total score [Table 3]. A large effect is seen in the total score and the questions about running ear, discharge and visits to the general practitioner. A medium positive size effect is seen in the questions about hearing in noisy surroundings, discomfort, dizziness, tinnitus, medication use and the mental aspect of the patient. In the questions about the hearing at home and quality of life and impact on work, we note a small positive size effect.

The previously published cut off value of 8 for the COMQ-12 was used, meaning that a total score of 8 or lower can be categorised as a normal HRQOL [8]. The post-operative evaluation in this study has a mean score of 9,35 ± 7,73 which is not very different from the cut off value. Between one and two year after surgery 50% (n=13) of our patients scored “normal” concerning HRQOL measured with this tool. The other 50% scored up to a level “very close to normal”. In the latter subgroup the mean postoperative score is 15,4 (median 14) and the preoperative mean score is 28,2 (median 27). Even though they are not statistically normalised, they still made a significant improvement (p = 0,003) [Figure 1].

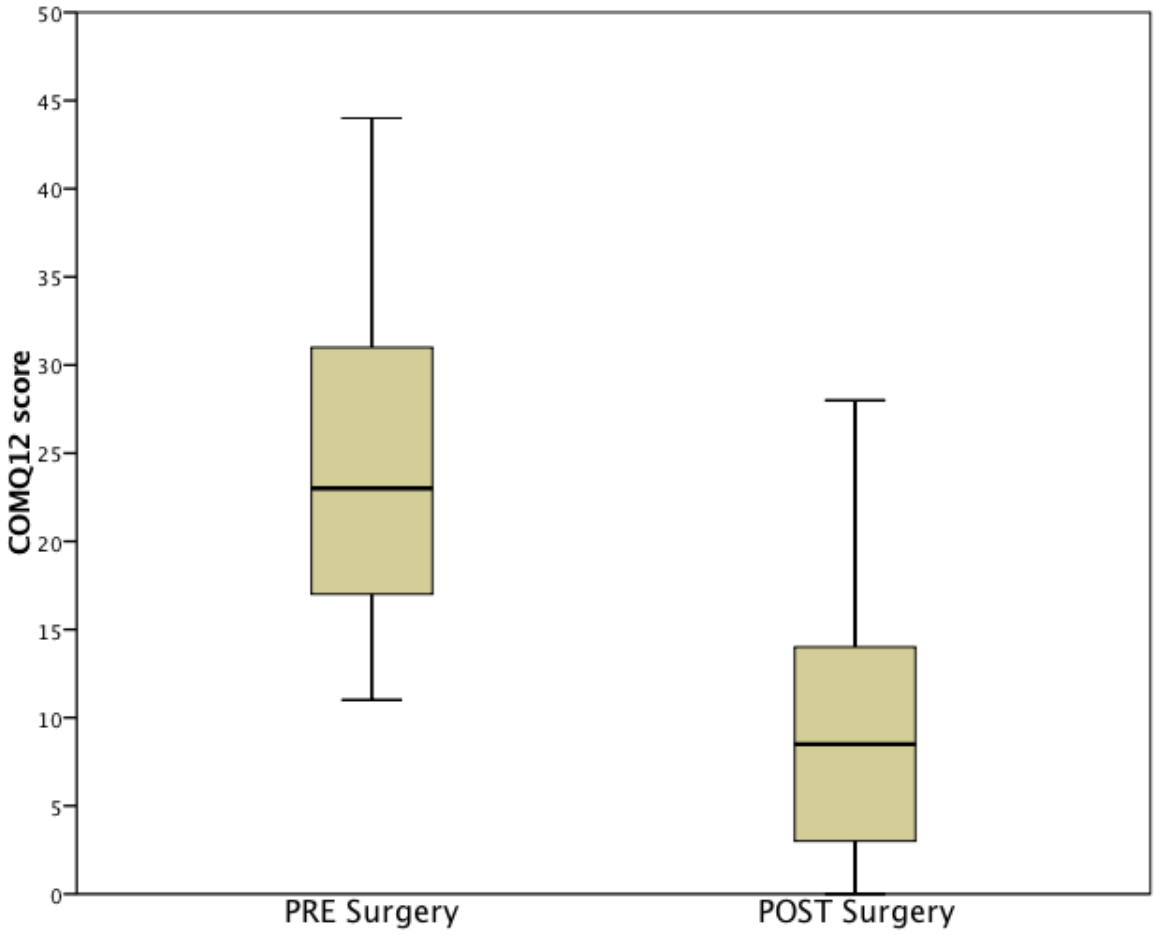

Figure 1. Box and Whisker plots of the *COMQ-12 score* (chronical otitis media questionnaire 12) for 26 patients operated with the canal wall up bony obliteration tympanoplasty technique; *PRE Surgery*, the preoperative COMQ-12 score; *POST Surgery*, the postoperative COMQ-12 score; Postoperatively in 50% (n = 13) of the patients have a score below the cut off score of 8 which categorizes them as "normal" concerning health related quality of life measured with this tool. The other postoperative 50% improved to a level "very close to normal"; Bars, minimum to maximum values; rectangles, 25th - 75th percentile, bars in rectangles, median value; dots outlying values.

Analysis of the outliers for each question learn that patients with disease recurrence (n=1), myringitis or retraction pockets, score less than patients with the absence of these problems.

Discussion

The COMQ-12 is a useful HRQOL questionnaire [5]. At the level of item format, when "before" and "after" are collected on separate occasions or periods, the COMQ-12 is a useful patient reported outcomes measures (PROMs) [12]. In 2017 a new mixed generic

and specific dynamic PROMs for adult middle ear disease, named the chronic otitis media benefit inventory (COMBI) was developed and validated [9]. The COMBI's one-shot format offers convenience over available single-occasion status instruments for chronic middle ear disease that require completion both preintervention and postintervention. Carr et al. stated that the QOL is determined by expectations and experience [13]. Differences obtained by subtraction or baseline adjustment (COMQ-12) may be more bias-free. This is the reason why we prefer to use the COMQ-12 instead of the COMBI.

This study, which investigates the symptom severity, life and work impact and health impact of COM over the past 6 months, by the COMQ-12 pre and postoperatively, shows a significant improvement in almost all aspects and a positive effect for all of the 12 questions. A non-significant improvement is seen in the questions concerning hearing (Q3,Q4,Q7) and lifestyle and work impact (Q8,Q9).

The long-term effect of the CWU-BOT for cholesteatoma concerning safety and hygienic restoration is well established [14-16]. The relative impact of the hearing situation becomes more and more important in the resulting postoperative situation [4, 17]. A postoperative hearing situation with an air-bone gap within 20 dBHL is achieved in only 50-60% of the adult patients operated with the CWU-BOT technique [4, 18]. The hearing remains thus an unresolved limiting factor, especially in children operated for extensive cholesteatoma and is therefore possibly the most important negative influencing factor for the HRQOL [19]. This finding is confirmed by the data of Lailach, who obtained similar results concerning hearing using the COMOT-15 questionnaire. With 7 out of 15 items asking about the hearing situation, this questionnaire is highly overweighed concerning the hearing aspect in HRQOL in COM [20].

Based on preliminary results of very long follow up, we can carefully predict that the questions evaluating the hearing (Q3, Q4) might remain the only significant factors negatively influencing the long-term postoperative HRQOL in patients operated for cholesteatoma with the CWU-BOT. However this COMQ-12 data is only postoperative and not comparable with a preoperative score. Secondly the mean age at the moment of questionnaire completion was 28 years (range 14-32) and the mean age at the time of surgery was 11,4 years (range 6-16), so the patients were children at time of the operation and the operation was performed with a mean of 17 years before completing the questionnaire [21]. Nowadays this type of analysis could have been perfomed with the COMBI [9, 22].

In this relatively short-term study other factors than hearing are also influencing the results. Beside the presence of recurrence, myringitis or retraction pockets, patients with COM with cholesteatoma who underwent ear surgery could stay anxious to have a recurrence of disease or infection. They might be very careful not to have water contact, they might avoid dusty environment and noisy situations especially the first years after

surgery. Long-term analysis could give more information about this possible effect. We hope to report further on this in the near future.
To better understand the HRQOL – PROM of our patient, we now introduced a protocol in our clinical practice. Preoperatively, patients are asked to complete the COMQ-12. Postoperatively patients complete the COMQ-12 together with the follow up MRI at 1, 3 and 5 years postoperatively. Patients who did not complete the COMQ-12 preoperatively or who were operated before the start of our protocol are asked to complete the COMBI postoperatively at the same intervals. With this protocol we expect to obtain an improved insight in the HRQOL of our patients.

Conclusion

The COMQ-12 pre and postoperatively in patients operated for COM with cholesteatoma with the CWU-BOT technique to evaluate the HRQOL shows a clear decrease in the severity of the symptoms, life and work impact and health care between one and two years after surgery. In 50% patients became normal concerning HRQOL, the remaining 50% improved to a level very close to normal.

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APPENDIX A. Translated version of COMQ-12

Chronic Otitis Media Questionnaire–12 (COMQ-12):

Deze vragen zijn om te achterhalen hoe erg uw oorproblemen u beïnvloeden. Geen enkele machine kan dit voor u doen: enkel u kan ons dit vertellen. Wij verwachten dat de resultaten van deze vragenlijst ons helpen te begrijpen welke van uw oor symptomen het meest belangrijk voor u zijn. Deze wetenschap zal ons helpen om de wijzen waarop patiënten met oorproblemen worden verzorgd te verbeteren.Beantwoord alstublieft onderstaande vragen door zorgvuldig elke gestelde vraag te overwegen en vervolgens het geschikte cijfer te omcirkelen. De cijfers verwijzen elk naar een bepaalde beschrijving. Er zijn geen juiste of foute antwoorden, maar probeert u alstublieft goed na te denken over elke vraag voordat u het geschikte cijfer omcirkelt. Overweeg alstublieft elk probleem zoals het in de voorbije 6 maanden geweest is.

VOORBEELD:
Duid voor de volgende vraag alstublieft aan hoe vaak u deze activiteit uitvoert, gebruik makende van de onderstaande schaal en door het geschikte cijfer te omcirkelen:
0 Nooit
1 Minstens éénmaal per drie maanden
2 Minstens éénmaal per maand
3 Minstens éénmaal per week
4 De meeste dagen in de week
5 Heel de tijd
Hoe vaak eet u toast voor ontbijt? 0 1 2 3 *4* 5
Een persoon die zodanig antwoordt, geeft aan dat hij/zij gewoonlijk toast eet als ontbijt doch niet altijd.

Als u enig probleem ondervindt bij het beantwoorden van de vragen, vraag dan hulp aan een lid van de klinische staf. Dank u.
Duid voor de volgende vragen alstublieft aan hoe ernstig de verscheiden beschreven elementen u beïnvloeden, gebruik makende van de onderstaande schaal door het geschikte cijfer te omcirkelen.
0 Stoort me helemaal niet
1 Een beperkt ongemak
2 Een matig ongemak
3 Een groot ongemak maar ik kan er mee omgaan
4 Een groot ongemak en ik vind het zwaar om ermee om te gaan
5 Het ergste dat mijn leven ooit heeft getroffen

Symptoom ernst:

1. Lopend oor of drainage van het oor	0 1 2 3 4 5
2. Een 'slecht ruikend oor' hebben	0 1 2 3 4 5
3. Gehoorproblemen thuis, bv vereisend dat het volume van de TV of radio wordt opgedreven	0 1 2 3 4 5
4. Gehoorproblemen wanneer men spreekt met mensen in groepen of in lawaaierige omgevingen	0 1 2 3 4 5
5. Discomfort in en/of rondom het oor	0 1 2 3 4 5

6. Duizeligheid of gevoel van “instabiliteit” 0 1 2 3 4 5
7. Tinnitus of lawaai in het oor 0 1 2 3 4 5

Duidt u voor de volgende vragen alstublieft aan hoe vaak de verscheiden beschreven elementen u beïnvloeden, door gebruik te maken van de onderstaande schaal en door het geschikte cijfer te omcirkelen.
0 Minder frequent dan eenmaal per 6 maanden
1 Minstens eenmaal per 6 maanden
2 Minstens eenmaal per 3 maanden
3 Minstens eenmaal per maand
4 Minstens eenmaal per week
5 De meeste dagen in de week

Levensstijl en werk impact:
Hoe vaak bent u NIET in staat geweest om:
8. Uw normale dagelijkse activiteiten thuis/op het werk uit te voeren 0 1 2 3 4 5
9. U te wassen, te douchen of te baden zoals u zou willen
bv. Hoe vaak bent u angstig geweest dat deze activiteiten
een oorontsteking veroorzaken? 0 1 2 3 4 5

Gezondheidszorg impact
10. Hoe vaak bent u langsgegaan bij uw huisarts omwille van
uw oorproblemen? 0 1 2 3 4 5
11. Hoe vaak bent u genoodzaakt medicijnen in te nemen
(inclusief oordruppels) voor uw oorprobleem? 0 1 2 3 4 5

Voor de volgende vraag, duid alstublieft aan hoe erg de dingen zijn, schaal van ‘0’ tot ‘5’. ‘0’ betekent helemaal niet erg, ‘5’ betekent het ergste dat u zich ooit kan inbeelden:

Algemeen:
12. In welke mate halen uw oorproblemen u ‘onderuit’? 0 1 2 3 4 5

Controleert u alstublieft dat u een antwoord heeft geformuleerd op elke vraag en vraag om hulp indien u dit moeilijk vindt.

Heel erg bedankt om deel te nemen.

Chapter 5.3

Validity and Test-Retest Reliability of the Dutch Version of the COMBI

De Greve G*, van Dinther JJS*, Maryn Y, Vanspauwen R, Zarowski A, Offeciers E

J Int Adv Otol. 2019 Apr;15:34-7.

*both first authors contributed equally

Abstract

Objectives: We aimed to test the validity and test-retest reliability of the Dutch translation of the Chronic Otitis Media Benefit Inventory (COMBI) questionnaire.
Materials and methods: In total, 30 chronic otitis media (COM) patients with a previous ear surgery completed the questionnaire; 30 patients with a negative medical history of COM complaints and with previous non-otologic surgery as the control group completed the questionnaire. For estimating the test–retest reliability, patients of the COM group completed the questionnaire twice; the scores were compared to those of the control group to test the validity.
Results: The overall COMBI score ranged as 32–60 in the patient test group, 32–60 in the patient retest group, and 35–40 in the control group. A mean (standard deviation) score of 43.87 (6.81) in the patient test group, 44.4 (6.83) in the patient retest group, and 36.7 (1.29) in the control group was noted. Post-intervention, the COM patients had a significantly higher absolute COMBI score compared to the control group. The diagnostic accuracy was investigated, and a cut-off score of 38.5 was found to have a high sensitivity and specificity in distinguishing a significant positive change from an insignificant change after the intervention. The average-measures intra-class correlation coefficient for absolute agreement (ICCAA) was 0.985 (95% confidence interval: 0.969–0.993), indicating an excellent test–retest reliability in the control group.
Conclusion: The Dutch version of the COMBI questionnaire has a good validity, diagnostic accuracy, and test-retest reliability.

Introduction

Chronic otitis media (COM) is a prevalent disease with a serious impact on patient's overall health status, which affects approximately 2% of the population [1]. The assessment of the physical and psychosocial impact of a disease from patients' perspective has gained interest in recent years. Hence, health-related quality of life (HRQoL) measures and patientreported outcome measures (PROM) have been developed, although they are not interchangeable terms. HRQoL measures are used to assess the patient's overall health status, whereas the PROM is used for disease-specific items in addition to QoL items, thereby creating the ability to monitor the outcome of interventions.
In otology, single clinical, radiological, and audiology findings may inter-relate poorly and may also predict the HRQoL poorly. It has been shown that the use of HRQoL measures aids the patient to prioritize their symptoms and subsequently direct them to the clinical

management of their individual expectations [2, 3]. In 2014, Philips et al. [4] developed the Active COM Questionnaire 12 (COMQ-12) as a mixed generic and specific PROM. A Dutch version was developed and validated in 2015. In this study, a cut-off value between normal individuals and COM patients was established. A good validity, diagnostic accuracy, and test–retest reliability was achieved, making the COMQ-12 a useful tool in clinical evaluation studies to assess the impact of surgery on patient's complaints [5]. However, one shortcoming of COMQ-12 was its inability to evaluate the "responsiveness" after treatment as reported by Philips in 2016 in the systematic review on the role of PROM in the assessment of chronic ear diseases [6]. Therefore, in 2017, the COM Benefit Inventory (COMBI) questionnaire was developed and validated by Philips as its dynamic equivalent [7].

In analogy with our previous study, the aim of the present study was to culturally adapt the COMBI to Dutch and to obtain measures of the validity and test-retest reliability of the Dutch translation [5]. The diagnostic accuracy or the ability of the COMBI to discriminate between significant alteration and no significant alteration of a disease-specific burden (after surgical intervention) was also investigated.

Materials and methods

Firstly, the original COMBI developed by Phillips was translated by both first authors. The translation was sent to a native English-speaking person who has lived in Flanders for more the 40 years and is fluent in both English and Dutch. Secondly, this person translated the Dutch version back into English. Both original and translated English versions of the COMBI were then compared by the first authors. As no substantial differences between the two English versions were noted, it was decided to adopt the Dutch version for further scientific and clinical use (Appendix A).

The questionnaire consists of 12 questions divided into 2 categories to compare the diseasespecific burden with the pre-intervention status. The first category focuses on the severity of symptoms, whereas the second category focuses on the psychosocial impact on the lifestyle and work. The initial validation of the questionnaire has been completed, and it provides a useful dynamic tool for the assessment of COM [7]. As in the original COMBI, COM patients and the control group patients (i.e., patients without ear problems) were asked to rate the level of inconvenience or frequency of the complaints they experienced compared with the preoperative status. Each question is provided with five response options ranging between maximal amelioration and maximal deterioration, namely "much worse," "a little or somewhat worse," "no change," "a little or somewhat better," and "much better" as scores 1–5, respectively.

Study population

In total, 60 individuals were asked to complete the Dutch version of the COMBI. All the participants provided written consent. The patient group consisted of 30 patients who underwent COM surgery (such as primary or revision myringoplasty and tympanoplasty for non-cholesteatoma and cholesteatoma ears). This group comprised 15 females with a mean age of 47.2 years (standard deviation [SD]=15.0; range=21–72) and 15 males with a mean age of 46.0 years (SD=16.0; range=18–71). The patients completed the questionnaire twice at an interval of approximately 2 weeks. The first completion was achieved 6 to 12 months after the surgery. The dataset of the first completion of the COMBI (i.e., test) was called "patient test group." The dataset from the second completion was referred to as "patient retest group."

The control group consisted of 30 patients. They were selected based on a negative medical history of COM complaints and recent non-otologic surgery, such as rhinoplasty, septoconchaplasty, functional endoscopic sinus surgery, parotidectomy, tonsillectomy, or thyroidectomy. They were administered the questionnaire 2–6 months after the surgery. This group included 11 females with a mean age of 47.2 years (standard deviation [SD]=19.1; range=24–82) and 19 males with a mean age of 42.8 years [SD=16.6; range=17–72]. Patient information was de-identified for the data analysis.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) statistics version 20 (IBM Corp.; Armonk, NY, USA). For each analysis, a significance level of 5% was adopted. Various tests were used.

First, the normality of the data distribution was investigated using the one-sample Kolmogorov-Smirnov test, which showed a skewed distribution for the questionnaire scores; therefore, the non-parametric Mann-Whitney U test was used to assess the validity of the questionnaire.

To examine the diagnostic value of COMBI, several estimates of diagnostic precision were calculated: sensitivity, specificity, and the area under the receiver operating characteristics curve (A_{ROC}). The A_{ROC} statistic is interpreted as a score between 1.0 (for perfect discrimination between cases and non-cases) and 0.5 (for chance-level diagnostic accuracy). To facilitate the clinical interpretation of COMBI scores, a threshold score for distinguishing patients without a significant change after intervention from those with improvement after intervention was derived from the ROC curve.

Finally, to assess test–retest reliability, the average-measures type A intra-class correlation coefficient using an absolute agreement definition (ICC_{AA}) was calculated. Similar to other reliability coefficients, the ICC_{AA} ranged from 0.00 (i.e., total absence of reliability) to 1.00 (i.e., perfect reliability). Although there are no standard criteria for the

interpretation of ICC_{AA}, a general guideline states that values above 0.75 correspond good to excellent reliability, and values below 0.75 correspond to poor to moderate reliability [8].

An ethics committee approval was received for this study from the ethics committee of the Sint-Augustinus Hospital, GZA Antwerp. (BUN nr: B099201732917)

Results

Study Population

The overall COMBI score in the patient test group ranged as 32–60, with a mean value of 43.87 (SD=6.81). The overall COMBI score in the patient retest group ranged as 32–60, with a mean value of 44.4 (SD=6.83). The median score of the COMBI was 43 in the patient test group and 43.5 in the patient retest group. Data of both patient groups showed a normal distribution (rest group: Kolmogorov-Smirnov Z=0.144; p=0.116; retest group: Kolmogorov–Smirnov Z=0.132; p=0.195). In the control group, the overall COMBI score ranged as 35–40, with a mean value of 36.7 (SD=1.29). The median score of the COMBI was 36 in the control group. The distribution of the control group data was not normal (Kolmogorov–Smirnov Z=0.280; p=0.000). Non-parametric statistical methods were chosen based on the abnormal distribution of the data of the control group (Table 1).

Table 1. Descriptive statistics

	Number (n)	Min	Max	Range	Median	Mean	SD	SE
Patient test group	30	32	60	28	43	43.87	6.81	1.24
Patient retest group	30	32	60	28	43.5	44.40	6.83	1.25
Control group	28	35	40	5	36	36.7	1.29	0.24

Patient test group and retest group consist of patients who underwent a previous COM surgery. The control group consists of patient who underwent a non-otologic surgery.

COM: chronic otitis media; Min: minimum score; Max: maximum score; SD: standard deviation; SE: standard error

Validity

When the absolute COMBI scores of both patient groups (patient test group and patient retest group) was compared with that of the control group using the Mann-Whitney U test, the COMBI score of the COM patient was found to be significantly different from the control participants (U=110.00; p=0.000).

To determine the diagnostic accuracy of COMBI and its ability to distinguish between patient without COM and COM patients, an ROC curve was constructed (Figure 1). The value of A_{ROC} with COMBI scores as the test variable and the group (i.e., patient group=1

and control group=0) as the state variable was 0.878, which revealed high discriminatory power to distinguish significant change after intervention from insignificant change (with a statistical significance at p<0.001). The ROC curve-based Youden index was also used to identify the cut-off point that achieved the best balance between sensitivity and specificity and would provide optimal discrimination between the experimental and control groups. In this regard, a COMBI cutoff score of 38.5 produced estimates of sensitivity and specificity of 0.867 and 0.933, respectively. Therefore, using this threshold, 87% of patients were correctly classified as having a significant change, whereas 93% of patients were correctly categorized as having insignificantly change (Figure 2).

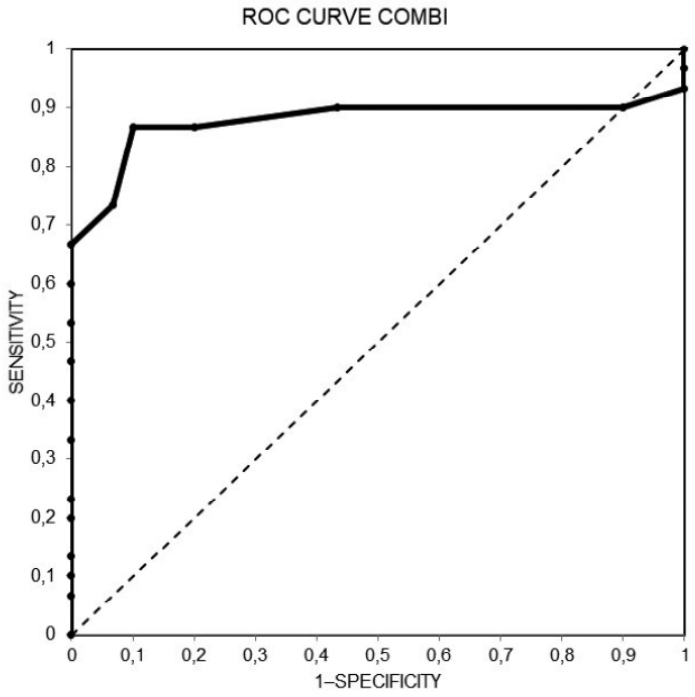

Figure 1: ROC curve. The ability of COMBI to discriminate between a significant change post-intervention from an insignificant change is represented by AROC. To facilitate the clinical interpretation of COMBI scores, a threshold of 38.5 was derived from the ROC curve.
AROC: area under the receiver operating characteristics curve; COMBI: Chronic Otitis Media Benefit Inventory

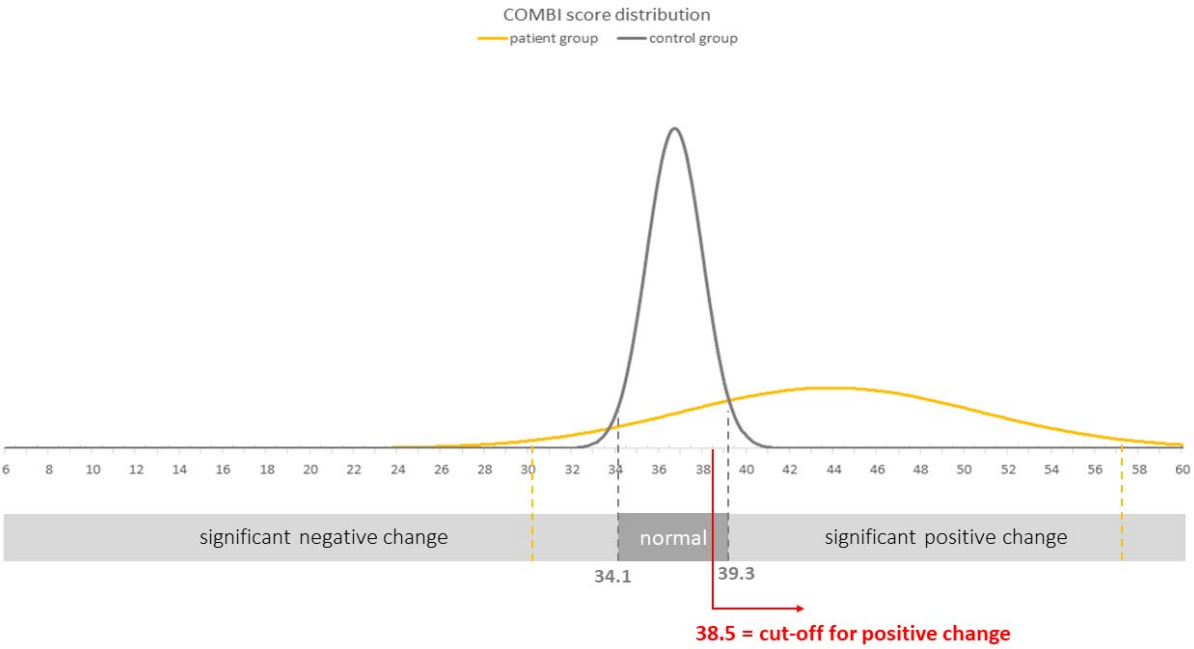

Figure 2. The COMBI score normal distribution. The overall COMBI score in the patient group (mean=43.8; SD=6.81) is significantly different from that in the control group (mean=36.7; SD=1.29). Normal scores ranged from 34.1 to 39.3 (i.e., the 95% confidence interval deducted from the data of the control group). The cut-off score for positive change is 38.5.
COMBI: Chronic Otitis Media Benefit Inventory; SD: standard deviation

Test-Retest Reliability

The average-measures of ICC_{AA} was 0.985 (95% confidence interval=0.969–0.993), which clearly exceeds the ICC threshold of 0.75 and confirms that there was excellent test–retest reliability within the control subjects.

Discussion

The measurement of patient-based perception of QoL due to their illness has become very important in healthcare. COMBI is a patient-related outcome questionnaire that has been constructed to obtain information regarding the dynamic change in the physical and psychosocial burden post-intervention. It allows a clinician to get rapidly yet a general idea of the impact of the intervention and the residual complaints that need to be managed. Therefore, its implementation is of great use in a patient follow up setting. We translated the original COMBI into Dutch and tested it for validity, diagnostic accuracy, and test–retest reliability.

The scores for the control group varied from 35 to 40, with a mean score of 36.7 (SD=1.29) and a median score of 36. A score of 36 is obtained when “zero change” is the response to all questions. Whenever responses were different from “zero change,” they

were most frequently seen with the second category of questions regarding the psychosocial impact, lifestyle, and work. This can be attributed to the generic quality of the questions.

The analysis of the diagnostic accuracy and the ability to distinguish COM from normal participants produced a cut-off score of 38.5 with reasonable sensitivity and specificity. Scores higher than 38.5 indicate a significant positive alteration post-intervention. Unfortunately, it was not possible to determine a cut-off score to indicate a significant negative alteration post-intervention because all individuals in the patient group reported an overall positive change.

The questionnaire used in this study was a Dutch translation of the original COMBI questionnaire. Although an expansion to seven response options was suggested by Phillips et al. [7] for avoiding bias in answers due to the observed ceiling effect, we chose to use a translation of the original questionnaire with five response options. Through this approach, we contributed to the ambition of multiple studies with a larger number of participants in distinct clinical populations for achieving the psychometrical appraisal of a QoL instrument [7].

Conclusion

The COMBI questionnaire is a patient-reported measurement tool with a good validity and rest-retest reliability, which aims at obtaining a dynamic evaluation of physical and psychosocial impact in COM patients after intervention. A cut-off score to distinguish a significant positive change from an insignificant change post-intervention was determined. A cut-off score to distinguish a negative change could not be determined in our study. The COMBI questionnaire is a useful tool complementary to the COMQ-12 in daily clinical practice.

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Appendix A

Onderstaande vragen zijn om te achterhalen hoe erg uw oorproblemen u beinvloeden in vergelijking met de situatie voor de operatie/behandeling. Geen enkele machine kan dit voor u doen: enkel u kan ons dit vertellen. Wij verwachten dat de resultaten van deze vragenlijst ons helpen om te begrijpen welke klachten voor u onvoldoende positief gewijzigd zijn. Deze wetenschap zal ons helpen om de wijze waarop patienten met oorproblemen worden verzorgd te verbeteren.

Beantwoord alstublieft onderstaande vragen zorgvuldig door elke gestelde vraag te overwegen en vervolgens het geschikte cijfer te omcirkelen.
De cijfers verwijzen elk naar een bepaalde beschrijving die eronder vermeldt staat. Er zijn geen juiste of foute antwoorden, maar probeert u alstublieft goed na te denken over elke vraag voordat u het geschikte cijfer omcirkelt.

Ernst van de symptomen

1. Sedert uw operatie/behandeling, is uw oorloop of drainage van uw oor verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

2. Sedert uw operatie/behandeling , hoe zou u de verandering beschrijven in het hebben van een ‘slecht ruikend oor’? Is dit verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

3. Sedert uw operatie/behandeling, is uw gehoor thuis (bijv. de televisie of de radio luider moeten zetten) verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

4. Sedert uw operatie/behandeling, is uw gehoor wanneer u met anderen in groep spreekt (of wanneer u in een lawaaierige omgeving bent) verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

5. Sedert uw operatie/behandeling, is het discomfort in en/of rond het oor verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

6. Sedert uw operatie/behandeling, is uw duizeligheid of uw gevoel van ‘instabiliteit’ verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

7. Sedert uw operatie/behandeling, is uw tinnitus of lawaai in het oor verbeterd of verslechterd?

5	4	3	2	1
Veel beter	Een beetje beter	Onveranderd	Een beetje slechter	Veel slechter

Gevolgen voor levensstijl, werk en gezondheidszorg

8. Betreffende uw gewone dagelijkse activiteiten thuis en op het werk, zou u zeggen dat u meer problemen of minder problemen ondervindt, sedert uw operatie/behandeling?

5	4	3	2	1
Veel meer problemen om activiteiten uit te voeren	Meer problemen om activiteiten uit te voeren	Onveranderd	Meer problemen activiteiten uit te voeren	Veel minder problemen om activiteiten uit te voeren

9. Betreffende de mogelijkheid om u te wassen of te douchen of te baden zoals u zelf zou willen sedert uw operatie/behandeling, hebt u dan meer angst of minder angst om een oorontsteking te krijgen door deze activiteiten?

5	4	3	2	1
Veel meer angst dat het oor nat wordt	Meer angst dat het oor nat wordt	Onveranderd	Minder angst dat het oor nat wordt	Veel minder angst dat het oor nat wordt

10. Sedert uw operatie/behandeling, bent u vaker of minder vaak naar uw huisarts gegaan omwille van uw oorproblemen?

5	4	3	2	1
Veel vaker	Vaker	Onveranderd	Minder vaak	Veel minder vaak

11. Sedert uw operatie/behandeling, heeft u vaker of minder vaak medicijnen (met inbegrip van oordruppels) moeten nemen voor uw oorprobleem?

5	4	3	2	1
Veel vaker	Vaker	Onveranderd	Minder vaak	Veel minder vaak

Algemeen

12. Sedert uw operatie/behandeling, bent u meer of minder ‘onderuit gehaald’ door uw oorprobleem dan ervoor?

5	4	3	2	1
Veel meer dan voorheen	Meer dan voorheen	Onveranderd	Minder dan voorheen	Veel minder dan voorheen

Heel erg bedankt om deel te nemen.

Chapter 6

Supporting Surgical Techniques in Cholesteatoma Surgery

Chapter 6.1

The M-meatocanalplasty: a Modification of the M-meatoplasty to Address the Superior Quadrants and the Bony Canal

van Dinther JJS, Zarowski A, Somers T, Offeciers E
Eur Arch Otorhinolaryngol. 2017 Sep;274:3291-3.

Abstract

The meatoplasty of the external auditory canal is a frequently performed otologic procedure in recurrent otitis externa, eczema or frequent accumulation of cerumen due to a narrow meatus of the external ear canal. Numerous surgical techniques have been described. The M-meatoplasty described by Mirck for addressing the external meatus is widely used. However, this technique does not sufficiently enlarge the external ear canal in all cases. Specifically in patients where the ear canal narrowing is most prominent in the postero- and/or anterosuperior quadrants of the lateral meatus the technique needs some modifications. In these cases, an oblique conversion of the M-meatoplasty, the MO-meatocanalplasty, is useful. In cases where the bony canal is also narrow this modification allows for a bony canalplasty while avoiding a retro-auricular approach. The MO-meatocanalplasty can be used in combination with myringoplasty and tympanoplasty.

Introduction

The meatoplasty of the external auditory canal is a frequently performed otologic procedure. Indications include recurrent otitis externa refractory to medical treatment, eczema and/or frequent accumulation of cerumen due to a narrow meatus of the external ear canal. In canal wall down surgery for chronic otitis media it is an essential step to achieve a dry and easily cleanable cavity. Numerous surgical techniques have been described on how to do a meatoplasty [1,2]. In our department, we used to perform the M-meatoplasty technique, described by Mirck [3]. This procedure has proven to be easy to perform, adjustable to the individual patient, efficient and aesthetically acceptable [4].

However, in several cases, we found that the M-meatoplasty did not sufficiently enlarge the external ear canal. This is specifically the case in patients where ear canal narrowing was most prominent in the postero- and/or anterosuperior quadrants of the lateral meatus and/or when a bony canalplasty was necessary. In the present report, we describe the modification of the M-meatoplasty to the MO-meatocanalplasty to adequately address meatal and canal narrowing in these difficult cases.

Materials and methods

Surgical technique

The surgical procedure can be done under local or general anaesthesia using an operating microscope. The cavum concha and the lateral part of the external meatus are infiltrated with a 2% xylocaine 1:100.000 epinephrine solution. The tragus and antitragus are retracted using a silk 4-0 suture, if they block direct visualisation of the external meatus.

Part of the incision is identical to the Mirck M-meatoplasty [3]. A semilunar incision along the border of the external meatus is made from the 6 o'clock position to the 12 o'clock position, overlying the anterior rim of the conchal cartilage (Fig. 1a: dashed line from A via B to C). A V-incision is then made in the skin of the cavum conchae, with the point of the V directed anteriorly (Fig. 1a: dashed lines from D to B, and from E to B). This creates three triangular flaps (Fig. 1b: nr. 1, 2 and 3). The flaps are dissected away from the underlying cartilage, from point to base. The base remains fixed to the cartilage. The free points are then everted outward by subcutaneously inserting a silk 4-0 suture in the point of the flaps. The superior suture is lead over the helix, the middle suture straight back and the inferior suture around the lobule. The sutures are weighted down backward by mosquito clamps, thus keeping the triangular flaps away from the exposed conchal cartilage. Subsequently, conchal cartilage and subcutaneous tissue are widely excised using a Beaver blade and monopolar electrocoagulation (Fig. 1c).

The following stages are different from the technique described by Mirck [3]. Instead of incising the external auditory canal skin longitudinally towards the lateral margin of the bony canal, the semilunar incision is extended superiorly to create a smooth curve running medially and towards the anterosuperior part of the bony external auditory canal (Fig. 1c: line from C via F to G). This oblique incision can be modified depending on the need for a bony canalplasty and/or the need for addressing anterior collapse of the external auditory canal and is made from G via F to C with a backcut from G to H. Part 1 (M-meatoplasty) and part 2 (MO-meatocanalplasty) of the incision are often made in one go, in order to make it a smooth continuum (if performed in one go it is easier to go from G via F, C and B to A with a back cut from H to G followed by the triangular flaps). The oblique part of the incision is not made perpendicular to the skin surface, but oblique through the soft tissue (Fig. 1e, f: *). This allows to dissect away the superfluous subdermal soft tissue causing the narrowing of the superior meatus, while leaving a thin layer of soft tissue covering the bone (Fig. 1e: **o**). This avoids leaving denuded bone in the superior part of the canal. It is important to keep the skin surface intact when thinning it down to the required thickness during this stage. Quite often a cartilaginous extension needs to be cut out posteriorly, where the skin is attached to the posterior bony canal. To facilitate the rotation of the skin flap, its medial connection to the bony canal can be

freed by a back cut from anterosuperior to posterosuperior (Fig. 1a, e: from point G to H). This allows the skin flap to rotate more easily outwards. The need for and size of this back cut depends on skin tension while rotating the flap. The flap can then be fitted to the initial external skin incision. The inferior and posterior triangular flaps are removed (Fig. 1c: nr. 3 and 2) and the inferior-based meatal flap is sutured to the conchal skin using absorbable 4-0 sutures (Fig. 1e: from A via D to E). The superior triangular flap is rotated medially and sutured and/or glued (Fig. 1e: nr. 1). The free triangular skin flaps (Fig. 1f: nr. 2 and 3) can be used, after thinning, to cover any remaining bare bone in the canal. They are glued in place with tissue glue.

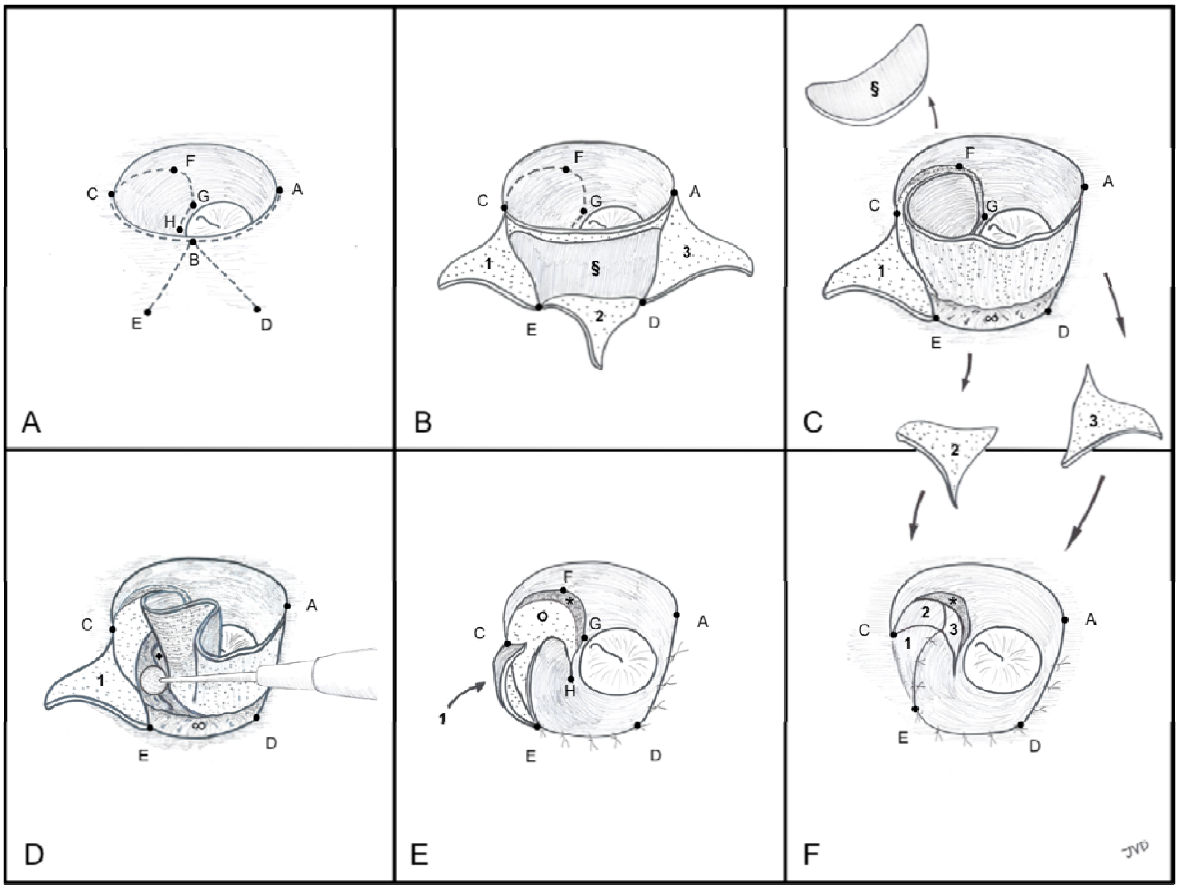

Figure 1. The surgical steps of the MO-meatocanalplasty. **a** Planning of the incisions: semilunar incision from *A* via *B* to *C*; *V-shaped* incision from *D* to *B* and from *E* to *B*; oblique incision from *C* via *F* to *G*; back cut incision from *G* to *H*. **b** Creation and eversion of three *triangular flaps* (nr. 1–3) with conchal cartilage exposure (*section sign*). **c** Conchal cartilage and subcutaneous tissue removal; oblique incision from *G* via *F* to *C*; back cut incision from *G* towards *H*; producing, thinning and fitting of the inferiorly based skin flap; removal of the inferior and posterior *triangular flaps*. **d** Bony canalplasty. **e** Rotation, fitting and suturing of the inferiorly based meatal flap to the conchal skin; medial rotation and suturing of the superior triangular skin flap (nr. 1). **f** Closing of the remaining skin defect with the free triangular skin flaps (nr. 2 and 3)

This technique leads to significant widening of the meatus and lateral external auditory canal (Fig. 1f). The wide exposure of the superior, posterior and inferior bony canal also allows for performing a bony canalplasty if needed while avoiding a retro-auricular approach (Fig. 1d).

The packing of the external auditory canal is done by means of a cylindrical multiperforated plastic sheet, filled with synthetic sponges soaked in an antibiotic-steroid ointment to expand the cylindrical bandage. The bandage is removed 2 weeks after surgery in the outpatient clinic. Followed by the removal of the packing the external auditory canal is further treated with the suspension version of the same antibiotic steroid ointment until the complete healing of the skin.

Discussion

The reported modification of the M-meatoplasty to the MO-meatocanalplasty can be used to achieve adequate meatal and/or canal widening in patients where additional narrowing is present in the superior quadrants of the lateral meatus and/or when bony canal widening is necessary while avoiding a retro-auricular approach. In our centre, this type of meatocanalplasty is used in a significant part of the canal wall up bony obliteration tympanoplasty (CWU-BOT) patients if a narrow meatus or canal is present, especially in the paediatric cholesteatoma patient population [5]. This procedure can be performed as a first-stage procedure in patients with severe chronic otitis media and narrowing of the lateral meatus and/or canal before performing the CWU-BOT. We believe that the described technique not only improves the per-operative visualisation and the postoperative healing and aftercare. The MO-meatocanalplasty may also result in a lower incidence of delayed epithelialisation of the tympanic graft, persistent myringitis, or granulation tissue formation. In cases with a milder narrowing of the meatus and/or canal, the procedure can be combined with the CWU-BOT during the same procedure. In case of delayed epithelialisation or myringitis following any type of myringoplasty or tympanoplasty, this technique can be performed as a second-stage procedure.

Conclusion

The MO-meatocanalplasty is a useful modification of the widely used M-meatoplasty for the narrow meatus and external auditory bony canal while avoiding a retro-auricular approach.

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Chapter 6.2

The MO-meatocanalplasty: Long-Term Results in the Narrow External Auditory Canal with Recurrent Otitis Externa or the Inability to Wear a Hearing Aid

De Greve G*, van Dinther JJS*, Vanspauwen R, Maryn Y, Verstreken M, Zarowski A, Offeciers E

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*Both first-authors contributed equally

Abstract

Objective: The MO-meatocanalplasty is the oblique modification of the M-meatoplasty. The MO-meatocanalplasty was designed to address the superior quadrants of the meatus and the bony canal without the need for a retro-auricular incision. This retrospective analysis was performed to evaluate the long-term results of the MO-meatocanalplasty in patients with a narrow external auditory canal (EAC) with recurrent otitis externa or in patients unable to wear a hearing aid.

Methods: Twenty-two ears in twenty consecutive patients who received a MO-meatocanalplasty for a narrow EAC with recurrent otitis externa or the inability to wear a hearing aid were analysed retrospectively. There were no patients included with any type of previous or planned second stage tympanoplasty procedures. A follow up period of 3 years was analysed for post-operative recurrent narrowing, the self-cleaning capacity of the EAC, the recurrence of otitis externa, the inability to wear a hearing aid, change in hearing level and for all types of esthetical complaints.

Results: The MO-meatocanalplasty procedure was effective in 81,8% (n=18). Post-operative recurrent narrowing was detected in 9,1% (n=2). Insufficient self-cleaning capacity of the EAC was 9,1% (n=2). The ability to wear a hearing aid was restored in all patients with the need for a hearing aid. No esthetical complaints were reported.

Conclusion: The MO-meatocanalplasty is an effective, safe and esthetical accepted procedure to address the narrow meatus and external auditory canal. With this procedure, there is no need for a retro-auricular incision in order to create a well aerated, dry and self-cleaning EAC in patients with a narrow EAC with recurrent otitis externa or in patient with the inability to wear a hearing aid.

Introduction

The meatoplasty of the external auditory canal (EAC) is a frequent otologic procedure which aims to create a sufficient widened and well-aerated EAC. Indications include narrow EAC with recurrent otitis externa, therapy resistant eczema, frequent cerumen accumulation or inability to wear a hearing aid. The meatoplasty is also an essential part in canal wall down mastoidectomy for chronic otitis media to create a dry and easy cleanable cavity. The Modified Oblique (MO)-meatocanalplasty was introduced as a useful modification to the M-meatoplasty to address the posterosuperior or anterosuperior quadrants of the lateral meatus while avoiding a retro-auricular approach.[1, 2] The aim of this study is to report the long term results of the MO-

meatocanalplasty in the narrow EAC with recurrent otitis externa or in patients unable to wear a hearing aid.

Materials and methods

Data collection

This study was performed in our tertiary referral centre. Data was collected retrospectively and pseudonymised for analysis. All patients who received a MO-meatoplasty for recurrent otitis externa or inability to wear a hearing aid with a follow up period of at least three years at our department were included. Patients with any type of previous or planned second stage tympanoplasty procedures were excluded to avoid influence of chronical otitis media symptoms. Selected outcome measures were recurrent narrowing, the self-cleaning capacity of EAC, ability to wear a hearing aid, change in pure tone average hearing level and all types of esthetical complaints.

Surgical technique

Informed consent was obtained preoperatively after detailed discussion of potential short term and long-term complications including post-operative wound infection, bleeding, recurrent narrowing, stenosis, recurrence of otitis externa and hearing loss. The operation was carried out under general anaesthesia or local anaesthesia using an operating microscope. No prophylactic antibiotic was given. Povidone-iodine 10% solution was used as local antiseptic agent. A 2% xylocaine with epinephrine 1:100.000 solution was infiltrated at the cavum concha and the lateral part of the external meatus. The tragus and the antitragus were retracted with a silk 4/0 suture for optimal exposure of the EAC. Incision identical to M-meatoplasty was made, i.e. a semilunar incision along the border of the external meatus from the 6 o' clock position to 12 o'clock position and a V-incision at the skin of the cavum conchae (Fig. 1a: dashed line from A via B to C, dashed lines from B to D, and from B to E). Three triangular skin flaps were created by separating the skin from the underlying cartilage. The base remained fixed to the cartilage (Fig. 1b: nr. 1, 2 and 3). The free apices of the three skin flaps were everted with a silk 4/0 suture placed subcutaneously to expose the underlying soft tissue and conchal cartilage. Wide excision of the cartilage was performed using a Beaver blade and a thin monopolar electrocauterization tip. Subsequently, the semilunar incision was extended superiorly to create a smooth curve running medially and toward the anterosuperior part of the bony EAC (Fig. 1c: dashed line from C via F to G). This incision was made oblique through the soft tissue (Fig. 1e,f: *) and could be adjusted according to the need for a bony canalplasty addressing anterior narrowing of the EAC. Progressive thinning of the EAC skin

and removal of underlying soft tissue until the posterior bony EAC was reached (Fig. 1c). A bony canalplasty with a diamond burr could be performed when needed (Fig. 1d) The inferior and posterior triangular skin flaps were removed and preserved for transposition at a later stage (Fig. 1c: nr. 2 and 3). The inferior-based meatal skin flap was sutured to the conchal skin using absorbable 4/0 sutures (Fig. 1e: from A via D to E). The superior triangular flap was rotated medially and sutured to the meatal skin (Fig. 1e: nr.1). After thinning of the free triangular skin grafts, they could be used to cover possible remaining denuded bone or soft tissue of the EAC (Fig. 1f: nr. 2 and 3). These flaps were fixated with tissue glue. Packing of the EAC was done by means of a cylindrical multiperforated plastic sheet, filled with synthetic sponges soaked in an antibiotic-steroid ointment to expand the cylindrical bandage. This packing was removed after 2 weeks at the outpatient clinic. Further treatment includes applying suspension of the same antibiotic-steroid agent in the EAC until the skin was completely healed (Figure 2). [1] Additional illustrative visual material can be found in Online Resource 1.

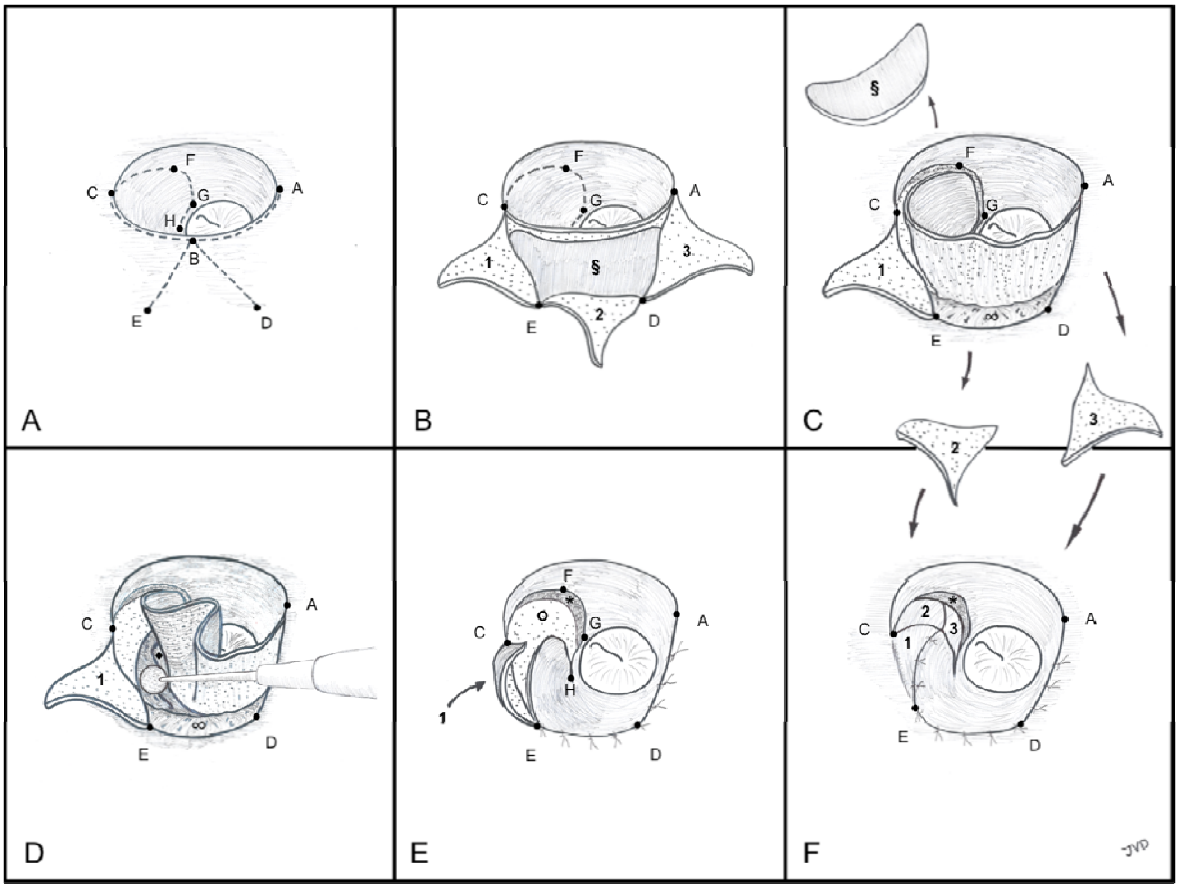

Figure 1. Surgical steps of Modified Oblique-meatocanalplasty.

Table 1. Patient characteristics

Case No.	Sex	Age (y)	Side	Indication	Recurrent narrowing	Self-cleaning EAC	Recurrent OE	Hearing Level (Δ db HL PTA)	Hearing aid	Esthetical complaint	
1	F	52	L	Inability to wear HA	No	+	No	-7	+	No	
2	F	24	R	Rec otitis ext	No	+	No			No	
3	F	41	L	Rec otitis ext	No	+	No			No	
4	F	41	L	Rec otitis ext	No	+	Yes			No	
5	M	34	R	Rec otitis ext	No	+	No			No	
6	M	59	R	Rec otitis ext + Inability to wear HA	No	+	No	+8	+	No	
7	M	14	L	Rec otitis ext	No	+	No	+3		No	
8	F	18	L	Rec otitis ext	No	+	Yes	-2		No	
9	F	66	L	Inability to wear HA	No	+	No	-2	+	No	
10	F	19	R	Rec otitis ext	No	+	No	0		No	
11	M	63	L	Inability to wear HA	No	+	No	-2	+	No	
12	M	15	R	Rec otitis ext	No	-	Yes	-10		No	
13	M	36	L	Rec otitis ext	Yes	+				No	Revision surgery
14	F	33	L	Rec otitis ext	No	+	No			No	
15	M	61	L	Rec otitis ext	No	+	No	-8		No	
16	F	52	R	Rec otitis ext	No	+	No	+2		No	

17	F	15	L	Rec otitis ext	Yes	-		-15		No	Revision surgery
18	F	20	L	Rec otitis ext	No	+	No	+2		No	
19	F	18	L	Rec otitis ext	No	-	No	-3		No	
20	M	45	L	Rec otitis ext	No	+	No			No	
21	M	58	R	Rec otitis ext	No	+	No	0		No	
22	F	28	L	Rec otitis ext	No	+	No	-7		No	

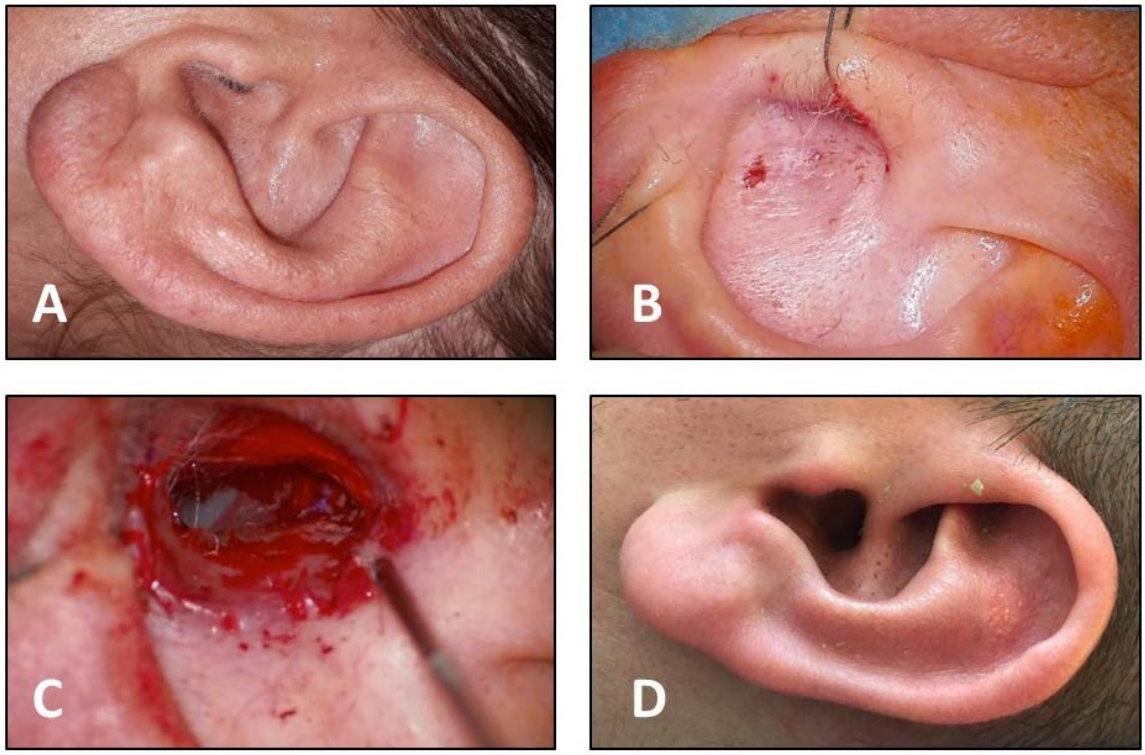

Figure 2. Panel A: Pre-operative view of EAC; Panel B: View of EAC immediately before incision; Panel C: View of EAC at the end of the procedure; Panel D: Post-operative view of EAC after several months.

Results

In total, 22 ears in 20 patients were surgically treated between 2009 and 2015 (Table 1). Data was analysed retrospectively. There were fourteen females with a mean age of 35 years [standard deviation (SD)= 17.3; range= 14-66] and eight men with a mean age of 42 years [SD = 18.9; range = [15-63]). The MO-meatocanalplasty was performed in eighteen patients for recurrent otitis externa, in three patients for inability to wear hearing aids and in one patient for recurrent otitis externa with inability to wear a hearing aid. All surgeries were performed under general anaesthesia in our cohort.

Post-operative recurrent narrowing of the EAC was found in 2 out of 22 patients (9,1%). In the first case postoperative healing was complicated by excessive granulation tissue at the meatal incision. Revision surgery 3 months after the first procedure showed excessive fibrous tissue at the level of the lateral border of the external meatus. In the second case, initial postoperative healing was uncomplicated. Follow up at 6 months showed recurrent narrowing of lateral external meatus. Revision surgery was performed 1 year and 9 months after the first procedure. Additional excision of conchal cartilage and bony

canalplasty was performed. In both cases revision MO-meatocanalplasty was performed in combination with skin grafts to cover denuded bone of the EAC. Based on our satisfying results in ears with acquired atresia we used split-thickness skin grafts harvested from the retro-auricular region. Further follow up showed no recurrence of narrow EAC or otitis externa in the first two years postoperatively.

Insufficient self-cleaning capacity of EAC was found in 2 out of 21 patients (9,1%). These patients still suffered from recurrent otitis externa despite surgery. They need follow up with regular cleaning of the EAC.

Postoperatively, we observed a mean improvement in air-conduction pure tone average (PTA) of 2,1 decibels hearing level (dB HL) (SD=7.1; range= [(-22)-8]), which is statistically not significant according to the Wilcoxon Signed Rank Test (p=0.261).

In none of the twenty-two cases esthetical complaints were reported (Figure 2D). Complications such as tympanic membrane perforation, facial nerve paralysis, exposure of the temporomandibular joint or inclusion cholesteatoma of the EAC were not reported. Hearing aids were well tolerated postoperatively in all patients with inability to wear a hearing aid prior to surgery.

Discussion

For decades, the meatoplasty is performed to tackle chronic otitis externa resistant to medical treatment. Literature on combined meatocanalplasty is scarce. The aim of this retrospective study was to report and analyse the long-term results of the MO-meatocanalplasty in narrow EAC with recurrent otitis externa or inability to wear a hearing aid. This procedure is frequently associated with surgery for chronical otitis media with cholesteatoma.[3] To exclude influence of chronic otitis media disease and its surgical treatment, we excluded those cases from our study.

The safety of this procedure is demonstrated by a low postoperative recurrent narrowing rate of 9,1% and the absence of any significant hearing loss. Postoperative wound infection was documented in 3 patients (13,6%) and treated with topical or systemic antibiotics. Only one out of these three patients presented with an episode of recurrent otitis externa on the long-term, the other two patients were without any infection up to now. Other complications such as tympanic membrane perforation, exposure of the temporomandibular joint or inclusion cholesteatoma of the EAC were not reported in our cohort.

The risk of recurrent narrowing is minimised by using the oblique incision in combination with free triangular skin flaps. This allows the meatal skin flap to be rotated and sutured to the meatal external skin incision whilst avoiding troublesome circumferential traction.

Furthermore, we might not underestimate the importance of meticulous packing of the EAC for two weeks postoperatively as well as accurate surveillance during the first months of follow up.

The MO-meatocanalplasty allows for bony canalplasty in an elegant way. A retro-auricular incision is avoided and thus possible complications, however scarce in this region, are prevented. Additionally, no esthetical complaints were reported in our cohort.

The importance of canalplasty was advocated by Paparella in 1981 and is confirmed by many others ever since.[4, 5] Recently van Spronsen et al. (2018) were able to provide evidence for a significant relationship between the shape of the bony EAC and recurrent or chronic otitis media.[6] When widening of the EAC leads to areas of denuded bone, free split-thickness skin grafts can be used to cover these areas.[4, 7]

Although the literature is scarce on the possible area of denuded EAC bone for subsequent secondary healing, we observed that the risk for stenosis and delayed healing time is reduced by using split-thickness skin grafts. The complete covering of the bony EAC is aimed for at the end of this surgery which in some cases, for instance in revision surgery, leads to the additional use of a free split-thickness skin graft harvested from the retro-auricular region.

We observed that the MO-meatocanalplasty was effective in 81,8% which is in concordance with the literature.[8] In healthy ears the self-cleaning capacity is the result of the combination of first the lateral epithelial migration of the skin of the osseous EAC and second a sufficient patency at the level of the meatus.[9] In our cohort no meatal stenosis or recurrent meatal narrowing was reported in the cases that presented with insufficient self-cleaning capacity of the EAC and recurrence of otitis externa. Therefore, accumulation of debris in the EAC might have been due to insufficient lateral epithelial migration. Whether this is the cause or effect of a long history of recurrent otitis externa is not known.

This small retrospective series comprises a homogenous group as a limited amount of indications were selected for this study. About the effect of meatocanalplasty in these conditions, little is published. We deliberately excluded patients with previous or planned second stage tympanoplasty as we aimed to extract the effect of the MO-meatocanalplasty on the state of the EAC, however much more experience with performing this technique in combination with the canal wall up bony obliteration tympanoplasty for chronical otitis media with cholesteatoma in children and adults is gained. In these tympanoplasty cases we observed a significant improved preoperative and postoperative visualisation of the tympanic membrane and middle ear structures, postoperative healing and aftercare.[3]

Prospective studies with standardised pre- and post-operative documentation of objective clinical outcome measures and subjective patient reported outcome measures

are needed to provide more evidence on the added value of the meatocanalplasty as well as to compare different surgical techniques. For example: the healing time; pre- versus post-operative size of the meatus (largest possible ear speculum); self-cleaning capacity of the EAC (need and/or interval for suction cleaning); the frequency of outpatient clinic visits; the visibility of the tympanic membrane quadrants including the anterior annulus; the frequency of otitis externa; and the presence of complications; are useful clinical outcome measures. Subjective patient reported outcome measures (PROMs) could be obtained through a questionnaire similar to the Chronic Otitis Media Questionnaire 12 (COMQ-12) and the Chronic Otitis Media Benefit Inventory (COMBI) to assess patient satisfaction and possibly quality of life, or in the latter responsiveness to treatments like MO-meatocanalplasty.[10-14] Such a questionnaire should at least cover possible esthetical complaints and the self-reported ability to wear a hearing aid.

Conclusion

The MO-meatocanalplasty is an effective, safe and esthetical accepted procedure to address the narrow meatus and external auditory canal to create a well aerated, dry, self-cleaning EAC in narrow EAC with recurrent otitis externa and/or inability to wear a hearing aid. Overall, analysis of relatively long-term results showed a low rate of postoperative recurrent narrowing (4,8%) and a low rate of recurrent otitis externa (9,5%). No significant hearing loss, esthetical complaints or other complications were reported.

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Chapter 6.3

Subarcuate Supralabyrinthine Approach for Supralabyrinthine Petrosal Cholesteatoma

van Dinther JJS, Vercruysse JP, De Foer B, Somers T, Zarowski A, Casselman J, Offeciers E

Ann Otol Rhinol Laryngol. 2010 Jan;119:42-6.

Abstract

Congenital cholesteatomas of the petrosal apex account for 1% to 3% of all cholesteatomas and often present an important surgical challenge. This report describes an exceptional case of a “nondestructive” translabyrinthine surgical approach to a large congenital petrosal cholesteatoma that threatened the vestibulum, superior semicircular canal, facial nerve, and internal auditory canal. We applied a nonconventional transmastoid subarcuate supralabyrinthine approach in a 20-year-old patient by accessing the lesion through the center of the superior semicircular arch without damaging the integrity of the canal. This led to a complete removal of the petrosal cholesteatoma with preservation of hearing and vestibular function. Follow up imaging performed 1 and 2 years after operation by means of non–echo-planar diffusionweighted imaging did not show residual cholesteatoma. This report describes the first successful use of a subarcuate supralabyrinthine approach through the arches of the superior semicircular canal in a case of petrosal cholesteatoma.

Introduction

Petrosal cholesteatomas, defined by the presence of cholesteatoma medial to the otic capsule, comprise both congenital and acquired cholesteatomas,(1) and account for 4% to 9% of all petrous lesions.(2,3) Petrosal cholesteatomas often present a difficult diagnostic and surgical challenge because of their relation to important structures (eg, cochleovestibular labyrinth, facial nerve, internal carotid artery, jugular bulb, and brain stem). In only a small number of petrosal cholesteatomas — most frequently, the supralabyrinthine type with limited extension — can hearing preservation be considered.(4-6) To eradicate supralabyrinthine petrosal cholesteatomas, the subtotal petrosectomy provides the best access to the petrosal apex, but it sacrifices hearing. The hearing will also be sacrificed by a (modified) transcochlear approach and will potentially be affected by a trans–superior semicircular canal (SSC) supralabyrinthine approach.(7) In contrast, the middle cranial fossa approaches potentially allow hearing preservation, but they necessitate a craniotomy, with the ensuing potential comorbidity (eg, bleeding, headache).(8) Moreover, a middle fossa approach can limit the access to the space above the vestibule just me dial to the SSC. The surgical removal of a congenital supra laby rinthine petrosal cholesteatoma, as reported in our case, extending medial to the SSC and eroding the roof of the vestibule, is therefore quite a challenging task if the secondary goal is hearing preservation.

Suspicion of a petrosal cholesteatoma with destruction according to a computed tomography (CT) scan can nowadays be unequivocally confirmed by use of magnetic resonance imaging (MRI) non– echo-planar diffusion-weighted imaging (non–echoplanar DWI) sequences.(9-14) This MRI sequence has become the gold standard in our department for the preoperative workup and follow up of cholesteatoma. Documentation of the extension and the associated labyrinthine and/or intracranial invasion of a petrosal cholesteatoma is crucial to deciding on the surgical approach.

Case report

Medical History

A 20-year-old woman was referred to our otolaryngology and radiology departments for the diagnostic workup of a large residual cholesteatoma on the left side. At first surgery, performed elsewhere 2 years before, this large cholesteatoma fulfilled all of the Derlacki criteria1 for a congenital petrosal cholesteatoma. Otomicroscopic examination prior to revision surgery showed the presence of a dry perforation of the posterosuperior quadrant of the tympanic membrane. Preoperative audiometric evaluation showed a left-sided conductive hearing loss with an air-bone gap of 48.3 dB hearing level (HL) on pure tone average (PTA) frequencies (500, 1,000, and 2,000 Hz). The bone conduction thresholds were normal (Fig 1). The contralateral ear was normal.

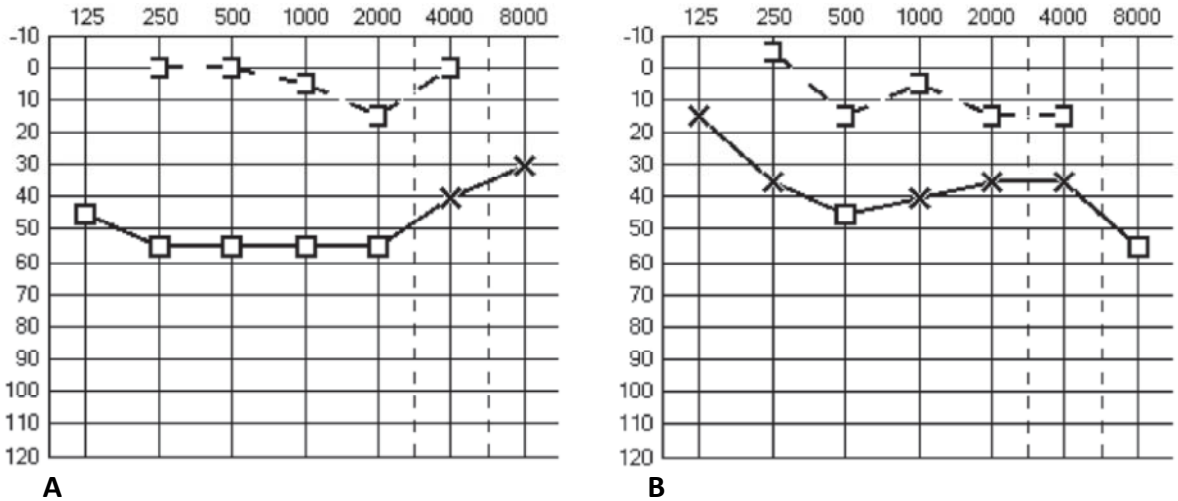

Figure 1. **A)** Preoperative and **B)** 12-month postoperative air and bone conduction thresholds of operated ear. Note preservation of inner ear function and 15-dB gain in air conduction thresholds (pure tone average).

Imaging

A high-resolution CT scan performed before revision surgery revealed the presence of a large eroding soft tissue mass filling the mastoidectomy cavity. The lesion eroded the

tegmen tympani, destroyed the bony layer covering the geniculate ganglion and the labyrinthine segment of the facial nerve, reached the internal auditory canal, and presumably caused fistulization of the SSC and the vestibule (Fig 2). Use of MRI, including standard sequences, late gadolinium-enhanced T1-weighted images, and non–echo-planar DWI,(9-14) confirmed the suspicion of a large cholesteatoma involving the petrosal apex (Fig 3). T2-weighted MRI showed normal enhancement of the membranous part of the labyrinth and cochlea, indicating the lack of an existing layer of reactive fibrous tissue that could protect the inner ear function at the moment of surgical excision of the cholesteatoma.

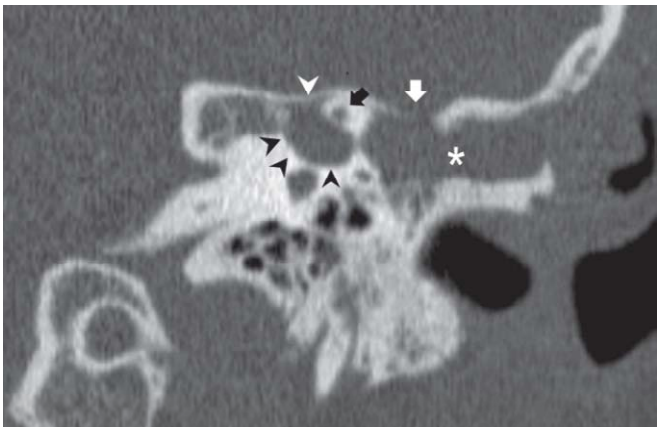

Figure 2. Preoperative coronal reformatted high-resolution computed tomographic image of left ear shows large eroding soft tissue mass filling mastoidectomy cavity (asterisk) and breaching tegmen tympani (white arrow). Supralabyrinthine extension of cholesteatoma (white arrowhead) has eroded vestibule (black arrowheads) and arch of superior semicircular canal (black arrow).

Surgical Aspects

Surgical revision comprised a conventional canal wall–up technique with wide posterior tympanotomy. The cholesteatoma, which filled the complete mastoidectomy cavity, extended laterally, superiorly, and medially to the SSC via supralabyrinthine extension. The facial nerve was nearly completely exposed from its tympanic segment up to the level of the geniculate ganglion and the labyrinthine segment. After partial resection of the lateral part of the cholesteatoma, the SSC was identified by carefully delineating its bony capsule.

In order to respect the integrity of the labyrinth (ie, SSC), we performed a subarcuate supralabyrinthine approach (SaSLA) by accessing the lesion through the center of the SSC arch without damaging the integrity of the canal, progressively following the subarcuate cell tract medially, resulting in an “eyeshaped” structure (Fig 4). Subsequently, the anterosuperior border of the SSC was defined by following the cholesteatoma and the superior prelabyrinthine cell tracts to the medial side of the SCC. In this manner, the cholesteatoma was progressively pushed out through the arch of the SSC (the “eye”) in

the lateral direction. A bony breach of the inner part of the anterior leg of the SSC and the roof of the vestibule were identified, and the fibrous delineation of the SSC remained intact throughout the dissection. After complete eradication of cholesteatoma, the external ear canal wall was reconstructed and the bony obliteration technique was applied.(15,16) The tympano-ossicular reconstruction was performed with an allograft tympanic membrane and malleus handle in one piece with interposition of a sculpted allograft malleus between the malleus handle and the footplate.

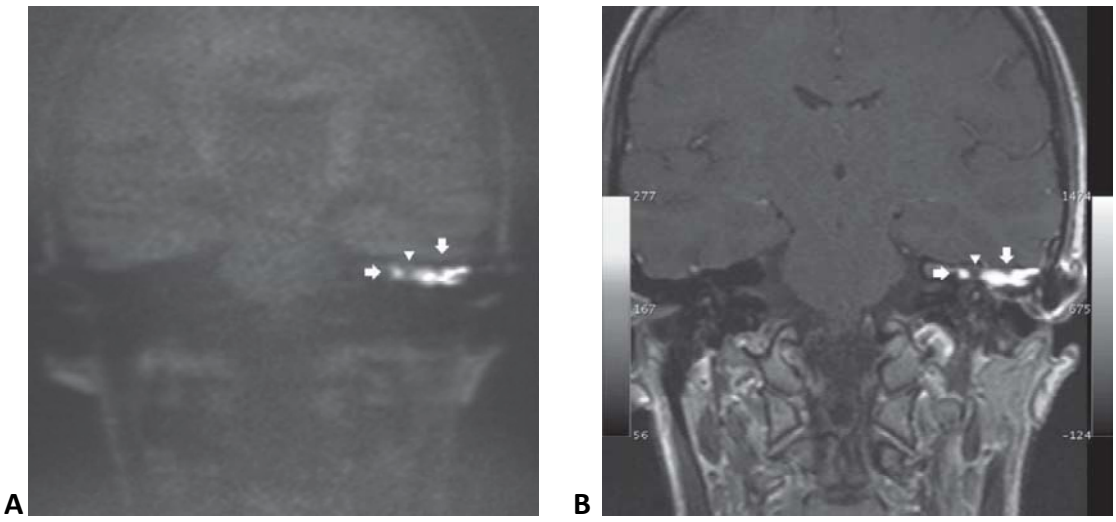

Figure 3. **A)** Preoperative magnetic resonance non–echo-planar diffusion-weighted imaging shows marked hyperintensity in temporal bone, suggestive for presence of large cholesteatoma. Cholesteatoma from mastoid (vertical arrow) extends superiorly to superior semicircular canal (arrowhead) and further medially via supralabyrinthine path (horizontal arrow).
B) Fusion of magnetic resonance non–echo-planar diffusion-weighted image and delayed contrast-enhanced T1 image was accomplished with image fusion software (OsiriX).

Follow up Results

Immediately after the operation, normal facial nerve function, an absence of vestibular dysfunction, and normal bone conduction thresholds were noticed. Postoperative otomicroscopic evaluation performed 1 year after surgery showed the presence of an intact tympanic membrane and an aerated middle ear. The hearing improved, resulting in an air-bone gap of 28.3 dB HL on the PTA frequencies at 12 months with preservation of bone conduction thresholds (Fig 1). Follow up by MRI, including non–echo-planar DWI(11) 16 and 24 months after surgery, showed no residual disease.

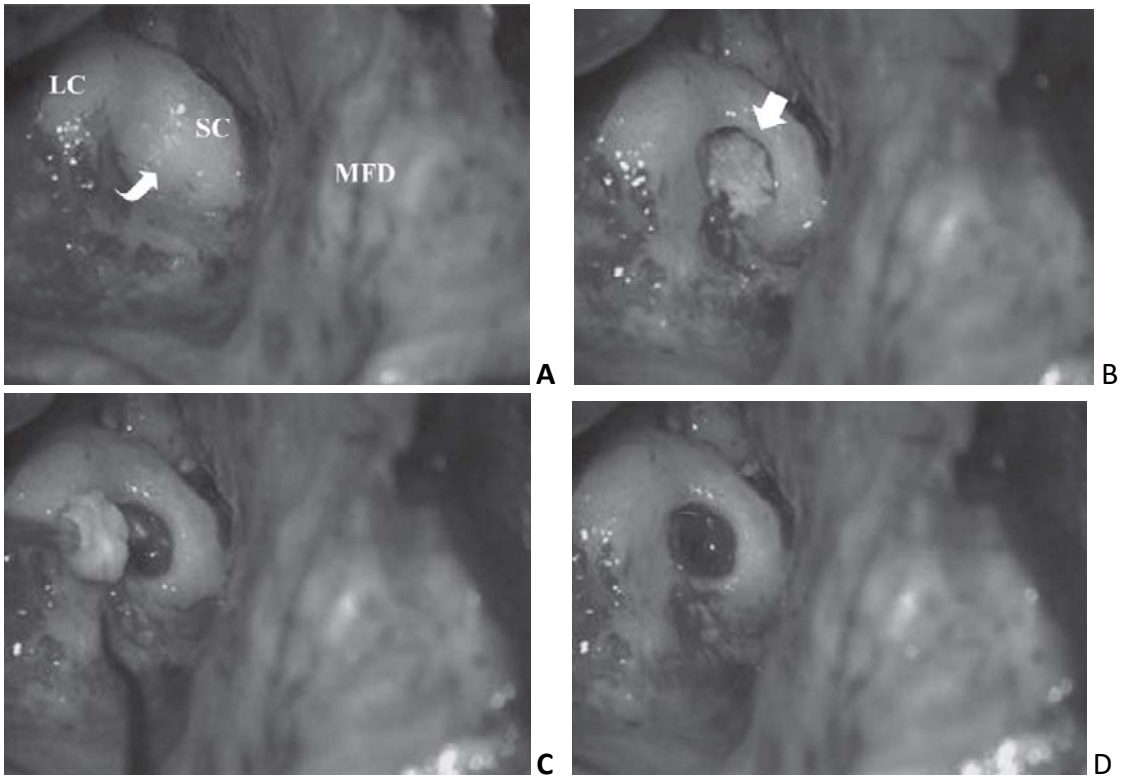

Figure 4 Intraoperative views. **A)** View prior to opening subarcuate cell tract (arrow shows direction of drilling). MFD —middle fossa dura; SC — superior semicircular canal; LC — lateral semicircular canal. **B)** Opening of subarcuate cell tract presenting supralabyrinthine cholesteatoma (arrow). **C)** Removal of cholesteatoma. **D)** View subsequent to removal of supralabyrinthine part of cholesteatoma

Discussion

To eradicate supralabyrinthine petrosal cholesteatomas without craniotomy and with hearing preservation, only a few surgical approaches can be used. Kobayashi et al (7) in 1997 first described the trans-SSC supralabyrinthine approach in their anatomic study on 21 temporal bones and in 3 clinical cases of supralabyrinthine cholesteatoma removal. They transected the arch of the SSC with a drill and immediately obliterated the labyrinthine defects with fascia before cleaning the apex of cholesteatoma. After complete cholesteatoma removal, the defects in the labyrinth were further closed with bone paste. All 3 cases preserved hearing. A supralabyrinthine approach through the arch of the SSC was first described by Frenckner (17) in 1932. He successfully used a 1-mm curette to drain the petrosal apex in 2 cases of purulent apicitis (Gradenigo's syndrome).
Both our "nondestructive" SaSLA and the "destructive" trans-SSC supralabyrinthine approach of Kobayashi (7) are only possible in selected cases of limited supralabyrinthine cholesteatomas with enough space between the tegmen and the superior border of the

SSC. If a supralabyrinthine approach with a transection of the SSC (7) is performed, good access to the upper part of the apex is possible. However, in the case at hand, we preferred our SaSLA. Opening and plugging an SSC, with or without opening the membranous labyrinth, carries a definite risk of sensorineural hearing loss, even in noninflamed, noninfectious ears, as documented by reports on use of the surgical technique in cases of SSC dehiscence (18) and by animal studies. (19) Moreover, opening the SSC in an inflamed ear with cholesteatoma could enhance the risk of labyrinthitis and its ensuing sensorineural hearing loss. In selected cases, our technique provides fairly good visibility and offers excellent odds for hearing preservation, because the membranous labyrinth remains untouched. However, in case of intracranial, internal auditory canal, cochlear, or labyrinthine invasion, complete eradication of the disease takes precedence over hearing preservation. Therefore, the SaSLA should not be used in those cases.

Since MRI non–echo-planar DWI allows detection of a cholesteatoma of at least 2 mm with a sensitivity and specificity approaching 100% (after correction for motion artifacts and self-cleaning cavities), this technique in combination with high-resolution CT scanning has become the standard procedure in our department for the preoperative evaluation of primary cholesteatoma and, even more important, in the follow up screening for residual disease. (9-14) Thanks to this major breakthrough in cholesteatoma imaging, the preoperative counseling of patients related to hearing preservation and facial and vestibular function and the surgical planning have become more precise. The fact that in the present case we were sure at the preoperative stage that the SSC, the internal auditory canal, and the intracranial compartment were not invaded allowed us to use this “nondestructive” SaSLA.

After the removal of cholesteatoma, we now perform follow up screening for residual disease after 1 and 5 years by MRI non–echo-planar DWI. If residual disease is visualized, a second-stage surgery is planned. (11)

Conclusions

Our case documents the possibility of preserving hearing, facial, and vestibular function by using this “nondestructive” SaSLA. A state-of-the-art radiologic workup is absolutely necessary to make a detailed plan of the surgical approach and to give fair, realistic counseling to the patient. The SaSLA can be recommended in cases of supralabyrinthine petrous cholesteatomas with no intracranial, cochlear, or labyrinthine invasion.

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Chapter 7

Discussion

Introduction

With an incidence of 9.2 per 100.000 per year in adults and 3 per 100.000 per year in children, chronic otitis media with cholesteatoma still is a potentially life-threatening disease due to intracranial complications, if not treated efficiently.(1,2,3)

Although the aims of cholesteatoma management are globally clear and agreed on, the literature shows quite an important variation in how to treat and follow up the patients, both throughout the world and within given countries. Due to the differences in the socio-economic environment impacting on the logistics and quality of the follow up, on the skills and training level of the ear surgeon, and on the goals, one wants to achieve in a given patient, this leads to different management options. The prevention of per-operative complications such as facial nerve palsy, sensory hearing loss, vestibular symptoms and intracranial complications is an evident goal, which is more related to the surgical skills and the training level of the surgeon than to the used technique. It is globally accepted that safety is the primary goal of all the different treatment options. Safety has two aspects: first the complete removal of the disease to prevent residual disease, because it will lead to re-growth of the original cholesteatoma; and secondly the prevention of recurrence, i.e. a new cholesteatoma. A third important goal is to achieve an acceptable postoperative hygienic status of the ear. It should be dry, self-cleaning and water proof. For the patient this means that the ear is not chronically infected, not discharging, not smelling badly with possible relational problems, not giving rise to discomfort, not painful, not inducing vestibular symptoms, allowing the patient to swim, and to use ear plugs for noise protection, as well as hearing aids or hearables. Self-cleaning means that the patient doesn't need to visit the otologist on a regular life-long basis, which would be a significant socio-economic burden.(4,5)

Generations of otologists debated on which surgical approach to use to best achieve these goals, which culminated in the controversy and heavily fought debate between the advocates of open versus closed techniques. The open technique – the canal wall down (CWD) tympanoplasty – removes the posterior and superior bony wall of the ear canal and marsupialises the disease to the ear canal. It focuses mainly on safety and on the avoidance of residual and/or recurrent disease and accepts the inherently higher risk for a worse hygienic status.(6,7,8) The closed technique – the canal wall up (CWU) tympano-plasty – leaves or reconstructs the bony canal wall. It tries to combine acceptable safety with a better hygienic status, but it accepts higher residual and recurrent disease levels as well as the need for stricter follow up and a higher re-operative rate, especially in children.(9,10,11) The bonus is more dry, self-cleaning, waterproof ears and probability of

a higher quality of life – at least for those patients that don't have residual or recurrent cholesteatoma. The choice for open versus closed tympanoplasty can thus be seen as a trade-off between safety and comfort.

The bony obliteration tympanoplasty (BOT), like other mastoid and epitympanic obliteration techniques, is a closed technique. The ears end up with a normal size of the external ear canal. In the obliteration techniques, the mastoid and epitympanic cavity is excluded and closed off by filling it with bone or its alternative materials. The BOT seems to fulfill both the safety and hygienic goals. There is no longer a trade-off.(5)

Other important goals that need to be evaluated are the postoperative hearing level (4) and the disease-specific health-related quality of life (12). Finally, we add some additional surgical techniques to the BOT that positively influence the long-term outcome, such as the MO-meatocanalplasty.

Chapter 1 is the introduction of this PhD thesis.

In **chapter 1.1** a general introduction gives an overview of some important milestones in the history of chronic otitis media with cholesteatoma and its treatment.(13) The definition and behaviour of cholesteatoma are explained by means of the recently published European Academy for Otology & Neurotology (EAONO) cholesteatoma classification system.(14) The epidemiology, the etiopathogenetic facts and theories, and the diagnostic work-up options are summarily explained.(1,2,15,16) A brief historical overview of the relevant surgical techniques is given, including the obliteration technique as reported by different schools, as the most recent and successful treatment option.(5,7,8,17,18) The current disease follow up strategies are described, with a crucial role for the non-echo planar Diffusion-Weighted MRI sequence (non-EP DW MRI).(19,20) Chapter 1.1 also introduces the use of disease-specific health-related quality of life evaluation by means of patient reported outcome measures (PROMs) in chronic otitis media with cholesteatoma. (12,21)

Chapter 2 treats the various long-term outcome measures after cholesteatoma removal using the single-staged, canal wall up, bony obliteration tympanoplasty (CWU+BOT) with tympano-ossicular allograft (TOA) reconstruction in a paediatric patient population.

In **chapter 2.1** we present the first complete 5-year follow up regarding safety and hygienic results of the CWU+BOT.(22) The paediatric cholesteatoma patients as a

subgroup is a special challenge.(1,2,23,24,25,26,27,28,29) Most authors have reported much worse outcomes in children than in adults regarding residual and recurrent disease, when CWU techniques **without obliteration** were used.(24,25,26,27,28,29) When CWU techniques **with obliteration** were used the results were dramatically better, especially in children.(30,31,32,33,34) Also, in our adult population, the single-stage CWU+BOT technique with TOA reconstruction markedly improved the results concerning safety. The residual and recurrent rates were both 2.9% after a mean follow up of 6.4 years (range 4.5–9.5) with good hygienic outcome.(35)

The 5-year results of this long-term monitored cohort of paediatric patients operated with the single-stage CWU+BOT with TOA reconstruction performed by a single surgeon show that this is a reliable and safe technique. It reduces the number of operations needed to reach the safety and hygienic goals we set ourselves. These results indicate that in paediatric cholesteatoma patients it is safe 1) to obliterate the mastoid and epitympanic space in one stage, 2) to abandon the routine exploratory second-look operation and replace it by yearly micro-otoscopy and repeated non-EP DW MRI follow up. In our residual cholesteatoma patients, the residual disease was found to reside in the middle ear cleft, never in the obliterated paratympanic space. One could argue that the reduction in residual rate compared with the formerly used CWU technique without obliteration is partially due to the Hinohara effect.(36) This effect makes it unlikely for residual skin to grow into a cholesteatoma in a bony obliterated space and is in itself an argument in favour of bony obliteration. Another factor contributing to the reduction of the residual disease rate could be that, when preparing the mastoid and epitympanic space for obliteration, one is more thorough in eliminating all soft tissues from the cavity, thus reducing the likelihood that keratinocytes are left behind.

In the majority of cases the technique resulted in a dry and trouble-free graft and in safe, dry, self-cleaning, and waterproof ears. A normal-sized external meatus, solid bony canal wall boundaries and a well-placed tympanic membrane in its normal position form an ideal basis for a stable hygienic condition of the ear. Moreover, if the functional result remains insufficient and cannot be improved by functional revision surgery, a conventional hearing aid, even with an ear canal occlusion mould, can be safely worn. In this way, the more costly and less well received hearing rehabilitation technique with a (percutaneous) bone anchored hearing device can be avoided. The use of tympano-ossicular allografts (TOA) for middle ear reconstruction allows for the combination with other reconstructive materials in revision surgery, such as cartilage reinforcement of the retraction pockets in the tympanic allograft or in case of a threatening recurrence. As an alternative for the TOAs, a cartilage–perichondrium graft and a columellar reconstruction

with a partial or total ossicular replacement prosthesis can be used. Recently, we started using hydroxyapatite bone cement as a complement for the fixation and the reconstruction of the canal wall.

The results in this paediatric series indicate that the mastoid and epitympanic BOT is a valuable addition to the CWU approach tympanoplasty technique for diminishing residual and recurrence rates. On the basis of our 5-year results, we can conclude that the CWU+BOT offers an excellent surgical solution in paediatric cholesteatoma patients. If well executed, the likelihood of residual cholesteatoma in the bony obliterated spaces is low. However, for reasons of long-term safety, the application of non-EP DW MRI monitoring remains mandatory to exclude residual disease in the middle ear cleft. We typically perform this at 1, 3, and 5 years post-op, and in case of doubt we repeat the examination. Also, clinical monitoring by micro-otoscopy and audiometry remains mandatory to exclude recurrent disease and to monitor hearing, even later than 5 years post-op. Therefore, we advise yearly otoscopy for at least 10 years on an annual basis, and at least a 3-yearly micro-otoscopic and audiometric follow up after 10 years post-op.

In **chapter 2.2** we present our 5-year follow up hearing results of the CWU+BOT with TOA reconstruction in a paediatric cholesteatoma patient population. We only included cases in which the incudo-mallear complex was destroyed by the pathology.(22,37) Cholesteatoma cases with a (nearly) intact ossicular chain and good pre-operative hearing were excluded from this series since this situation is not suitable for epitympanic bony obliteration because of the presence of a still well-functioning incus body and malleus head in the attic space. In the more extensive cholesteatoma cases these structures are either destroyed by the disease or cannot be preserved without the risk for leaving cholesteatoma behind. Because the attic in these cases is no longer useful for hearing it can be obliterated, and the ossicular chain reconstruction is then limited to the tympanic cavity.(5)

The paediatric cholesteatoma patients are also a special challenge regarding hearing results, and most authors have reported inferior hearing outcomes in children.(24,26,27,28,29,30,33,34) But when we compare the hearing gain between our former series of CWU without obliteration and the CWU+BOT group in this study, there seems to be no significant difference. However, this former CWU without obliteration group is positively biased concerning the hearing results: first because this study also included ears with a small attic cholesteatoma with an intact ossicular chain, and second because the former group had a higher re-operative rate with extra opportunities to improve the final hearing level.(28)

In our opinion the somewhat disappointing hearing outcomes in this study are biased by at least five negatively influencing factors. A first negative factor is the status of the remaining ossicular chain: in 18% of the cases the stapes footplate was fixed; in 65% of the cases the stapes superstructure was absent; in 94% of the cases the malleus was absent or could not be preserved; and in every case the incus was absent or could not be surgically preserved. Different authors published about decreased hearing outcome in these situation.(38,39) A second negatively influencing factor is the relatively good pre-operative hearing due to sound conduction by the cholesteatoma, called “cholesteatoma hearing”, even when the stapes superstructure is destroyed (65%). The odds for hearing improvement or preservation of the pre-operative hearing level are then unfavourable. A third negative bias in this study is the exclusion of small cholesteatoma cases. From the literature and by personal experience we know that the small epitympanic cases with preservation of an intact ossicular chain after cholesteatoma dissection often have a near-normal hearing level, both pre- and postoperatively, with air-bone gaps ≤ 15 dBHL after closed tympanoplasty techniques.(40) In cases with minor destruction of the long process of the incus we are nowadays able to easily and successfully reconstruct the chain with hydroxyapatite bone cement, thus safeguarding the normal tri-ossicular structure of the chain.(41) In these types of small cholesteatoma, we do not disrupt the ossicular chain in the epitympanic space and therefore we do not obliterate the epitympanic space. In our practice, these situations represent between 10 and 15% of the paediatric cholesteatoma cases. A fourth negative bias in this study is the high number of referred revision cases (50%), which might negatively influence the results. A fifth negative influence is a concomitant cleft palate (3%).

We found only a few studies in the literature, reporting on hearing outcome after obliteration tympanoplasty in children, to compare our results with. These studies, with significant loss in follow up rates concerning hearing, only report on short term postoperative hearing results.(30,33) Based on our 5-year results, we can conclude that our series of CWU+BOT for extensive cholesteatoma in children has at least comparable results with other obliterating techniques in children. Given all the negative predictive factors in our series this is better than we could hope for.

An interesting finding at the 5-year follow up of the postoperative bone conduction thresholds is the slight deterioration of these levels in six cases (17.6%), as compared to the 1-year follow up BC levels (3%). It is not clear what caused this deterioration. Possibly there is an influence of ongoing mucosal inflammation of the middle ear. Another possibility is the replacement of a tri-ossicular structure of the chain with a columellar

reconstruction, thus taking away the protective function of the dampening effect of the normal tri-ossicular chain.

The 5-year results of this long-term monitored cohort of paediatric patients show that this is a reliable and safe technique resulting in a stable hygienic condition of the ear. The mastoid and epitympanic bony obliteration technique is a valuable addition to the combined approach tympanoplasty technique. It reduces the residual and recurrence rates as well as the number of operations needed to reach the safety, hygienic and functional goals we set ourselves. In our hands the hearing results are somewhat better in this series of CWU+BOT than in our previous series of CWU without obliteration. Nevertheless, a better hearing outcome in this group of children is needed. This remains a challenge. Since even unilateral hearing loss is negatively influencing the development of children and adolescents, prevention of this irreversible lifelong developmental damage by restoring the binaural situation is urgent and mandatory in every single paediatric and adolescent case.(42) If the functional result remains insufficient after surgery, a conventional hearing aid (when needed with an ear canal occlusion mould) can be safely worn in these intact and dry external ear canals. If the air-bone gap cannot successfully be overcome with conventional hearing aids, rehabilitation with a bone anchored hearing solution needs to be considered in every paediatric and adolescent ear when the bone conduction levels allow for it. Although as chronic ear surgeons we always hope to develop new techniques to improve hearing, completely eroded ossicular chains and non-aerated middle ears are part of the chronic middle ear reality. It will always be a huge challenge to surgically rehabilitate these ears to a normal hearing situation. Since we do not know what future developments will bring, we believe it is best to preserve or reconstruct the external auditory canal and tympanic cavity to their normal anatomical dimensions. This keeps open all the options for hearing rehabilitation with new techniques in the future.

Chapter 3 reports on the results of a series of adult cholesteatoma patients who underwent CWU+BOT surgery in a single stage procedure. The surgery was executed by a single surgeon, other than the surgeon who executed the series reported on in Chapter 2. Various materials were used to reconstruct the middle ear, and their influence on outcome is discussed.

In **chapter 3.1** we present the retrospective 3-year follow up results of single-staged canal wall up with bony obliteration (CWU+BOT) surgery in adult cholesteatoma patients, performed by a single surgeon during his learning curve, i.e. the first four years of his almost fulltime otology practice.(43) Only extensive cholesteatoma cases were included,

viz. cases in which the ossicular chain could not be preserved. Cases in which the tri-ossicular configuration of the chain could be preserved or easily reconstructed with hydroxyapatite cement were not included in this series. Since those patients were not considered candidates for complete epitympanic bony obliteration, a partial obliteration technique, keeping the attic and its ossicular content intact, or a conservative CWU approach was chosen in order to get the best possible hearing outcome.(40)

Postoperative hearing outcome was evaluated prior to any revision tympanoplasty. The patient selection criteria result in a negative selection bias concerning hearing outcome compared to other reports on cholesteatoma surgery.

In terms of safety outcome (levels of residual or recurrent disease) and hygienic outcome (a dry, self-cleaning and waterproof ear) the results were comparable to the results by other experienced surgeons at our department, including those of the surgeon who developed and implemented the CWU+BOT technique.(5,22,37,44) This shows that the CWU+BOT is a safe technique with a predictable outcome. The limited recurrence level (3,27%) and the absence of residual disease at 3 years after surgery belong to the lowest numbers in literature. Some of the patients included in this study have now been clinically followed-up at our centre for well over 5 years, of which some have already received their 5-year follow up non-EP DW MRI. None of these patients currently show any clinical tendency of change in the reported outcomes.

Because routine exploratory second look surgery has been replaced by the non-invasive non-EP DW MRI sequence and owing to the very low levels of residual and recurrent disease, we have seen a tremendous drop in the re-operative rate. This made it interesting to perform a thorough assessment of the hearing outcome after the single stage CWU+BOT. In all cases reported in this study the incudomallear block was taken out because of its pathological involvement. Despite the earlier mentioned negative selection bias the hearing outcome in this study can be considered to be at least equal to the functional outcome in previous reports on cholesteatoma surgery with extensive disease and the need for ossicular disarticulation. The incidence of residual and recurrent disease shows remarkably low levels and is comparable to the low incidence reported by the experienced surgeon who was first to develop and implement the CWU+BOT technique.(22) As opposed to previous reports on the CWU+BOT technique this study includes a variety of grafts used for tympanic membrane reconstruction. No difference in recurrent or residual disease could be found between cases with a tympano-ossicular allograft (TOA) tympanic membrane reconstruction or more widely used tympanic membrane reconstructions with autologous musculus temporalis fascia or cartilage-

perichondrium grafts. One case of recurrence occurred in both the cartilage-perichondrium autograft and the TOA group, which were roughly equally sized groups. This indicates that the low recurrence rate in the CWU+BOT is not necessarily attributable to the use of TOAs but more likely to the obliteration technique itself.

Although the type of tympanic membrane reconstruction did not show a significant effect on overall hearing outcome, a trend was seen favouring the group in which a TOA was used for tympanic membrane reconstruction. A clearly significant positive effect on postoperative air-bone gap (ABG) and ABG improvement was found in favour of the TOAs in all ears with a normal mobility of the footplate and intact stapedial superstructure compared to the cartilage-perichondrial autografts. This significant effect might be caused by the optimal sound transmission due to the rotation of the malleus handle of the tympanic-ossicular allograft towards the oval window niche. Another factor might be the rigidity of the cartilage-perichondrial autografts causing a potentially suboptimal sound transmission. However, no evidence of such an effect was found in the literature but high-quality data on this feature are not available.(45) This study also shows a trend towards a smaller postoperative ABG in autologous fascia tympanic membrane reconstructions compared to the cartilage-perichondrial grafts, which could give the argument of a difference in physical quality of the grafts some weight.

Future studies might be needed to evaluate the effect on hearing outcome and residual or recurrent disease in more conservative BOT approaches such as partial obliteration with ossicular preservation or ossicular restoration by hydroxyapatite or glass ionomer cement.

Overall, this study shows that the CWU+BOT is a safe and reliable technique in different surgeons' hands, including those of a younger otologist. Reproducible safety, hygiene and hearing results with limited recurrence and residual disease can be obtained by different surgeons performing the CWU+BOT for extensive cholesteatoma.

A variety of grafts for tympano-ossicular reconstruction can be used. The knowledge that multiple grafts can be used for tympanic membrane reconstruction with similar levels of recurrent and residual disease might help this technique to become more widely implemented. The TOA might nevertheless show superior hearing results when a functioning intact stapes is present.

Chapter 4 is about the reconstruction of troublesome cavities.

In **chapter 4.1** an adult patient group (n=50) with troublesome cavities after canal wall down (CWD) surgery, who had their canal wall reconstructed (CWR) and their cavities obliterated with bone (BOT), is retrospectively analyzed. The paper discusses the outcome after a long-term mean follow up of 101.8 months.(44) The CWD mastoidectomy technique yields lower cholesteatoma recurrence and residual rates than conventional canal wall up (CWU) mastoidectomy techniques without obliteration. However, it often requires regular cavity cleaning and is associated with recurrent otorrhea because of inflammation/infection, water intolerance, caloric-induced vertigo, and the diminished ability to comfortably wear a hearing aid. The problem of recurrent inflammation and infection is mainly caused by the loss of the self-cleaning capacity of the ear, which leads to accumulation of epithelial debris and thus necessitates regular cleaning of the mastoid cavity.

When a cavity is unstable, it is often perceived by the patient as a major inconvenience. By reconstructing such ears with the BOT technique, our aim is to create a safe ear and a stable hygienic condition. This obviates the need for regular suction cleaning, makes the ear water resistant and allows the patient to comfortably wear an air conduction hearing aid, even with an open canal fitting when the hearing outcome is sufficiently good.

However, this patient group represents the worst category of cholesteatoma cases, having ended up with a troublesome cavity after 1 to 9 previous operations. Therefore, it is important to document the long-term safety and stability outcome of our reconstructive BOT technique in this group. At a mean follow up of 101.8 months, the CWR+BOT resulted in a safe ear without recurrent or residual cholesteatoma in 96% (49/50) of the ears. A residual cholesteatoma was detected by imaging in 2% (1/50) of the patients. We observed a recurrent cholesteatoma in 2% (1/50). A safe dry, and trouble-free graft and a self-cleaning external auditory canal (EAC) were achieved in 94% (47/50). The 1 and 5-year imaging follow up revealed no other recurrent or residual disease.

We concluded that the CWR+BOT is a safe and very effective option for the management of problematic, unstable CWD cavities, resulting in dry, trouble-free ears.

Chapter 5 is dedicated to quality of life evaluation in chronic otitis media (COM).

In **chapter 5.1** we translated an English quality of life questionnaire, the Chronic Otitis Media Questionnaire 12 (COMQ-12), to the Dutch language.(46)

Quality of life measurements have become very important in healthcare.(47) The COMQ-12 is a patient-related outcomes questionnaire that is constructed to obtain information about the symptoms that are most important for the patient. It allows the clinician to get an idea of the expectations of patients regarding therapy and to choose an adequate management strategy that is consistent with these expectations.(48,49) We translated the original COMQ-12 into Dutch and tested it for validity, diagnostic accuracy, and test-retest reliability.(46)

The scores for normal subjects in a test-retest setup in the same group, i.e. healthy subjects in a normal population - which varied from 0 to 11 in the test and from 0 to 6 in the retest on a scale of 0 to 60. The mean scores were 1.43 in the test and 1.34 in the retest. The modal scores of 0 (i.e. the best score, meaning no symptoms impacting on their quality of life) which were found in 51.4% and 60% of the control participants for completion and recompletion, respectively, are comparable to the values for normal subjects calculated by Phillips et al.(48)

By using a ROC curve, a cut-off value of 8 was determined to distinguish between the absence and presence of COM, although in the control group one 44-year-old subject had a COMQ-12 score of 11 (test) and 6 (retest) in the absence of Chronic Otitis Media (COM). This can be explained by a high score for the questions regarding hearing, which can be diminished in the absence of COM. Also, two patients with chronical otitis media reported COMQ-12 scores of 7 and 9. One had COM for years and had undergone several operations for this problem. Because the COMQ-12 is a patient-based measurement, the subjective inconvenience is assessed, and this patient was probably able to cope very well with his COM. The other patient had a small attic cholesteatoma in the absence of otorrhea and with good hearing, which was discovered because of a sensation of ear fullness and tinnitus.

The Dutch version of the COMQ-12 has good reproducibility and high diagnostic accuracy for detecting COM and can be used in clinical evaluation studies to assess the impact of surgery on patients' complaints.(46)

In **chapter 5.2** the Chronic Otitis Media Questionnaire 12 (COMQ-12) is applied to cholesteatoma patients before and after canal wall up with bony obliteration tympanoplasty.(50)

The COMQ-12 is a useful health-related quality of life (HRQOL) questionnaire.(48) At the level of item format, when “before” and “after” are collected on separate occasions or periods, the COMQ-12 is a useful patient reported outcomes measure (PROM).(49) In 2017 a new mixed generic and specific dynamic PROM for adult middle ear disease, named the chronic otitis media benefit inventory (COMBI) was developed and validated.(51) The advantage of COMBI’s one-shot format is convenience, while the available single-occasion status instruments for chronic middle ear disease require completion of the questionnaire at both pre-intervention and post-intervention. Carr et al. stated that QOL is determined by expectations and experience. Differences obtained by subtraction or baseline adjustment (COMQ-12) may be more bias-free.(52) This is the reason why we prefer to use the COMQ-12 over the COMBI.

This study, which investigates the symptom severity and the impact of COM with cholesteatoma on life, work and health over the 6 months preceding the evaluation, by applying the COMQ-12 pre- and postoperatively, shows a significant improvement in almost all aspects and a positive effect for all of the 12 questions. Only for the questions concerning hearing (Q3, Q4, Q7) and impact on lifestyle and work (Q8, Q9) the improvement is non-significant.

The long-term effect of the CWU+BOT on safety and hygienic outcome is well established.(22,37,53) Hearing, in contrast, often remains an unresolved issue, especially in children operated for extensive cholesteatoma with the BOT technique.(5,22,54) Good postoperative hearing, with an air-bone gap within 20 dBHL, is achieved in only 50-60% of the adult patients.(5,43) This explains why the items concerning quality of hearing and communication negatively influence the HRQOL score.(37) This finding is confirmed by the data of Lailach, who obtained similar results concerning hearing using the COMOT-15 questionnaire. In our opinion, this questionnaire with 7 out of 15 items asking about quality of hearing, attributes too much weight to the hearing aspect in HRQOL in COM.(55) However, QOL evaluation shows that the hearing outcome of tympanoplasty is emotionally very important to the patients. The ear surgeon has the important task to pre-operatively counsel the patient in realistic terms about hearing expectations and should tone them down to the known facts. Counseling should also include alternative hearing rehabilitation strategies in case the postoperative hearing level would turn out to be disappointing.

Based on preliminary results of another long-term follow up cohort, we can prudently predict that the questions evaluating the hearing (Question 3, Question 4) might remain the only significant factors negatively influencing the long-term postoperative HRQOL in patients operated for cholesteatoma with the CWU+BOT. However, this COMQ-12 data is only postoperative and not comparable with a preoperative score. Secondly the mean age at the moment of questionnaire completion was 28 years (range 14-32) and the mean age at the time of surgery was 11,4 years (range 6-16), so the patients were children at time of the operation and the operation was performed in the mean 17 years before the questionnaire was completed.(56) Nowadays this type of analysis could have been performed with the COMBI.(52,57)

In this study other factors than the hearing are also influencing the results. Beside the presence of recurrence, myringitis or retraction pockets, patients with COM with cholesteatoma who underwent ear surgery could stay anxious to have a recurrence of disease or infection. They might be very careful not to have water contact, they might avoid dusty environment and noisy situations especially the first years after surgery. Long-term analysis could give more information about this possible effect. We hope to report further on this in the near future.

To better understand the HRQOL – PROM of our patient, we have introduced a standard protocol in our clinical practice. Preoperatively, patients are asked to complete the COMQ-12. Postoperatively patients complete the COMQ-12 together with the follow up MRI at 1, 3 and 5 years postoperatively. Patients who did not complete the COMQ-12 preoperatively or who were operated before the start of our protocol are asked to complete the COMBI postoperatively at the same intervals. With this protocol we expect to obtain an improved insight in the HRQOL of our patients.

In **chapter 5.3** we translated an English quality of life questionnaire, the Chronic Otitis Media Benefit Inventory (COMBI) to the Dutch language.(57) The measurement of patient-based perception of QoL change due to their illness has become very important in healthcare. COMBI is a patient related outcome questionnaire that has been constructed to obtain information regarding the dynamic change in the physical and psychosocial burden post-intervention. It allows a clinician to rapidly get a general idea of the impact of the intervention and the residual complaints that need to be managed. Therefore, its implementation is of great use in a patient follow up setting.(51)

We translated the original COMBI into Dutch and tested it for validity, diagnostic accuracy, and test–retest reliability. The scores for the control group varied from 35 to 40, with a mean score of 36.7 (SD=1.29) and a median score of 36. A score of 36 is obtained when “zero change” is the response to all questions. Whenever responses were different from “zero change,” they were most frequently seen for the second category of questions regarding the psychosocial impact, lifestyle, and work. This can be attributed to the generic quality of the questions. The analysis of the diagnostic accuracy and the ability to distinguish COM from normal participants produced a cut-off score of 38.5 with reasonable sensitivity and specificity. Scores higher than 38.5 indicate a significant positive alteration post-intervention. Unfortunately, it was not possible to determine a cut-off score to indicate a significant negative alteration post-intervention because all individuals in the patient group reported an overall positive change.

The questionnaire used in this study was a Dutch translation of the original COMBI questionnaire.(51) Although an expansion to seven response options was suggested by Phillips for avoiding bias in answers due to the observed ceiling effect, we chose to use a translation of the original questionnaire with five response options. Through this approach, we contributed to the ambition of multiple studies with a larger number of participants in distinct clinical populations for achieving the psychometrical appraisal of a QoL instrument.

The COMBI questionnaire is a patient-reported measurement tool with a good validity and rest-retest reliability.(51) Its aim is to provide a dynamic evaluation of the physical and psychosocial impact of surgical treatment on COM patients.(51) The questionnaire was completed post-operatively between 2 and 6 months in the control surgery group and between 6 and 12 months in the COM surgery group. A cut-off score to distinguish a significant positive change from an insignificant change post-intervention was determined. A cut-off score to distinguish a negative change could not be determined in our study. The COMBI questionnaire is a useful tool complementary to the COMQ-12 in daily clinical practice.(57)

Chapter 6 is reporting on the supporting techniques and strategies used in the bony obliteration tympanoplasty.

In **chapter 6.1** the MO-meatocanalplasty is stepwise illustrated in a “How we do it” structured manuscript.(58) Meatoplasties and/or meatocanalplasties are generally

accepted supportive steps in tympanoplasty to achieve adequate meatus and canal diameters.(59,60)

The reported oblique modification of the M-meatoplasty (61,62) to the MO-meatocanalplasty can be used in a transmeatal approach, thus avoiding a retro-auricular incision. Its goal is to achieve adequate meatal and/or canal widening in patients where, in addition to a posterior narrowing by the protruding conchal cartilage, also soft tissue narrowing is present in the superior quadrants of the lateral meatus and/or when bony canal widening is necessary.

In our institute, this type of meatocanalplasty is used in a significant part of the canal wall up with bony obliteration tympanoplasty (CWU+BOT) patients if a narrow meatus or canal is present, especially in the paediatric cholesteatoma patient population.(22)

This procedure can be performed as a first-stage procedure in patients with severe chronic otitis media and narrowing of the lateral meatus and/or canal before performing the CWU+BOT. We believe that the described technique not only improves the per-operative visualization and the postoperative healing and aftercare. The MO-meatocanalplasty also results in a lower incidence of delayed epithelialisation of the tympanic graft, persistent myringitis, or granulation tissue formation at the fundus of the meatus. In cases with a milder narrowing of the meatus and/or canal, the procedure can be combined with the CWU+BOT during the same procedure. In case of delayed epithelialisation or myringitis following any type of myringoplasty or tympanoplasty, this technique can be performed as a second-stage procedure.(22,58)

In **Chapter 6.2** is the long-term outcome of the MO-meatocanalplasty technique is evaluated in a group of patients with a narrow external canal meatus presenting with recurrent eczema or otitis externa, or with the inability to wear a hearing due to extreme narrowness of the canal or to recurrent inflammation of the external canal skin.(57).

For decades, the meatoplasty is performed to tackle chronic otitis externa resistant to medical treatment. Literature on combined meatocanalplasty is scarce. The aim of this retrospective study was to report and analyse the long-term results of the MO-meatocanalplasty (58) in narrow external auditory canal (EAC) with recurrent otitis externa or inability to wear a hearing aid. This procedure is frequently associated with surgery for chronical otitis media with cholesteatoma. (22) To exclude influence of chronic otitis media disease and its surgical treatment we excluded those cases from our study.

The safety of this procedure is demonstrated by a low postoperative recurrent narrowing rate of 9,1% and the absence of any significant hearing loss. Postoperative wound infection was documented in 3 patients (13,6%) and treated with topical or systemic antibiotics. Only one out of these three patients presented with an episode of recurrent otitis externa on the long-term, both others were without any infection up to now. However possible, other complications such as tympanic membrane perforation, exposure of the temporomandibular joint or inclusion cholesteatoma of the EAC were not reported in our cohort.

The risk of recurrent narrowing is minimised by using the oblique incision in combination with free triangular skin flaps. This allows the meatal skin flap to be rotated and sutured to the meatal external skin incision whilst avoiding troublesome circumferential traction. Furthermore, we might not underestimate the importance of meticulous packing of the EAC for two weeks postoperatively as well as accurate surveillance during the first months of follow up.

The MO-meatocanalplasty allows for bony canalplasty in an elegant way. A retro-auricular incision is avoided and thus possible complications, however scarce in this region, are prevented. Additionally, no esthetical complaints were reported in our cohort.

The importance of canalplasty was advocated by Paparella in 1981 and is confirmed by many others ever since.(63,64) Recently van Spronsen et al. were able to provide evidence for a significant relationship between the shape of the bony EAC and recurrent or chronic otitis media.(65) When widening of the EAC leads to areas of denuded bone, free split-thickness skin grafts can be used to cover these areas.(63,66)

Although the literature is scarce on the possible area of denuded EAC bone for subsequent secondary healing, we observed that the risk for stenosis and delayed healing time is reduced by using split-thickness skin grafts. The complete covering of the bony EAC is aimed for at the end of this surgery which in some cases, for instance in revision surgery, leads to the additional use of a free split-thickness skin graft harvested from the retro-auricular region.

We observed that the MO-meatocanalplasty was effective in 81,8% which is in concordance with the literature.(67) In healthy ears the self-cleaning capacity is the result of the combination of first the lateral epithelial migration of the skin of the osseous EAC and second a sufficient patency at the level of the meatus.(68) In our cohort no meatal stenosis or recurrent meatal narrowing was reported in the cases that presented with

insufficient self-cleaning capacity of the EAC and recurrence of otitis externa. Therefore, accumulation of debris in the EAC might have been due to insufficient lateral epithelial migration. Whether this is the cause or effect of a long history of recurrent otitis externa is not known.

This small retrospective series comprises a homogenous group as a limited amount of indications were selected for this study. About the effect of meatocanalplasty in these conditions, little is published. We deliberately excluded patients with previous or planned second stage tympanoplasty as we aimed to extract the effect of the MO-meatocanalplasty on the state of the EAC, however much more experience with performing this technique in combination with the canal wall up bony obliteration tympanoplasty for chronical otitis media with cholesteatoma in children and adults is gained. In these tympanoplasty cases we observed a significant improved preoperative and postoperative visualisation of the tympanic membrane and middle ear structures, postoperative healing and aftercare.(22)

Prospective studies with standardised pre- and post-operative documentation of objective clinical outcome measures and subjective patient reported outcome measures are needed to provide more evidence on the added value of the meatocanalplasty as well as to compare different surgical techniques. For example: the healing time; pre- versus post-operative size of the meatus (largest possible ear speculum); self-cleaning capacity of the EAC (need and/or interval for suction cleaning); the frequency of outpatient clinic visits; the visibility of the tympanic membrane quadrants including the anterior annulus; the frequency of otitis externa; and the presence of complications; are useful clinical outcome measures. Subjective patient reported outcome measures (PROMs) could be obtained through a questionnaire similar to the Chronic Otitis Media Questionnaire 12 (COMQ-12) and the Chronic Otitis Media Benefit Inventory (COMBI) to assess patient satisfaction and possibly quality of life, or in the latter responsiveness to treatments like MO-meatocanalplasty.(12,48,51,62,69) Such a questionnaire should at least cover possible esthetical complaints and the self-reported ability to wear a hearing aid.

The MO-meatocanalplasty is an effective, safe and esthetical accepted procedure to address the narrow meatus and external auditory canal to create a well aerated, dry, self-cleaning EAC in narrow EAC with recurrent otitis externa and/or inability to wear a hearing aid. Overall, analysis of relatively long-term results showed a low rate of postoperative recurrent narrowing (4,8%) and a low rate of recurrent otitis externa (9,5%). No significant hearing loss, esthetical complaints or other complications were reported.

In **chapter 6.3** the subarcuate supralabyrinthine approach (SaSLA) for supralabyrinthine petrosal cholesteatoma is explained.(70) To eradicate supralabyrinthine petrosal cholesteatomas without craniotomy and with hearing preservation, only a few surgical approaches can be used. Kobayashi et al. in 1996 first described the trans-superior semicircular canal supralabyrinthine approach in their anatomical study on 21 temporal bones and in 3 clinical cases of supralabyrinthine cholesteatoma removal. They transected the arch of the superior semicircular canal (SSC) with a drill and immediately obliterated the labyrinthine defects with fascia before cleaning out the cholesteatoma from the apex of the temporal bone. After complete cholesteatoma removal the defects in the labyrinth were further closed with bone pâté. All 3 cases preserved hearing.(71) A supralabyrinthine approach through the arch of the SCC was first described by Frenckner in 1932.(72) He successfully used a 1 mm curette to drain the petrosal apex in two cases suffering from purulent apicitis or Gradenigo's syndrome.

Both our 'non-destructive' subarcuate supralabyrinthine approach (70) and Kobayashi's 'destructive' trans-superior semicircular canal supralabyrinthine approach (71), are only possible in selected cases when the supralabyrinthine cholesteatomas is limited in size and when there is enough space between the tegmen and the superior border of the SSC. If a supralabyrinthine approach with a transection of the SSC (71) is performed, a wider access to the upper part of the apex is possible.

However, in the described case at hand, we preferred our subarcuate supralabyrinthine approach (SaSLA).(70) Opening and plugging a semicircular canal, with or without opening the membranous labyrinth, carries a definite risk for sensorineural hearing loss, even in non-inflamed non-infectious ears, as documented by the reports on the surgical technique in cases with SSC dehiscence (73) and by animal studies (74). Moreover, opening the SSC in an inflamed cholesteatoma ear could enhance the risk for labyrinthitis and its ensuing sensorineural hearing loss. In selected cases our technique provides enough visibility to dissect the cholesteatoma and offers excellent odds for hearing preservation, because the membranous labyrinth remains untouched. However, in case of intracranial, internal auditory canal, cochlear or labyrinthine invasion, complete eradication of the disease takes precedence over hearing preservation. Therefore, the subarcuate supralabyrinthine approach (SaSLA) should not be used in those cases.

Since non-echo-planar DW MRI allows detection of a cholesteatoma of at least 2mm with high sensitivity and specificity, this technique in combination with high resolution CT-scanning has become the standard procedure in our department for the preoperative

evaluation of primary cholesteatoma and, even more important, in the follow up screening for residual disease.(5,19,34,35,75,76,77) Thanks to this major breakthrough in cholesteatoma imaging, the preoperative counselling of patients, related to hearing preservation, facial and vestibular function, as well as the surgical planning have become more precise. The fact that in the present case we were sure at the preoperative stage that the SSC, the internal auditory canal and intracranial compartment were not invaded allowed the senior author of this paper to use this 'non-destructive' subarcuate supralabyrinthine approach (SaSLA).(22)

Concluding Remarks

The bony obliteration tympanoplasty in both canal wall up and canal wall down is an excellent solution for extensive cholesteatoma and troublesome cavity revision cases. It creates a situation with excellent safety concerning residual rates and recurrence rates, without significant complications and with preserved inner ear function. The hygienic outcome is very good, i.e. a self-cleaning and dry ear, which is waterproof and can be comfortably fitted with a conventional hearing aid if needed. The bony obliteration tympanoplasty results in acceptable postoperative hearing in comparison to other techniques. In contrast, when a canal wall up tympanoplasty technique without obliteration is used in these extensive cases, it leads to significant higher long-term residual and recurrence rates and to a significant increase in the number of operations needed. This effect is even more pronounced in children.

Since cholesteatoma is most often a unilateral pathology, the ensuing hearing loss is usually restricted to one ear. However, the deleterious effect of unilateral hearing loss is often underrated. The known socio-economic effects of unilateral hearing loss in children and adults should be further explored in cholesteatoma patients. In the future more research on hearing rehabilitation is needed in these patients. If reconstruction of the middle ear mechanism doesn't yield good enough hearing, hearing aids and implants should be considered and offered, especially in children and adolescents, where the impact of unilateral hearing loss could have a devastating effect on their cognitive development and academic potential.

The bony obliteration tympanoplasty is not exclusively used in combination with tympano-ossicular allografts. Other techniques for tympanic membrane reconstruction give comparable results. However, in case of an intact stapes superstructure, the use of tympano-ossicular allografts tends to produce better hearing results. With proper training

the safety, hygienic and hearing results are reproducible in the hands of different surgeons in different centres.

The first results of health-related quality of life outcome after the bony obliteration tympanoplasty are very promising with half of patients scoring at normal levels and the other half close to normal and significantly better than chronic otitis media patients. However, more long-term evaluation and comparison with other techniques used for these same indications is needed. The use of a universal disease-specific tool translated and validated in different languages such as the COMQ-12 and COMBI is helpful and should be encouraged.

Meatocanalplasty is a supportive technique which each otologist should be able to use when managing chronic otitis media with cholesteatoma. Various meatoplasty and canalplasty techniques are available, although not all of them are esthetically acceptable. The MO-meatocanalplasty is a useful technique, consisting of logical surgical steps which can be adjusted to the individual case and which allows for a bony canalplasty without a retro-auricular incision.

Considering the widely variable results of CWU and CWD tympanoplasty without (bony) obliteration published by various authors, the implementation of an obliteration technique in cases of extensive cholesteatoma or troublesome cavities should be considered in every ear clinic. The willingness to change one's technique and get out of one's comfort zone depends on different factors. First, surgeons should evaluate their own results and compare them with the results published in the literature. Embarrassingly enough this is frequently not the case. Secondly, one should be able to learn these obliteration techniques in dedicated temporal bone courses, which are still not broadly available. Thirdly, one must invest in extra operation time in each and every patient since the obliteration techniques are more time consuming compared to non-obliterative procedures, even in very skilled hands. Finally, the use of extra operation time and the reduction of the total number of ear procedures per time unit is a serious cut in a department's budget.

Proper long-term prospective study protocols and/or databases will be helpful and will probably lead to stronger arguments for using specific techniques in specific situations, such as the bony obliteration tympanoplasty in extensive cholesteatoma. The proper outcome measures and tools should be agreed on and used for evaluation. To allow comparison between different surgical treatment strategies, safety, hygienic results,

hearing and quality of life all need to be consistently measured in well-defined patient groups, using universal outcome parameters.

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Chapter 8

Summary – Samenvatting

Summary

Cholesteatoma has an incidence of 9.2 per 100.000 adults per years and 3 per 100.000 children per year. Chronic otitis media with cholesteatoma still is a potentially life-threatening disease due to intracranial complications, if not treated effectively.(1-3) The aims of cholesteatoma management are globally clear and agreed on. The literature shows quite an important variation in how to treat and follow up the patients. Safety is the primary goal of all the different treatment options and has three aspects: the prevention of per-operative complications such as facial nerve palsy, sensory hearing loss, vestibular symptoms and intracranial complications; the complete removal of the disease to prevent residual disease; and the prevention of recurrent disease. A second important goal is to achieve an acceptable postoperative hygienic status of the ear. It should be dry, self-cleaning and waterproof. For the patient this means that the ear is not chronically infected, not discharging, not smelling badly with possible relational problems, not giving rise to discomfort, not painful, not inducing vestibular symptoms. Furthermore, it allows the patient to swim, to use ear plugs for noise protection, and to wear hearing aids or hearables. Self-cleaning means that the patient doesn't need to visit the otologist on a regular life-long basis, which would be a significant socio-economic burden.(4,5) The third goal that needs to be evaluated is the postoperative hearing level.(4) The disease-specific health-related quality of life (6) forms an important fourth goal. Which surgical approach to use to best achieve these goals is part of the debate between the advocates of open versus closed techniques. The bony obliteration tympanoplasty (BOT), like other mastoid and epitympanic obliteration techniques, is a closed technique. The ears end up with a normal size of the external ear canal. In the obliteration techniques, the mastoid and epitympanic cavity are excluded and closed off by filling it with bone or its alternative materials. The BOT seems to fulfill both the safety and hygienic goals.(5)

In **chapter 1.1**, the introduction of this PhD thesis, a general introduction gives an overview of some important milestones in the history of chronic otitis media (COM) with cholesteatoma and its treatment.(7) The definition and behaviour of cholesteatoma are explained by means of the recently published cholesteatoma classification system of the European Academy for Otology & Neurotology (EAONO).(8) The epidemiology, the etiopathogenetic facts and theories, and the diagnostic work-up options are summarily explained.(1,2,9,10) A brief historical overview of the relevant surgical techniques is given, including the obliteration technique as reported by different schools, as the most recent and successful treatment option.(5,11-14) The current disease follow up up strategies are described, with a crucial role for the non-echo planar Diffusion-Weighted MRI sequence (non-EP DW MRI).(15-17) Chapter 1.1 introduces the use of disease-

specific health-related quality of life evaluation by means of patient-reported outcome measures (PROMs) in chronic otitis media with cholesteatoma.(6,18)

In **chapter 2.1** we present the first 5-year complete follow up up outcome measures regarding safety and hygienic results after cholesteatoma removal using the single-staged, canal wall up, bony obliteration tympanoplasty (CWU+BOT) with tympano-ossicular allograft (TOA) reconstruction performed by a single surgeon in a paediatric patient population.(19) It shows that this is a reliable and safe technique and that it reduces the number of operations needed to reach the safety and hygienic goals we set ourselves. These results indicate that in paediatric cholesteatoma patients it is safe 1) to obliterate the mastoid and epitympanic space in one stage, and 2) to abandon the routine exploratory second-look operation and replace it by yearly micro-otoscopy and repeated non-EP DW MRI follow up up. In the majority of cases the technique resulted in a dry and trouble-free graft and in safe, dry, self-cleaning, and waterproof ears.

In **chapter 2.2** we present our 5-year follow up up hearing results of the CWU+BOT with TOA reconstruction in a paediatric cholesteatoma patient population. We only included extensive cases in which the incudo-mallear complex was destroyed by the pathology.(19,20) Because the attic in these cases is no longer useful for hearing it can be obliterated, and the ossicular chain reconstruction is then limited to the tympanic cavity.(5) In our opinion the somewhat disappointing hearing outcomes in this study are biased by at least five negatively influencing factors. A first negative factor is the inferior status of the remaining ossicular chain. A second negatively influencing factor is the relatively good pre-operative hearing due to sound conduction by the cholesteatoma, called “cholesteatoma hearing”. A third negative bias in this study is the exclusion of small cholesteatoma cases. A fourth negative bias in this study is the high number of referred revisions. A fifth negative influence is a concomitant cleft palate. Nevertheless, a better hearing outcome in this group of children is needed. This remains a challenge.

In **chapter 3.1** we present the retrospective 3-year follow up up results of single-staged CWU+BOT using various reconstructive materials in adult cholesteatoma patients, performed by a single surgeon during his learning curve.(21) Only extensive cholesteatoma cases were included, viz. cases in which the ossicular chain could not be preserved. In terms of safety outcome (levels of residual or recurrent disease) and hygienic outcome (a dry, self-cleaning and waterproof ear) the results were comparable to the results by other experienced surgeons at our department, including those of the surgeon who developed and implemented the CWU+BOT technique.(5,20-23) This shows that the CWU+BOT is a safe technique with a predictable outcome. The limited

recurrence level (3,27%) and the absence of residual disease at 3 years after surgery belong to the lowest numbers in literature. As opposed to previous reports on the CWU+BOT technique this study includes a variety of grafts used for tympanic membrane reconstruction. No difference in recurrent or residual disease could be found between cases with TOA tympanic membrane reconstruction or more widely used tympanic membrane reconstructions with autologous musculus temporalis fascia or cartilage-perichondrium grafts. This indicates that the low recurrence rate in the CWU+BOT is not necessarily attributable to the use of TOAs but more likely to the obliteration technique itself. Despite the earlier mentioned negative selection bias, the hearing outcome in this study can be considered to be at least equal to the functional outcome in previous reports on cholesteatoma surgery with extensive disease and the need for ossicular disarticulation. A significant positive effect on postoperative air-bone gap (ABG) and ABG improvement was found in favour of the TOAs in all ears with a normal mobility of the footplate and intact stapedial superstructure compared to the cartilage-perichondrial autografts.

In **chapter 4.1** an adult patient group with troublesome cavities after canal wall down (CWD) surgery, who had their canal wall reconstructed (CWR) and their cavities obliterated with bone (BOT), is retrospectively analyzed. The paper discusses the outcome after a long-term mean follow up up of 101.8 months.(24) When a cavity is unstable, it is often perceived by the patient as a major inconvenience. By reconstructing such ears with the BOT technique, our aim is to create a safe ear and a stable hygienic condition. This obviates the need for regular suction cleaning, makes the ear water resistant and allows the patient to comfortably wear an air conduction hearing aid, even with an open canal fitting when the hearing outcome is sufficiently good. This patient group represents the worst category of cholesteatoma cases, having ended up with a troublesome cavity after 1 to 9 previous operations. At a mean follow up up of 101.8 months, the CWR+BOT resulted in a safe ear without recurrent or residual cholesteatoma in 96% (49/50) of the ears. A residual cholesteatoma was detected by imaging in 2% (1/50) of the ears. We observed a recurrent cholesteatoma in 2% (1/50) of the ears. A safe dry, and trouble-free graft and a self-cleaning external auditory canal (EAC) were achieved in 94% (47/50). The 1 and 5-year imaging follow up up revealed no other recurrent or residual disease. We concluded that the CWR+BOT is a safe and effective option for the management of problematic and unstable CWD cavities, resulting in dry and trouble-free ears.

In **chapter 5.1** we translated an English quality of life questionnaire, the Chronic Otitis Media Questionnaire 12 (COMQ-12), to the Dutch language and tested it for validity,

diagnostic accuracy, and test-retest reliability.(23) The COMQ-12 is a patient-related outcomes questionnaire that is constructed to obtain information about the symptoms that are most important for the patient. It allows the clinician to get an idea of the expectations of patients regarding therapy and to choose an adequate management strategy that is consistent with these expectations.(25,26) The Dutch version of the COMQ-12 has good reproducibility and high diagnostic accuracy for detecting chronic otitis media (COM) and can be used in clinical evaluation studies to assess the impact of surgery on patients' complaints.(23)

In **chapter 5.2** the Chronic Otitis Media Questionnaire 12 (COMQ-12) is applied to investigate symptom severity and impact of COM in cholesteatoma patients before and after CWU+BOT.(27) This study shows a significant improvement in 7 of the 12 questions. Three questions concerning hearing and 2 questions concerning impact on lifestyle and work also revealed improvement, however not to a level of significance. Questions evaluating the hearing may remain the only significant factor negatively influencing the long-term postoperative health-related quality of life in patients operated for cholesteatoma with the CWU+BOT. In this study other factors than the hearing are also influencing the results. Beside the presence of recurrence, myringitis or retraction pockets, patients with COM with cholesteatoma who underwent ear surgery could stay anxious to have a recurrence of disease or infection. They might be very careful not to have water contact, they might avoid dusty environment and noisy situations especially the first years after surgery.

In **chapter 5.3** we translated an English quality of life questionnaire, the Chronic Otitis Media Benefit Inventory (COMBI), to the Dutch language and tested it for validity, diagnostic accuracy, and test-retest reliability.(28) COMBI is a patient-related outcomes questionnaire that has been constructed to obtain information regarding the dynamic change in the physical and psychosocial burden post-intervention. It allows a clinician to rapidly assess the impact of the intervention and the residual complaints that need to be managed. Therefore, its implementation is of great use in a patient follow up up setting.(29) The COMBI questionnaire is a useful tool complementary to the COMQ-12 in daily clinical practice.(28)

In **chapter 6.1** the MO-meatocanalplasty is stepwise illustrated in a "How we do it" structured manuscript.(30) The reported oblique modification of the M-meatoplasty (31,32) to the MO-meatocanalplasty can be used in a transmeatal approach, thus avoiding a retro-auricular incision. Its goal is to achieve adequate meatal and/or canal widening in patients where, in addition to a posterior narrowing by the protruding

conchal cartilage, also soft tissue narrowing is present in the superior quadrants of the lateral meatus and/or when bony canal widening is necessary. In our institute, this type of meatocanalplasty is used in a significant part of CWU+BOT patients if a narrow meatus or canal is present, especially in the paediatric cholesteatoma patient population.(23)

In **chapter 6.2** the long-term outcome of the MO-meatocanalplasty technique is evaluated in 22 ears with a narrow external auditory canal and meatus presenting with recurrent eczema, recurrent otitis externa, or with the inability to wear a hearing aid.(33) The safety of this procedure is demonstrated by a low postoperative recurrent narrowing rate of 9,1% and the absence of any important hearing loss. Postoperative wound infection was documented in 3 patients (13,6%) and treated with topical or systemic antibiotics. Other complications such as tympanic membrane perforation, exposure of the temporomandibular joint or inclusion cholesteatoma of the external auditory canal (EAC) were not reported in our cohort. The MO-meatocanalplasty allows for bony canalplasty in an elegant way. A retro-auricular incision is avoided and thus possible complications, however scarce in this region, are prevented. Additionally, no esthetical complaints were reported in this cohort. The MO-meatocanalplasty is an effective, safe and esthetically accepted procedure to address the narrow meatus and external auditory canal to create a well aerated, dry, self-cleaning EAC in narrow EAC with recurrent otitis externa and/or inability to wear a hearing aid.

In **chapter 6.3** the subarcuate supralabyrinthine approach (SaSLA) for supralabyrinthine petrosal cholesteatoma is explained.(34) To eradicate supralabyrinthine petrosal cholesteatomas without craniotomy and with hearing preservation, only a few surgical approaches can be used. Both the ‘non-destructive’ SaSLA (34) and the ‘destructive’ trans-superior semicircular canal supralabyrinthine approach (35) are only possible in selected cases when the supralabyrinthine cholesteatoma is limited in size and when there is enough space between the tegmen and the superior border of the superior semicircular canal (SSC). In selected cases the non-destructive technique provides enough visibility to dissect the cholesteatoma and offers excellent odds for hearing preservation, because the membranous labyrinth remains untouched. However, in case of intracranial, internal auditory canal, cochlear or labyrinthine invasion, complete eradication of the disease takes precedence over hearing preservation. Therefore, SaSLA should not be used in those cases. Due to excellent preoperative radiological imaging in this case, non-invasion of the SSC, the internal auditory canal and the intracranial compartment could be demonstrated pre-operatively, and consequently the ‘non-destructive’ SaSLA (34) could be applied.

Conclusion

The bony obliteration tympanoplasty in both canal wall up and canal wall down is an excellent solution for extensive cholesteatoma and troublesome cavity revision cases. It creates a situation with outstanding safety concerning residual rates and recurrence rates, without significant complications and with preserved inner ear function. The hygienic outcome is very good, i.e. a self-cleaning and dry ear, which is waterproof and can be comfortably fitted with a conventional hearing aid if needed. The bony obliteration tympanoplasty results in acceptable postoperative hearing in comparison to other techniques. In contrast, when a canal wall up tympanoplasty technique without obliteration is used in these extensive cases, it leads to significantly higher long-term residual and recurrence rates and to a significant increase in the number of operations needed. This effect is even more pronounced in children. The first results of health-related quality of life outcomes after the bony obliteration tympanoplasty are very promising with half of patients scoring at normal levels and the other half close to normal and significantly better than chronic otitis media patients. However, more long-term evaluation and comparison with other techniques used for the same indications is needed. The use of a universal disease-specific tool translated and validated in different languages such as the COMQ-12 and COMBI is helpful and should be encouraged.

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Samenvatting

Cholesteatoma heeft een incidentie van 9,2 per 100.000 volwassenen per jaar en 3 per 100.000 kinderen per jaar. Chronische otitis media met cholesteatoma is nog steeds een potentieel levensbedreigende ziekte als gevolg van intracraniële complicaties, indien niet effectief behandeld.(1-3) De doelstellingen van cholesteatomazorg zijn wereldwijd duidelijk en overeenstemmend. De literatuur toont een grote variatie in hoe de patiënten te behandelen en op te volgen. Veiligheid is het primaire doel van alle verschillende behandelingsopties en heeft drie aspecten: het voorkomen van peroperatieve complicaties zoals aangezichtsverlamming, sensorineuraal gehoorverlies, vestibulaire symptomen en intracraniële complicaties; de volledige verwijdering van de pathologie om residuele ziekte te voorkomen; en de preventie van recidief van de ziekte. Een tweede belangrijk doel is het bereiken van een acceptabele postoperatieve hygiënische status van het oor. Het moet droog, zelfreinigend en waterbestendig zijn. Voor de patiënt betekent dit dat het oor niet chronisch is geïnfecteerd, niet loopt, niet slecht ruikt met mogelijke relationele problemen, geen aanleiding geeft tot ongemak, niet pijnlijk is en geen vestibulaire symptomen veroorzaakt. Bovendien stelt het de patiënt in staat om te zwemmen, oordoppen te gebruiken voor bescherming tegen lawaai en om gehoorapparaten of hoor accessoires (hearables) te dragen. Zelfreinigend betekent dat de patiënt de oorarts niet op regelmatige basis hoeft bezoeken, hetgeen een aanzienlijke sociaal-economische weerslag heeft.(4,5) Het derde doel dat moet worden geëvalueerd, is de postoperatieve gehoorstatus.(4) De ziekte specifieke gezondheid gerelateerde kwaliteit van leven (6) vormt een belangrijk vierde doel. Welke chirurgische aanpak men aanwendt om deze doelen het beste te bereiken, maakt deel uit van het debat tussen de voorstanders van open of “canal wall down” (CWD) versus gesloten of “canal wall up” (CWU) technieken. De beenderige obliteratie tympanoplastie (BOT) is, net als andere mastoïd en epitympanale obliteratietechnieken, een gesloten techniek. De oren eindigen met een normale grootte van de externe gehoorgang. In de obliteratietechnieken worden het mastoïd en het epitympanum geëxcludeerd en afgesloten door deze op te vullen met bot of alternatieve materialen. De BOT lijkt zowel de veiligheids- als de hygiënische doelen te bereiken.(5)

In **hoofdstuk 1.1**, de inleiding van dit proefschrift, geeft een algemene introductie en overzicht van enkele belangrijke mijlpalen in de geschiedenis van chronische otitis media (COM) met cholesteatoma en de behandeling ervan.(7) De definitie en het gedrag van cholesteatoma worden verklaard door het recent gepubliceerde classificatiesysteem voor cholesteatoma van de European Academy for Otology & Neurotologie (EAONO).(8) De epidemiologie, de etiopathogenetische feiten en theorieën en de diagnostische opties

worden kort beschreven.(1,2,9,10) Een kort historisch overzicht van de relevante chirurgische technieken wordt gegeven, inclusief de obliteratietechnieken zoals gerapporteerd door verschillende scholen, als de meest recente en succesvolle behandelingsoptie.(5,11-14) De huidige strategieën voor de follow up up van de ziekte wordt beschreven, met een cruciale rol voor de non-echo planar Diffusion-Weigthed MRI-sequentie (non-EP DW MRI).(15-17) Hoofdstuk 1.1 introduceert het gebruik van ziekte specifieke gezondheid gerelateerde kwaliteit van leven-evaluatie door middel van patiënt gerapporteerde uitkomstmaten (PROM's) in chronische otitis media met cholesteatoma.(6,18)

In **hoofdstuk 2.1** presenteren we de eerste 5-jaars complete follow up up resultaten met betrekking tot veiligheid en hygiëne na verwijdering van cholesteatoma met behulp van de single-stage, canal wall up met beenderige obliteratie tympanoplastie (CWU+BOT) met tympano-ossiculaire allogreffe (TOA) reconstructie uitgevoerd door één chirurg in een pediatrische patiëntenpopulatie.(19) Het onderzoek laat zien dat dit een betrouwbare en veilige techniek is en dat het aantal handelingen vermindert dat nodig is om de veiligheids- en hygiënische doelen te bereiken die we onszelf stelden. Deze resultaten geven aan dat het bij pediatrische cholesteatoma patiënten veilig is 1) om het mastoïd en het epitympanum in één fase te oblitereren, en 2) om de routinematige verkennende second-look heroperatie te verlaten en te vervangen door een jaarlijkse micro-otoscopie en herhaalde non-EP DW MRI follow up up. In de meeste gevallen resulteerde de techniek in een droog en probleemloos transplant en in veilige, droge, zelfreinigende en waterbestendige oren.

In **hoofdstuk 2.2** presenteren we onze 5-jaars follow up up gehoorresultaten van de CWU+BOT met TOA-reconstructie in pediatrische cholesteatoma patiënten. Enkel gevorderde cholesteatoma gevallen waarbij het incudo-malleair complex is vernietigd door de pathologie werden geïncludeerd.(19,20) Omdat het atticus in deze gevallen niet langer nuttig is voor het gehoor, kan dit worden geëxcludeerd en is de reconstructie van de gehoorbeentjesketen dan beperkt tot de trommelholte.(5) Naar onze mening zijn de ietwat teleurstellende gehoorresultaten in dit onderzoek beïnvloed door ten minste vijf negatieve factoren. Een eerste negatieve factor is de inferieure status van de resterende ossiculaire keten. Een tweede negatief beïnvloedende factor is het relatief goede pre-operatieve gehoor als gevolg van geluidsgeleiding door het cholesteatoma, ook wel 'cholesteatoma horen' genoemd. Een derde negatieve vertekening in deze studie is de uitsluiting van kleine gevallen van cholesteatoma. Een vierde negatieve bias in deze studie is het hoge aantal revisies. Een vijfde negatieve invloed is een gespleten

gehemelte. Desondanks is een beter gehoor nodig bij deze groep kinderen. Dit blijft een uitdaging.

In **hoofdstuk 3.1** presenteren we de retrospectieve 3-jaars follow up up resultaten van een single-staged CWU+BOT met behulp van verschillende reconstructieve materialen bij volwassen cholesteatoma patiënten, uitgevoerd door één chirurg tijdens zijn leer-curve.(21) Alleen uitgebreide gevallen van cholesteatoma werden opgenomen, te weten gevallen waarin de ossiculaire keten niet kon worden bewaard. In termen van veiligheidsuitkomst (mate van residuele of recidiverende ziekte) en hygiënische uitkomst (een droog, zelfreinigend en waterbestendig oor) waren de resultaten vergelijkbaar met de resultaten van andere ervaren chirurgen op onze afdeling, inclusief die van de chirurg die de CWU+BOT techniek ontwikkelde en implementeerde. (5,20-23) Dit laat zien dat de CWU+BOT een veilige techniek is met een voorspelbaar resultaat. Het beperkte recidiefniveau (3,27%) en de afwezigheid van resterende ziekte op 3 jaar na de operatie behoren tot de laagste aantallen in de literatuur. In tegenstelling tot eerdere rapporten over de CWU+BOT-techniek omvat deze studie een aantal typen van transplantaten die worden gebruikt voor de reconstructie van het trommelvlies. Er kon geen verschil in recidief of residuele ziekte worden gevonden tussen gevallen met TOA-trommelvliesreconstructie of meer algemeen gebruikte trommelvliesreconstructies met autologe musculus temporalis fascia of kraakbeen-perichondriumtransplantaten. Dit geeft aan dat het lage recidiefpercentage in de CWU+BOT niet noodzakelijkerwijs te wijten is aan het gebruik van TOA's, maar eerder aan de obliteratiemethode zelf. Ondanks de eerdergenoemde negatieve selectiebias, kan het gehoorresultaat in dit onderzoek worden beschouwd als minimaal gelijk aan het functionele resultaat in eerdere rapporten over cholesteatoma chirurgie met uitgebreide ziekte en de noodzaak van ossiculaire disarticulatie. Een significant positief effect op postoperatieve air-bone gap (ABG) en ABG-verbetering werd gevonden ten voordele van de TOA's in alle oren met een normale mobiliteit van de voetplaat en intacte stapes superstructuur in vergelijking met de kraakbeen-perichondrium autotransplantaten.

In **hoofdstuk 4.1** wordt een volwassen patiëntengroep met onrustige radicaal holtes na een canal wall down (CWD) operatie, waarbij hun gehoorgang wand gereconstrueerd (CWR) en hun holten geëxcludeerd werden met de BOT, retrospectief geanalyseerd. Deze paper bespreekt de uitkomst na een gemiddelde lange termijn follow up up van 101,8 maanden.(24) Wanneer een radicaal holte onstabiel is, wordt deze door de patiënt vaak als een groot ongemak ervaren. Ons doel is om een veilig oor en een stabiele hygiënische toestand te creëren door dergelijke oren te reconstrueren met de BOT-techniek. Dit maakt de noodzaak voor een regelmatige oortoilet overbodig, maakt het oor water-

bestendig en stelt de patiënt in staat comfortabel een hoortoestel met luchtgeleiding te dragen, zelfs met een open kanaalpassing wanneer het gehoorresultaat voldoende goed is. Deze patiëntengroep vertegenwoordigt de ergste categorie gevallen van cholesteatoma, die na 1 tot 9 eerdere operaties uiteindelijk in een lastige radicaalholte resulteerde. Bij een gemiddelde follow up up van 101,8 maanden resulteerde de CWR+BOT in een veilig oor zonder recidief of residueel cholesteatoma in 96% (49/50) van de oren. Een residueel cholesteatoma werd gedetecteerd door beeldvorming in 2% (1/50) van de oren. We zagen een recidief cholesteatoma in 2% (1/50) van de oren. Een veilig, droog en probleemloos transplantaat en een zelfreinigende externe gehoorgang (EAC) werden bereikt bij 94% (47/50). Uit de beeldvorming follow up up na 1 en 5 jaar bleek geen andere recidiverende of resterende ziekte. We concludeerden dat de CWR+BOT een veilige en effectieve optie is voor het beheer van problematische en onstabiele CWD-holten, wat resulteert in droge en probleemloze oren.

In **hoofdstuk 5.1** hebben we een Engelse vragenlijst over kwaliteit van leven, de Chronic Otitis Media Questionnaire 12 (COMQ-12), vertaald naar de Nederlandse taal en getest op validiteit, diagnostische nauwkeurigheid en test-hertest betrouwbaarheid.(23) De COMQ-12 is een patiënt gerelateerde uitkomstenvragenlijst die is samengesteld om informatie te verkrijgen over de symptomen die het belangrijkst zijn voor de patiënt. Hiermee kan de arts een idee krijgen van de verwachtingen van patiënten met betrekking tot therapie en een geschikte managementstrategie kiezen die consistent is met deze verwachtingen.(25,26) De Nederlandse versie van de COMQ-12 heeft een goede reproduceerbaarheid en hoge diagnostische nauwkeurigheid voor het detecteren van chronische otitis media (COM) en kan worden gebruikt in klinische evaluatiestudies om de impact van chirurgie op de klachten van patiënten te beoordelen.(23)

In **hoofdstuk 5.2** wordt de Chronische Otitis Media-vragenlijst 12 (COMQ-12) toegepast om de ernst van de symptomen en de impact van COM bij cholesteatoma patiënten voor en na CWU+BOT (27) te onderzoeken. Deze studie toont een significante verbetering voor 7 van de 12 vragen. De 3 vragen over het gehoor en de 2 vragen over de impact op levensstijl en werk lieten ook verbetering zien, maar niet significant. Vragen die handelen over het gehoor kunnen de enige significante factor blijven die de postoperatieve gezondheid gerelateerde kwaliteit van leven op lange termijn negatief beïnvloedt bij patiënten die met de CWU+BOT worden geopereerd in verband met cholesteatoma. In deze studie beïnvloeden ook andere factoren dan het gehoor de resultaten. Naast de aanwezigheid van recidief, myringitis of retractiepockets, konden patiënten met COM met cholesteatoma die een ooroperatie ondergingen angstig blijven voor een herhaling van ziekte of infectie. Ze kunnen wellicht relatief voorzichtig zijn om watercontact, een

stoffige omgeving en lawaaierige situaties te vermijden, vooral de eerste jaren na de operatie.

In **hoofdstuk 5.3** hebben we een Engelse vragenlijst over de kwaliteit van leven, de Chronische Otitis Media Benefit Inventory (COMBI), vertaald naar de Nederlandse taal en getest op validiteit, diagnostische nauwkeurigheid en test-hertest betrouwbaarheid.(28) COMBI is een patiënt gerelateerde uitkomstenvragenlijst die is opgesteld om informatie te verkrijgen over de dynamische verandering in de fysieke en psychosociale last na interventie. Hiermee kan een arts snel de impact van de interventie beoordelen en de resterende klachten die moeten worden behandeld. Daarom is de implementatie ervan van groot nut in een instelling voor follow up up van patiënten.(29) De COMBI-vragenlijst is een handig hulpmiddel als aanvulling op de COMQ-12 in de dagelijkse klinische praktijk.(28)

In **hoofdstuk 6.1** wordt de MO-meatocanalplastie stapsgewijs geïllustreerd in een "How we do it" gestructureerd manuscript.(30) De gerapporteerde schuine modificatie van de M-meatoplastie.(31,32) in de MO-meatocanalplastie kan worden gebruikt in een transmeatale benadering, waardoor een retro-auriculaire incisie wordt vermeden. Het doel is het bereiken van voldoende gehoorgang verbreding bij patiënten waarbij, naast een posterieure vernauwing door het uitstekende conchale kraakbeen, ook weke delen vernauwing aanwezig is in de superieure kwadranten van de laterale gehoorgang en/of wanneer beenderige kanaal verruiming noodzakelijk is. In ons instituut wordt dit type meatocanalplastie gebruikt bij een aanzienlijk deel van CWU+BOT-patiënten als er een nauwe gehoorgang aanwezig is, vooral in de pediatrische patiëntenpopulatie met cholesteatoma.(23)

In **hoofdstuk 6.2** wordt het lange termijn resultaat van de MO-meatocanalplastie geëvalueerd in 22 oren met een smalle externe gehoorgang met recidief eczeem, recidiverende otitis externa of met het onvermogen om een gehoorapparaat te dragen.(33) De veiligheid van deze procedure wordt aangetoond door een lage postoperatieve vernauwing van 9,1% en de afwezigheid van enig belangrijk gehoorverlies. Postoperatieve wondinfectie werd gedocumenteerd bij 3 patiënten (13,6%) en behandeld met topische of systemische antibiotica. Andere complicaties zoals trommelvlies-perforatie, blootstelling van het kaakgewricht of inclusie cholesteatoma van de uitwendige gehoorgang werden niet gemeld in onze cohort. De MO-meatocanalplastie maakt beenderige kanaalverbreding op een elegante manier mogelijk. Een retro-auriculaire incisie wordt vermeden en daarmee worden mogelijke complicaties, hoe zeldzaam in deze regio ook, voorkomen. Bovendien werden in dit cohort geen esthetische

klachten gemeld. De MO-meatocanalplastie is een effectieve, veilige en esthetisch geaccepteerde procedure om de smalle gehoorgang aan te pakken en om een goed beluchte, droge, zelfreinigend gehoorgang te creëren in smalle uitwendige gehoorgangen met recidiverende otitis externa en/of het onvermogen om een gehoorapparaat te dragen.

In **hoofdstuk 6.3** wordt de subarcuate supralabyrinthine approach (SaSLA) voor supralabyrinthaire petrosale cholesteatoma beschreven.(34) (van Dinther 2010). Om supralabyrinthaire petrosale cholesteatoma zonder craniotomie en met gehoorbehoud te verwijderen, kunnen slechts enkele chirurgische benaderingen worden gebruikt. Zowel de 'niet-destructieve' SaSLA (34) als de 'destructieve' trans-superieure semicirculaire kanaal supralabyrinthaire benadering (35) zijn alleen mogelijk in geselecteerde gevallen wanneer het supralabyrinthaire cholesteatoma beperkt in omvang is en wanneer er voldoende ruimte is tussen het tegmen en de superieure grens van het superior semicirculair kanaal (SSC). In geselecteerde gevallen biedt de niet-destructieve techniek voldoende zichtbaarheid om het cholesteatoma te verwijderen en biedt dit uitstekende kansen voor gehoorbehoud, dit omdat het membraneuze labyrinth onaangeroerd blijft. In geval van intracraniële, interne gehoorgang, cochleaire of labyrinth invasie heeft volledige verwijdering van de ziekte voorrang op gehoorbehoud. Daarom mag SaSLA in die gevallen niet worden gebruikt. Vanwege uitstekende preoperatieve radiologische beeldvorming in dit geval kon de non-invasie van het SSC, de interne gehoorgang en het intracraniële compartiment preoperatief worden aangetoond, en bijgevolg kon de ‘niet-destructieve’ SaSLA (34) worden toegepast.

Conclusie

De beenderige obliteratie tympanoplastie is in zowel canal wall up als canal wall down een uitstekende oplossing voor uitgebreide gevallen van cholesteatoma alsook in de reconstructie van onrustige radicaalholtes. Het creëert een situatie met uitstekende veiligheid met betrekking tot residuele- en recidiefpercentages, zonder significante complicaties en met behoud van de binnenoorfunctie. Het hygiënische resultaat is zeer goed, d.w.z. een zelfreinigend en droog oor, dat waterbestendig is en indien nodig comfortabel kan worden uitgerust met een conventioneel gehoorapparaat. De beenderige obliteratie tympanoplastie resulteert in een acceptabel postoperatief gehoor in vergelijking met andere technieken. Wanneer in deze uitgebreide gevallen een canal wall up tympanoplastie techniek zonder obliteratie wordt gebruikt, leidt dit daarentegen tot aanzienlijk hogere residuele en recidiefpercentages op lange termijn en tot een

significante toename van het aantal benodigde operaties. Dit effect is zelfs meer uitgesproken bij kinderen. De eerste resultaten van gezondheid gerelateerde kwaliteit van leven na de beenderige obliteratie tympanoplastie zijn veelbelovend, waarbij de helft van de patiënten op normale niveaus scoort en de andere helft bijna normaal en aanzienlijk beter dan patiënten met chronische otitis media scoort. Er is echter meer lange termijn evaluatie nodig en vergelijking met andere technieken die voor dezelfde indicaties worden gebruikt. Het gebruik van een universele ziekte specifieke vragenlijst, vertaald en gevalideerd in verschillende talen, zoals de COMQ-12 en COMBI, is nuttig en moet worden aangemoedigd.

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Chapter 9

Curriculum Vitae

Curriculum Vitae

Joost van Dinther werd geboren op 16 maart 1976 te Dreumel in het Land van Maas en Waal, Nederland. In 1994 behaalde hij zijn vwo-diploma aan het Pax Christi College te Druten. Vervolgens studeerde hij geneeskunde aan de Universiteit Antwerpen alwaar hij in 2002 cum laude afstudeerde. Hij was o.a. Praeses in 1999-2000 van de Antwerpse Geneeskundige Faculteitsvereniging “Aesculapia”. In diezelfde jaren kwam hij in contact met de Antwerpse Otologische School. Na een korte inleidende research periode vatte hij in 2003 aan met zijn opleiding tot NKO-arts. Tijdens zijn assistentenjaren richtte hij in 2004 mee de Vereniging voor Assistenten NKO “VA-NKO” op en werd hier ook voorzitter van in 2007-2008. De passie voor de oorheelkunde werd hem door Prof. Erwin Offeciers en Dr. Andrzej Zarowski met de paplepel ingegoten. In 2008 verkreeg hij zijn erkenning als NKO-arts. Vervolgens genoot hij nog een fellowship Hoofd- en Halschirurgie onder begeleiding van Prof. Hubert Vermeersch in het UZGent. Vanaf 2009 werd hij na 2 jaar neurotologisch fellow als vast staflid benoemd in het European Institute for ORL-HNS van het Sint-Augustinus Ziekenhuis te Antwerpen. In 2014 richtte hij daar mee het Skillslab Antwerpen op voor hands-on training van voornamelijk neurotologische procedures. Hij startte in 2014 mee de Antwerp Bony Obliteration Tympanoplasty Course op met als eerste eregast Dr. Ulf Mercke. In april 2020 staat de 13de editie van deze cursus gepland. In 2014 kreeg het idee een proefschrift aan te vangen over het onderwerp cholesteatoom chirurgie onder begeleiding van promotores Prof. Cor Cremers en Prof. Erwin Offeciers vorm. In 2017 werd hij adjunct-diensthoofd van het European Institute for ORL-HNS. Momenteel is hij beheerder van de Tympano-Ossiculaire Weefselbank GZA, de donorbank voor gehoorbeentjes en trommelvliezen. In het kader van de opleiding van stagiairs geneeskunde en assistenten NKO is hij sedert 2011 stagementor en sedert 2019 stagemeester voor de huisartsenopleiding. Sedert 2012 is hij Gastlector aan Thomas More Hogeschool. Hij is LOK-verantwoordelijke sinds 2013. Joost heeft samen met zijn vrouw Janneke Schapendonk drie lieve kinderen: Mats, Saar en Kaat.

Chapter 10

Research Data Management Page

Research Data Management Page

This thesis is based on the results of human studies, which were conducted in accordance with the principles of the Declaration of Helsinki. Conform the general data protection regulation enforced on May 25th 2018, approval of the medical and ethical review board committee of GZA Hospitals was asked and provided for the two prospective studies as well as the later retrospective studies within this thesis.

The primary and secondary data obtained during my PhD at the European Institute for ORL-HNS, Department of Otorhinolaryngology – Head & Neck Surgery, Sint-Augustinus, GZA Hospitals, Antwerp have been captured, pseudonymised and stored on the local GZA server belonging to the department and accessible by the associated senior staff members and researchers involved in research. To ensure interpretability of the data, all filenames, primary and secondary data, metadata, descriptive files used to provide the final results are documented along with the data.

The privacy of the participants in this study is warranted by use of encrypted and unique individual subject codes. These codes correspond with the codes on the patient's and physician's booklets and were stored separately from the study data.

Published data generated or analyzed in this thesis are part of published articles and its additional files are available from the associated corresponding authors on request.

The data will be saved for 20 years after termination of the study. Using these patient data in future research will only be possible after a renewed permission by the patient.

Chapter 11

List of Publications

List of Publications

1. **Sinonasal Fibro-osseous Hamartoma: Case Presentation and Differential Diagnosis with other Fibro-osseous Lesions Involving the Paranasal Sinuses.**
   Boudewyns AN, **van Dinther JJS**, Colpaert CG.
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Sluydts M, Bernaerts A, De Foer B, Zarowski A, **van Dinther JJS**, Vanspauwen R, Offeciers E.
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35. **The MO-meatocanalplasty: Long-Term Results in the Narrow External Auditory Canal with Recurrent Otitis Externa or the Inability to Wear a Hearing Aid.**
De Greve G, **van Dinther JJS**, Vanspauwen, Maryn Y, Verstreken M, Zarowski A, Offeciers E.
Eur Arch Otorhinolaryngol. Accepted 2019.

Chapter 12

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Joost van Dinther

Chapter 13

Abbreviations

Abbreviations

3D	three-dimensional
AAOHNS	American Academy of Otolaryngology-Head and Neck Surgery
ABG	air-bone gap
AC	air conduction
ADC	apparent diffusion coefficient
AHEP	Amsterdam hearing evaluation plot
AIR	autograft incus remodeled
AT	autograft tympanum
ATp	autograft tympanum partial
AWp	autograft wall partial
BAHA	bone anchored hearing device
BAHD	bone anchored hearing device
BC	bone conduction
BOT	bony obliteration tympanoplasty
CBCT-scan	cone beam computed tomography scan
CES	chronic ear survey
COM	chronic otitis media
COM-5	chronic otitis media 5
COMBI	chronic otitis media benefit inventory
COMOT-15	chronic otitis media outcome test 15
COMQ-12	chronic otitis media questionnaire 12
CPA	cerebellopontine angle
CSF	cerebrospinal fluid
CT-scan	computed tomography scan
CWD	canal wall down
CWU	canal wall up
CWR	canal wall reconstruction
dB	decibel
dBHL	decibel hearing level
DW	diffusion-weighted
DWI	diffusion-weighted imaging
EAONO	European Academy for Otology and Neurotology
EAC	external auditory canal
EIORL-HNS	European Institute for ORL-HNS
ENT	ear, nose and throat
EO	Erwin Offeciers
EP	echo-planar
EP DW	echo-planar diffusion-weighted
GBI	Glasgow benefit inventory
GZA	Gasthuiszusters Antwerpen
kHz	kilohertz
HIR	homograft incus remodeled
HMR	homograft malleus remodeled
HRCT	High resolution CT-scan
HRQOL	health-related quality of life

HT	homograft tympanum
HTM	homograft tympanum + malleus
HTMI	homograft tympanum + malleus + incus
HTMISp	homograft tympanum + malleus + incus + stapes partial
HTMp	homograft tympanum + malleus partial
ICC	intraclass correlation coefficient
JVD	Joost van Dinther
mg	milligram
ml	milliliter
mm	millimeter
MO	M-oblique
MO-plasty	M-oblique meatocanalplasty
MR	magnetic resonance
MRI	magnetic resonance imaging
Non-EP DW	non-echo planar Diffusion-weighted
Non-EP DW MRI	non-echo planar diffusion-weighted MRI
O&NO	Otology & Neurotology
OS	original stapes
OSp	original stapes partial
OTMI	original tympanum + malleus + incus
OTMIS	original tympanum + malleus + incus + stapes
OTMp	original tympanum + malleus partial
Q	question
QOL	quality of life
ROC curve	receiver operating characteristic curve
PROM	patient-reported outcome measure
PROMs	patient-reported outcome measures
PROs	patient-reported outcomes (USA)
PTA	pure tone average
PTA-HF	pure tone average high frequency
SA	Sint Augustinus
SaSLA	subarcuate supralabyrinthine approach
SD	standard deviation
SNHL	sensorineural hearing loss
SPPS	statistical package for the social sciences
SSC	superior semicircular canal
SCCs	semicircular canals
STP	subtotal petrosectomy
TAO	tympano-ossicular allograft
TM	tympanic membrane