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Tesi di Laurea

PEDIATRIC TYMPANOPLASTY: ANALYZING THE IMPACT OF PROGNOSTIC FACTORS ON SURGICAL SUCCESS AND FUNCTIONAL OUTCOMES

TIMPANOPLASTICA IN ETA' PEDIATRICA: ANALISI DELL'IMPATTO DEI FATTORI PROGNOSTICI SUL SUCCESSO CHIRUGICO E FUNZIONALE

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1 INTRODUCTION

Tympanoplasty is the surgical repair of the tympanic membrane and/or the middle ear ossicles. The goal of tympanoplasty is the eradication of the disease and the anatomical and functional restoration of the middle ear. This consists of an intact tympanic membrane, a mobile ossicular chain and a healthy middle ear cavity (1) (2).

1.1 ANATOMY AND FUNCTION OF THE EAR

The ear is a uniquely constructed organ. It is perfectly designed to catch sound waves and transform them into electrical signals that can consequently be translated into auditory messages (3). The human ear is made up of three regions (Figure 1): the outer ear, comprising the auricle and ear canal, the middle ear, containing the tympanic membrane, the ossicles, and the middle ear cavity, and the inner ear, comprising the cochlea, semicircular canals, and internal auditory canals. The middle ear is contiguous with the Eustachian tube which is connected to the rhinopharynx (3) (4).

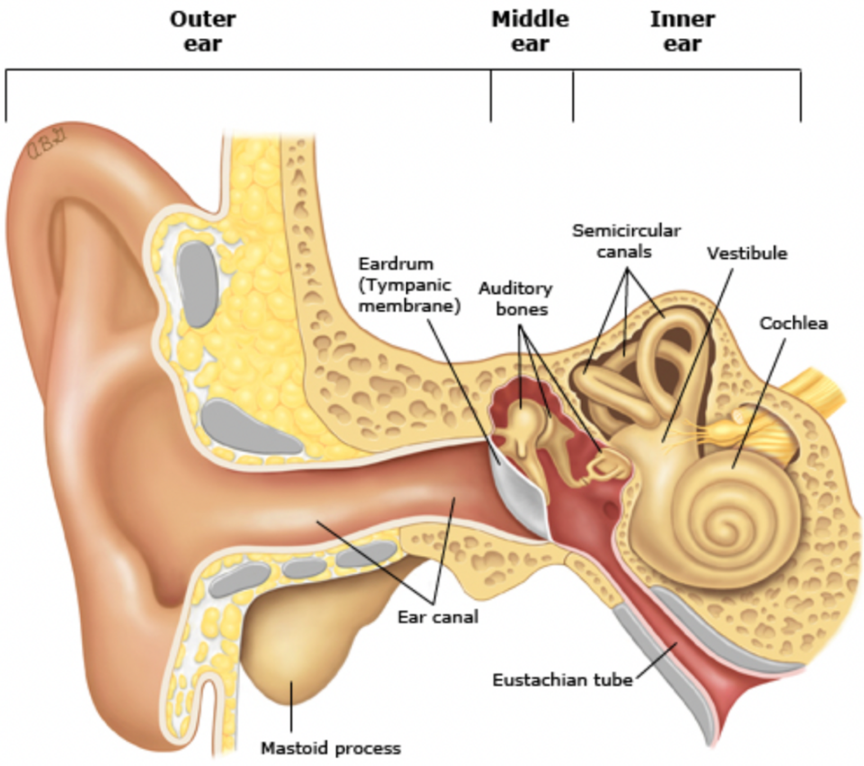


Figure 1: Normal structures of the outer, middle and inner ear (5).

1.1.1 TIMPANIC MEMBRANE

The tympanic membrane is thin, semi-transparent, and almost oval, though slightly wider at the top than the bottom. Its longest diameter, antero-inferiorly, is 9 - 10 mm, while the shorter diameter is 8 - 9 mm (Figure 2A) (6). Surrounding its circumference, there is a fibrous annulus composed of smooth muscle cells that plays a fundamental role in blood flow and in maintaining the membrane tension (7) (8). The plane of the tympanic annulus changes from a nearly horizontal orientation (34 degrees from the horizontal plane) in neonates to a more vertical orientation (63 degrees from the horizontal plane) in adults (9). This change in angulation is due to growth of the skull base and temporal lobe of the brain (3) (7).

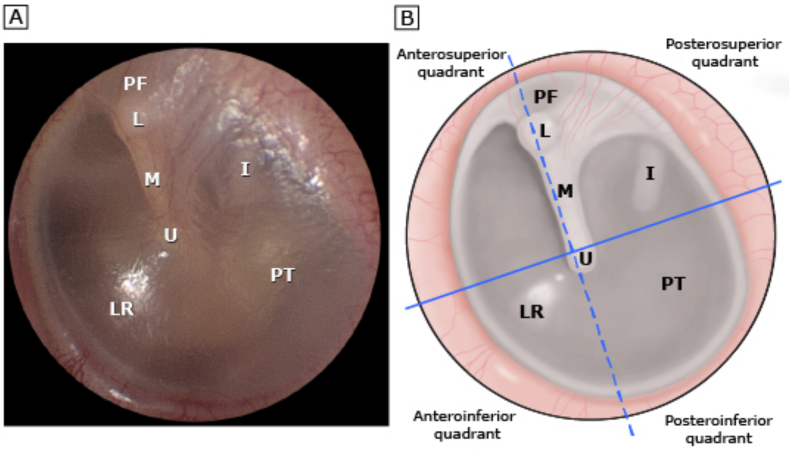


Figure 2: Otoscopic image (panel A) and schematic diagram (panel B) of a left tympanic membrane. A line drawn along the manubrium of the malleus divides the tympanic membrane into anterior and posterior halves (dashed line). A line drawn through the umbo (perpendicular to the first line) divides the tympanic membrane into superior and inferior halves (solid line).I: incus, long process; L: lateral process of the malleus; LR: light reflex; M: manubrium of the malleus; PF: pars flaccida; PT: pars tensa; U: umbo (5).

Focusing on the microscopic anatomy, the tympanic membrane consists of an outer cutaneous layer, a middle fibrous layer, and an inner mucous layer (Figure 3) (3) (6) (10). The cutaneous layer is composed of a keratinized squamous epithelium and a vascularized subepithelial tissue; it is contiguous with the skin of the external auditory canal. The fibrous layer consists of an outer layer of radial fibers spreading from the handle of the malleus and a deeper layer of circular fibers. Finally, the mucous layer is part of the mucosa of the tympanic cavity and is characterized by a single layer of very flat cells, with irregular microvilli on their luminal side (3) (7).

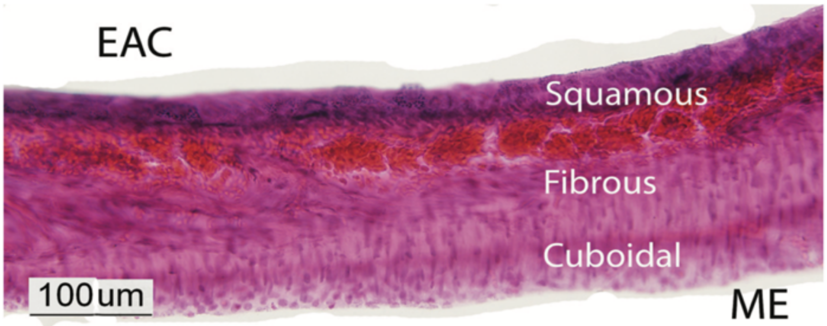


Figure 3: Transverse section of tympanic membrane of a 3-month-old child. EAC, external auditory canal; ME, middle ear (7).

In the tympanic membrane we can identified two portions: pars flaccida, which is the small portion of the tympanic membrane above the lateral process of the malleus, and pars tensa, which is thinner than the pars flaccida and is suspended from the fibrous tympanic annulus; it is the largest portion of the tympanic membrane and is the part in which the fibrous state is also present (3) (10).

If we imagine a line drawn along the manubrium of the malleus and a line through the umbo, we can identify the four quadrants that constitute the eardrum (Figure 2B) (4) (5)

Of the ossicles, only the malleus is normally in direct contact with the tympanic membrane (Figure 4) (3) (7).

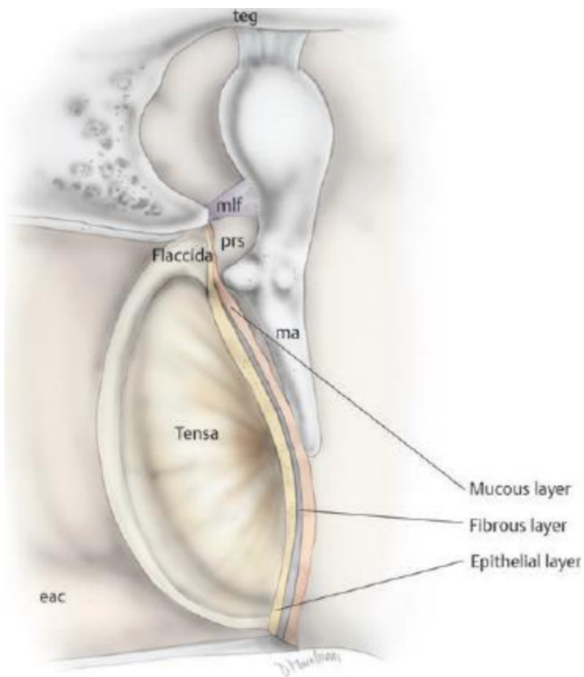


Figure 4: Right ear. Picture of the layers of the tympanic membrane and its relation to the ossicles (11).

1.1.2 THE OSSICLES

The malleus has a long handle, called manubrium, attached to the inner surface of the eardrum and a head, located in the epitympanic recess of the middle ear (Figure 5) (12) (3). The anterior body of the incus fits against the posterior head of the malleus in the epitympanum, forming the true diarthrodial incudomalleal joint. The slender long process of the incus terminates in a knob-like lenticular process. A diarthrodial incudostapedial joint connects the latter to the stapes head (also called capitulum). From its articulation with the incus, the stapes extends to the oval window. The two are united by an annular ligament that allows movement. The stapes is further supported by the stapedius muscle (3) (7).

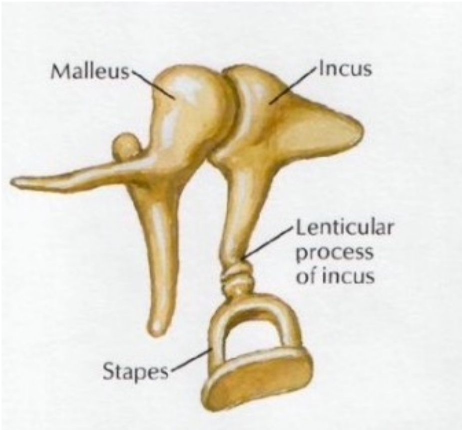


Figure 5: Ossicles articulated (12).

Four ligaments suspend the malleus in its anatomical position and are important surgical determinants. The anterior malleolar ligament extends from the neck of the malleus to the petrotympanic fissure. The ligament for tensor tympani extends from the medial surface of the upper end of the manubrium to the cochleariform process, which is an important landmark for the tympanic portion of the facial nerve. The lateral malleolar ligament extends from the malleolar neck to the tympanic notch and forms a fold that delineates the boundaries of Proussak's space. Finally, the superior malleolar ligament anchors the head of the malleus to the roof of the epitympanum, the tegmen timpany (1) (3).

The stapedial tendon extends from the apex of the pyramidal process to the posterior surface of the neck of the stapes. When stimulated, the tendon pulls the stapes posteriorly, thereby increasing the resonant frequency of the ossicular chain and attenuating sound (3) (10).

1.1.3 TIMPANIC CAVITY

The middle ear is an air-filled space bounded by the tympanic membrane laterally and the labyrinthic wall medially. Anteriorly, the carotid wall and pharyngotympanic tube are important anatomic landmarks. Posteriorly, the tympanic cavity is confluent with the mastoid cells of the temporal bone. Superiorly, the cavity is bounded by the tegmen tympani dividing it from the middle cranial fossa, and inferiorly by the jugular wall and styloid prominence (3) (10) (12) (13).

The anatomy of this very complex anatomic area has recently become more accessible as a result of the outstanding development of the endoscopic approach to ear pathologies (8) (7) (14). The adoption of the endoscope has made possible to add further details to the anatomical knowledge previously established through the microscopic view. In fact, the optical tip of an endoscope can bypass the narrowest point of the ear canal and generate a very broad wide view of the middle ear. Furthermore, placing the optic on an angle can further allow to explore the timpanic cavity (7) (8).

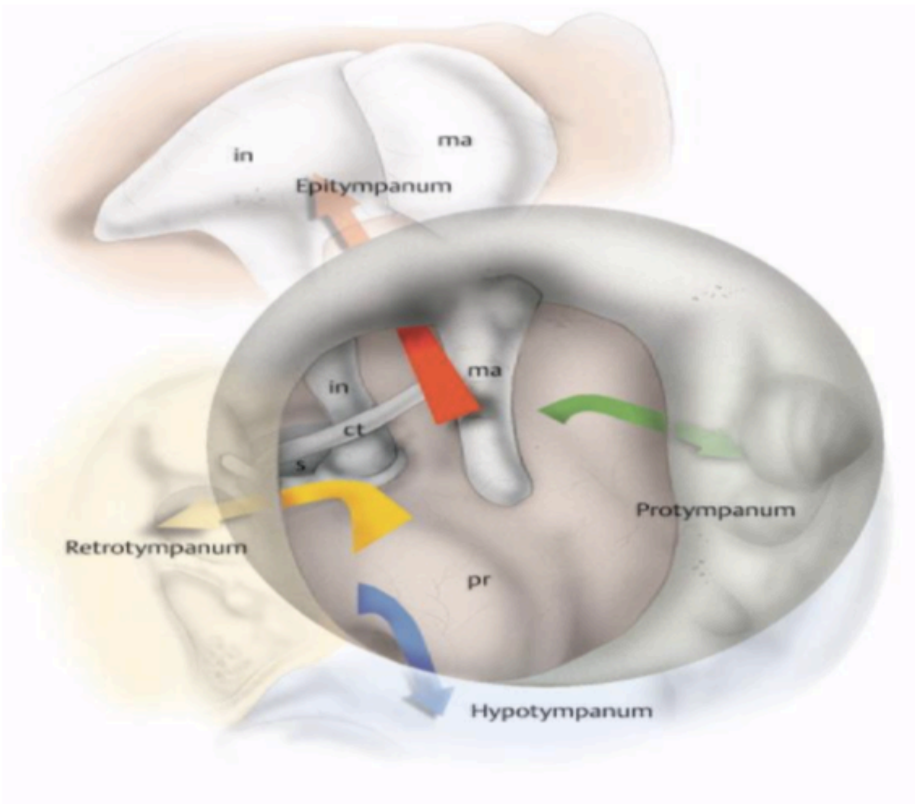


Figure 6: Anatomy of the tympanic cavity (11).

Diving deeper into the anatomy of the area, the tympanic cavity can be subdivided into five subsites (Figure 6). The circle represents the annulus of the tympanic membrane and directly behind it is the mesotympanum. Surrounding the latter, there are the epitympanum superiorly, the protympanum anteriorly, the hypotympanum inferiorly, and the retrotympanum posteriorly (8) (10).

The epitympanum contains the incudomalleal joint and is limited inferiorly by the facial nerve, a very important structure to preserve during surgery in this area. Part of the facial nerve is also the chorda tympani, which is a branch of its mastoid segment and passes above the incus, below the malleus, towards the petrotympanic fissure (3) (7).

In the protympanum lies the Eustachian tube, which leads to the nasopharynxs, and the tensor tympani muscle which arises near the first genu of the facial nerve (10) (8).

The mesotympanum contains the stapes and its tendon which emerges from the pyramidal process of the facial canal. The stapes footplate is therefore very close to the facial nerve. Another important area of the mesotympanum is the cochlear promontory with the round window that overlays the basal turn of the cochlea. Over it runs the tympanic nerve. A thick bone called the fustis leads up to the round window, separating it from the canaliculus (8) (3).

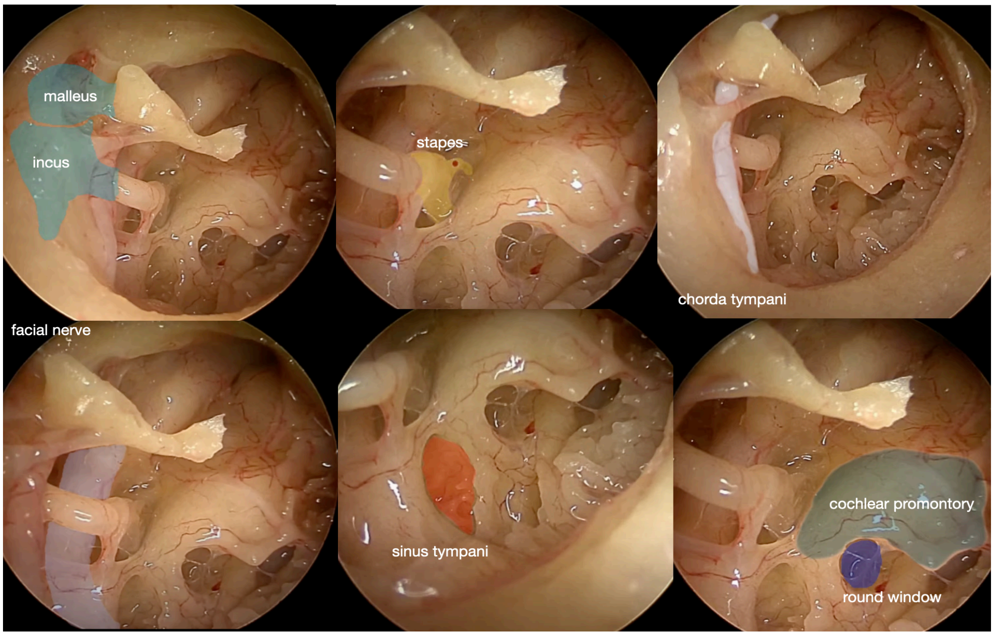


Figure 7: Endoscopic anatomy of the tympanic cavity (8).

The retrotympanum region is very complex and characterized by the presence of many recesses around the third portion of the facial nerve (8).

The sinus tympani is the largest of the recesses and lies between the ponticulus and the subiculum bones. It can be very deep, and it runs under the facial nerve. Another recess is the facial recess which, on the contrary, extends over the nerve. The hypotympanum represents the inferior compartment of the tympanic cavity and vascular structures can be found, such as the first genu of the internal carotid artery or the jugular bulb (8) (3).

Sensory innervation is provided by branches of the auriculotemporal nerve, which is a division of the trigeminal nerve, and by the tympanic branch of the glossopharyngeal nerve (3) (10).

The arterial vascularization of the middle ear comes mainly from the branches of the external carotid artery through the deep auricular artery, the anterior tympanic artery and the stylomastoid artery. Smaller arteries that also contribute to the vascularization of the tympanic cavity arethe inferior tympanic and the superficial petrosal branches of the middle meningeal artery, the superior tympanic branch of the ascending pharyngeal artery, a branch of the artery of the pterygoid canal and the tympanic branch of the internal carotid artery (12).

The venous drainage ends in the venous pterygoid plexus and in the superior petrosal sinus (3).

1.1.4 EUSTACHIAN TUBE

The Eustachian tube plays a crucial role in protecting the middle ear from bacterial and viral pathogens of the upper airways, besides being vital for removing middle ear secretions and achieving pressure balance (4) (10). Its epithelium works as a primary barrier against pathogens from the nasopharynx through the mucociliary flow associated with the secretion of antimicrobial agents. In infants and young children it is shorter, broader, and more horizontally compared to adults, easing the transmission of pathogens to the middle ear and therefore increasing the likelihood of developing otitis media (Figure 8) (15). As kids grow older, a shift downward in skull base elevation results in a gradual increase in length and inclination. From approximately 13 mm at birth it reaches 35 mm when fully grown-up (16). These adjustments, along with maturation in immune function, contribute towards a decreased auricular infective risk (4).

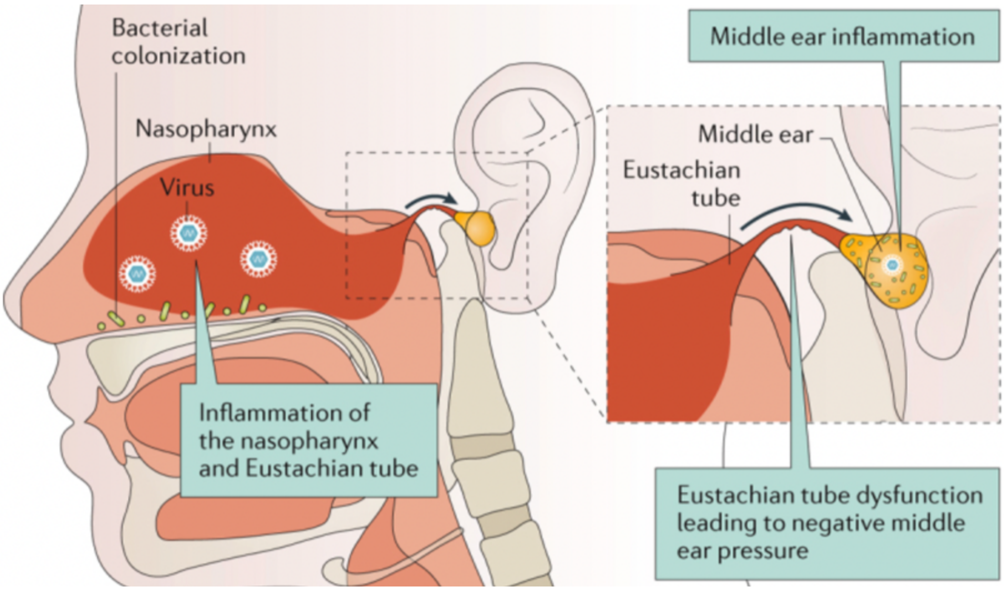


Figure 8: The child might have a pre-existing nasopharyngeal bacterial colonization, which does not cause symptoms. When the child contracts a common cold, the viral infection initiates inflammation of the nasopharynx and the Eustachian tube, leading to colonization of bacteria. Eustachian tube dysfunction follows, leading to negative middle ear pressure, which allows pathogens in the nasopharynx to move into the middle ear causing infection (17).

1.1.5 PHYSIOLOGY OF HEARING

Sound is a mechanical event that consists of oscillations through a transmitting medium, such as air. Air waves are propagated outward from vibrating sources. When pressure waves encounter another object, the vibration can be transmitted to the medium of that object (13). The ear is a very efficient transducer, transforming sound pressure of the air into a neural-electrical signal that is translated by the brain as sound (18).

Sound waves have three basic physical attributes: frequency, amplitude, and temporal variation. Frequency is the number of oscillations per unit of time, expressed in Hertz (Hz). The healthy, young auditory system can detect tones with frequencies ranging from approximately 20 to 20000 Hz in quiet environments (10) (18). Amplitude is the intensity of the sound, expressed in decibels (dB). The hearing capacity of the human ear is broad, ranging from barely perceptible sounds to very intense sounds (13) (18). Sounds that exceed 85 dB can be harmful to hearing in cases of prolonged exposure. Lastly there are many aspects to the temporal variation of sound, such as sound duration (19) (18).

The first structure sound waves encounter is the outer ear which funnels them down the external auditory canal to vibrate of the tympanic membrane. The outer ear also plays an important role of amplification of sound, especially for acute frequencies (18) (19). The oscillation transmitted to the tympanic membrane causes motion of the ossicles inside the middle ear, that results in a piston-like effect of the stapes footplate onto the oval window of the inner ear cochlea. The parameters of this motion are dependent on the intensity, frequency, and duration of the signal (20). Besides mechanical transmitting sound waves, the middle ear is important to adapt the impedance of sound waves between air and fluid mediums, which would otherwise be reflected, losing most of the sound energy (19). The most significant factors that prevent dispersion of sound energy are the difference in surface area of 14-15 times between the tympanic membrane and the oval window, and the lever mechanism provided by the ossicular chain at the oval window (18) (21) (22).

The cochlea has three separate fluid compartments, two, scala tympani and scala vestibuli, contain perilymph, similar to the body's extracellular fluid, and the other, scala media, contains endolymph, which is similar to intracellular fluids (3) (12). The basilar membrane divides scala media and scala tympany and tapers from base to apex of the cochlea. The neurosensorial hair cells lie on this membrane in a structure called the Corti organ. The inner hair cells are the auditory biotransducers translating sound vibration into electrical signals (10). Once sound waves have reached cochlear fluids, a traveling wave in the basilar membrane is stimulated. The lower chamber of the cochlea ends in the round window which acts as a pressure release mechanism, preventing echoes back down the cochlea (18). Bending of the stereocilia of the inner hair cells activates a neural-electrical potential that auditory nerve fibers of the eighth cranial nerve carry to the the auditory cortex nuclei (Figure 9).

Specific sections of the cochlea vibrate in response to sound with a particular frequency. All motions excite basal end of the basilar membrane, while only low frequencies get to the apex (18) (20). Furthermore, in the Corti organ there are outer hair cells that do not work as sensors but cause the ear to selectively change the gain of selected areas of the basilar membrane. The outer cells have very few afferent neural cells and many efferent cells, thus they appear to function in some way to control the biomechanics of the ear. It is believed that the brain sends signals back to the outer hair cells in a form of active feedback loop. This is thought to help in filtering out unimportant sounds (23).

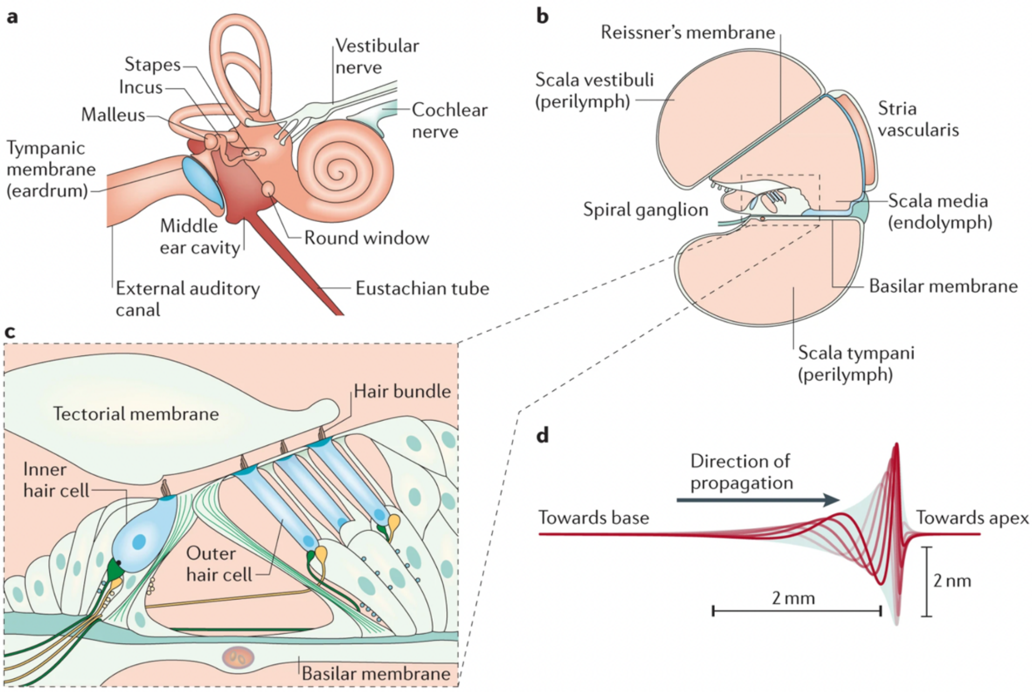


Figure 9: Cochlear structure (24).

The vestibulocochlear nerve synapses with neurons in the cochlear nuclei of the superior medulla. From here the signal is transmitted to the brainstem, in the superior olivary nucleus, then to the midbrain, to the medial geniculate nucleus of the thalamus and finally to the temporal lobe of the cerebral cortex (12) (25).

1.2 PEDIATRIC PATHOLOGIES REQUIRING TYMPANOPLASTY

Tympanic membrane perforation is a common pathology in the pediatric otolaryngological practice. Damage to the tympanic membrane in children is commonly the result of chronic otitis media, trauma from direct physical injury or head injury, or iatrogenic damage by inserting ventilating tube. Spontaneous resolution may occur but a persistent perforation can result in hearing loss and have a significant impact on development of language and school performance of pediatric population (26) (27) (28).

Otitis media is a spectrum of diseases, including acute otitis media, otitis media with effusion, chronic suppurative otitis media and cholesteatoma. These conditions are closely related and can overlap (17) (29). It is among the most common diseases in young children worldwide and it is important to prevent its recurrence in order to avoid complications and progressive hearing loss (28) (30) (31).

1.2.1 ACUTE OTITIS MEDIA AND RECURRENT ACUTE OTITIS MEDIA

Acute otitis media (AOM), also called purulent or suppurative, is characterized by the presence of middle ear effusion behind an intact tympanic membrane together with signs and symptoms of an acute infection. Ear pain is the most common symptom but not always present, especially in very young children. Bulging of the tympanic membrane during the otoscopy examination is a key diagnostic feature of AOM (Figure 10) (17) (29).

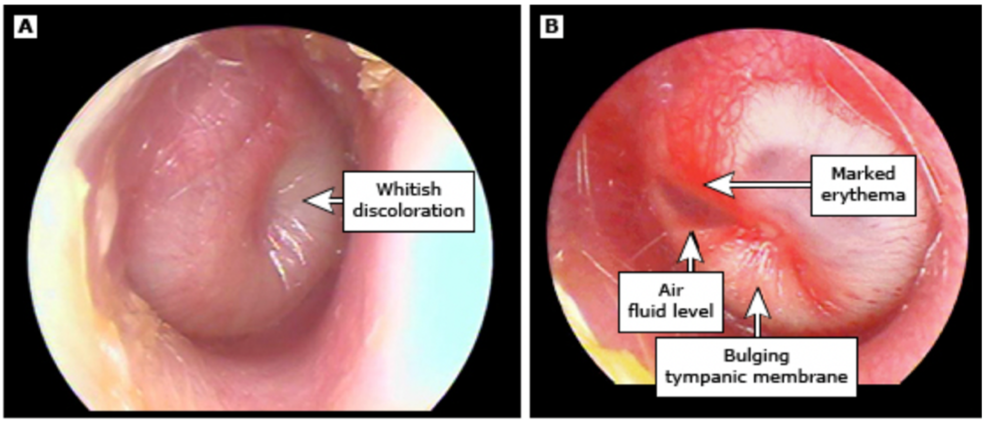


Figure 10: Examples of bulging tympanic membrane seen in acute otitis media. (A) A bulging tympanic membrane with minimal erythema. (B) Tympanic membrane bulging, marked erythema along the handle of the malleus, and an air-fluid level in the anterosuperior portion of the tympanic membrane (5).

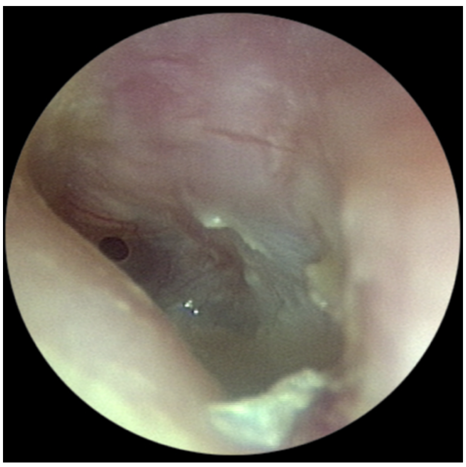


Figure 11: AOM complicated by perforation of the tympanic membrane (5).

Tympanic membrane perforation can be a consequence of the increased pressure in the middle ear cavity. It is easily identified by the presence of purulent otorrhea (Figure 11) (17) (15).

Symptomatic management of ear pain and fever with analgesics at the appropriate age-adjusted dose is the main approach for uncomplicated AOM treatment (17). Antibiotics should begiven only when there are risk factors for complications, mainly in children younger than 2 years of age with bilateral AOM and in those of any age presenting with acute ear discharge due to AOM or important comorbidities. In children with uncomplicated, non-severe AOM who are not at increased risk of complications, watchful waiting or delayed antibiotic prescription is recommended (17) (29).

Eardrum perforations allow drainage of the middle ear with rapid improvement of the symptoms. Usually, the perforation resolves on its own. If it does not heal spontaneously, it is important to seek additional intervention (4) (32).

Recurrent AOM is has been defined as the occurrence of 3 or more episodes of AOM in a 6-month period or the occurrence of 4 or more episodes of AOM in a 12-month period (that includes at least 1 episode in the preceding 6 months).These episodes should be well documented and separate acute infections (33) (34). The recurrence of AOM represents an important therapeutic challenge and prevention is the key factor. It can often result in chronic suppurative otitis media (29) (4).

1.2.2 CHRONIC SUPPURATIVE OTITIS MEDIA: EPIDEMIOLOGY, PATHOGENESIS AND RISK FACTORS

Chronic suppurative otitis media (CSOM) is one of the most common childhood infectious diseases worldwide and is a leading cause of hearing impairment in resource-limited settings (29) (4). It is a condition where there is prolonged inflammation of the middle ear mucosa and the mastoid space. This results in a chronic drainage from the middle ear associated with tympanic membrane perforation (17). It is estimated that there are 31 million new cases of CSOM per year worldwide, with nearly one-quarter occurring in children younger than 5 years old (4) (29). It occurs more frequently in resource-limited settings, with prevalence ranging from 6 to 46 percent depending on the geographic area and population studied (29). It is more commonly a unilateral disease, but it can also affect both sides. The reported frequency of bilateral disease ranges from 27 to 55 percent

(4). The complications of CSOM are a significant cause of avoidable hearing loss, particularly within developing countries.

CSOM generally results from unresolved or complicated acute otitis media. Infrequently, it can result from chronic otitis media with effusion or traumatic perforations (4) (17). It is more common in children because of the immaturity of their immune system and high susceptibility to upper respiratory tract infections. In its pathogenesis there are several factors involved, not only host related such as overproduction of mucin or decreased ciliary motion in the middle ear mucosa, and upregulation of proinflammatory cytokines, but also environmental and bacterial factors (17) (15). Studies regarding the relative frequencies of different pathogens vary depending on the geographic area and population studied. Commonly isolated bacteria include Staphylococcus aureus (methicillin-resistant and methicillin-sensitive), Pseudomonas, Proteus, coagulase-negative staphylococci, Enterococcus, and anaerobes. Polymicrobial growth is common (4). Eustachian tube dysfunction role is not fully clear yet, but it certainly has a role in the progression from AOM to CSOM. A recent literature review by Mihika Khairkar et al. explains how a tympanic membrane rupture breaks the pressure balance between middle ear, external air and nasopharynx, leading to backflow of upper respiratory pathogens in the tube (15).

Risk factors associated with this disease, other than having a history of multiple episodes of AOM or upper respiratory tract infections, are conditions that are common in resource limited settings: living in crowded conditions, low parental education level, unhygienic practices such as bathing in contaminated water, unsterile ear piercing, and cleaning ears with cotton buds. Furthermore, comorbid conditions such as cleft lip/palate, Down syndrome, Cri-du-chat syndrome, choanal atresia, and other craniofacial anomalies can predispose to CSOM (15) (17). A shared characteristic of these congenital abnormalities pertains to insufficient Eustachian tube functionality, a condition that elevates the vulnerability of affected children towards middle-ear infections (4). A history of tympanostomy tubes, which are small plastic tubes placed into the tympanic membrane to drain fluid from the middle ear, is also a potential risk factor (35).

1.2.3 CHRONIC SUPPURATIVE OTITIS MEDIA: CLINICAL PRESENTATION AND DIAGNOSIS

CSOM is clinically identified by a persistent purulent discharge from the middle ear which is not painful. The duration of the chronic discharge is of at least six weeks. If the patient is experiencing symptoms such as fever, dizziness, or pain the clinician should check for potential complications related to CSOM, like mastoiditis or intracranial infections (17) (15).

Hearing loss affects roughly 50 to 60 percent of CSOM sufferers, though the reported prevalence can differ significantly based on the criteria applied (36). It is more frequent in resource-limited settings. The hearing loss is typically a mild loss (10 to 20dB), though this may be worse with large perforations. Additionally, ossicular chain erosion can occur in some cases, causing a more profound audiologic alteration (50 to 70dB). It is crucial to exclude the presence of cholesteatoma in such instances (37). Conductive hearing loss is more common compared with sensorineural hearing loss, but both may occur (31) (30). Therefore, an important tool to evaluate children with CSOM is the audiologic assessment which allows the clinician to know the type and the degree of the hearing loss, and to detect the worse ear. Audiology investigates the ability to hear pure tones of various frequencies as a function of intensity measured in decibels (dB). The pure tone frequencies evaluated in a complete audiogram are 250, 500, 1000, 2000, 3000, 4000, and 8000 hertz (Hz). The threshold for each tone is determined by finding the intensity level at which the child can detect the tone 50 percent of the time. Hearing is tested with both air and bone conduction (4) (32). Air conduction, evaluated with earphones, tests the ability to hear when sound waves travel their normal route through the external auditory canal to the tympanic membrane. Bone conduction, performed with an oscillator placed on the mastoid bone, tests hearing by directly stimulating the cochlea and inner ear fluids through bone vibrations. Hearing loss is defined by the pure tone threshold: normal hearing has a threshold of 0 to 20 dB, mild hearing loss from 20 to 40 dB, moderate from 40 to 60 dB, severe from 60 to 80 dB. The audiogram of a child with a conductive hearing loss shows normal bone-conducted pure tone thresholds and abnormal air-conducted pure tone thresholds (Figure 12). The difference in the air- and bone-conducted thresholds is termed the air/bone gap (AB gap) (38).

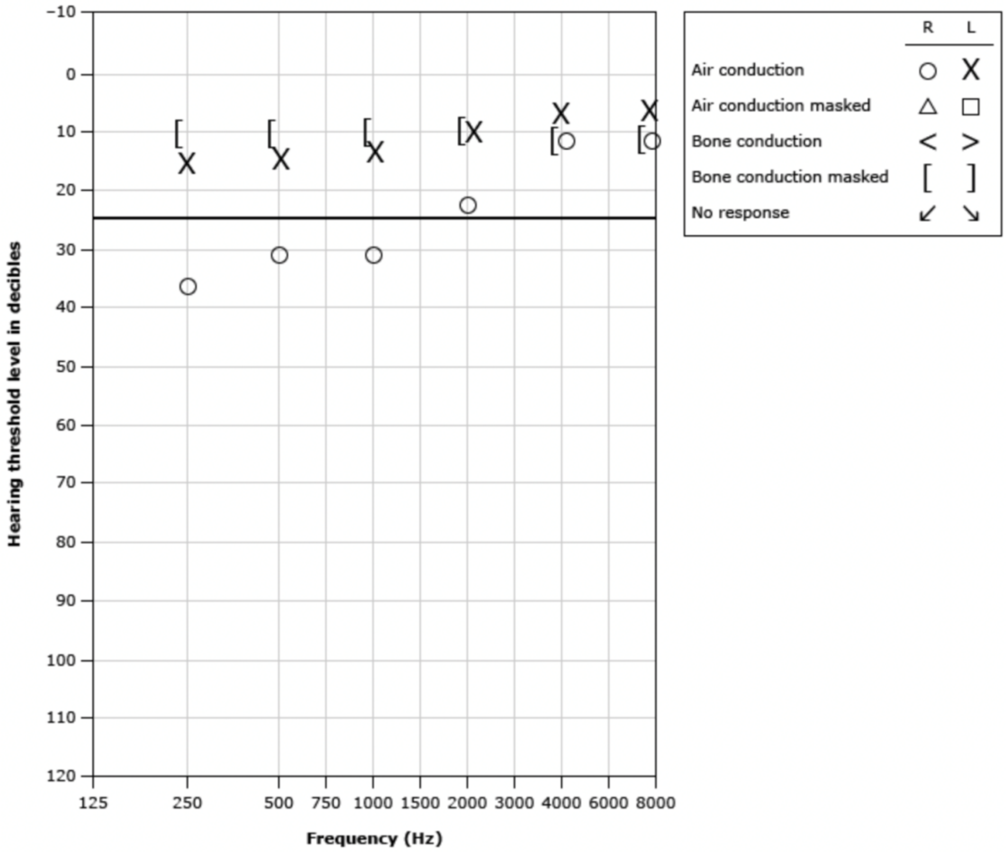


Figure 12: Conductive hearing loss audiometry (4).

In addition, to diagnose CSOM an otoscopic examination is necessary, showing perforation of the tympanic membrane and purulent discharge from the middle ear in affected patients (Figure 13) (17). A large central TM perforation is the most typical finding, while perforations in the posterosuperior quadrant are rarer (4) (17). While granulation tissue might be present, it is important to differentiate it from retraction-pocket cholesteatoma, where granulation tissue is found in the pars flaccida of the TM. It occurs in 1 to 18 percent of all patients with CSOM and it can be difficult to distinguish (4) (32).

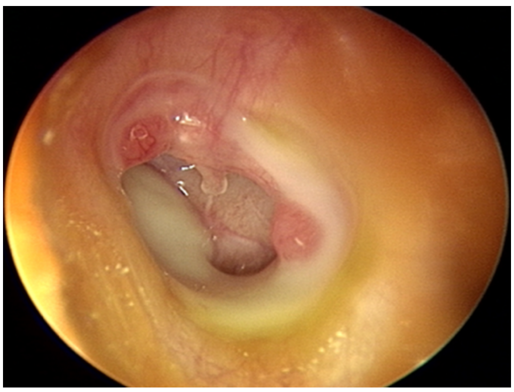


Figure 13: Draining tympanic membrane perforation in CSOM (4).

1.2.4 CHRONIC SUPPURATIVE OTITIS MEDIA TREATMENT

For patients with uncomplicated CSOM aural toilet associated with an ototopical fluoroquinolone is considered the first-line treatment approach (32) (39) .

Treatment is considered to have failed if otorrhea continues after approximately three weeks of medical therapy. It can be due to resistant organisms, poor adherence to the medical regimen, presence of a cholesteatoma, or underlying immunodeficiency (eg, HIV) (40). In case of failure, a trial of culture-directed topical antibiotics or oral antibiotics can be the next best step in the management of the disease (32). Finally, if the patient does not respond to the previous therapy, intravenus antibiotics or tympanoplasty surgery are the following approach (41) (42).

More often, CSOM is a remitting and relapsing disease. Most of the patients respond to the initial treatment but can later develop a recurrence of the disease. This is more likely to happen if the tympanic membrane remains perforated. Having an intact tympanic membrane is critical to have a safe and functional hearing system. Therefore, tympanoplasty surgery for patients with a persistent perforation of the tympanic membrane after resolution of CSOM is advocated (32) (42). Because the cochlear reserve is excellent in children, the potential for restoring middle ear function and preserving hearing is high. Early tympanoplasty can prevent ossicular damage, hearing disability and give a safe and dry ear too. However, there is much debate over the subject of tympanoplasty in the paediatric population (34) (43).

1.2.5 CHOLESTEATOMA

Cholesteatoma is characterized by the buildup of keratinized squamous epithelium in the middle ear (10) (44).

In children, there are two different types of cholesteatoma: acquired, which also affects adults, and congenital, which is specific to childhood. Various etiopathogenic theories have been proposed to account for the two forms of cholesteatoma. Despite recent research, the underlying mechanisms remain unknown (45) (44).

According to the retraction pocket theory, also referred to as a primary type cholesteatoma, an underlying Eustachian tube disfunction leads to poor aeration of the epitympanic space. This causes the pars flaccida, pars tensa or both to be drawn medially by retraction to the top of the malleus neck, forming a retraction pocket (44). This restricts the physiologic self-cleaning ability of the tympanic membrane enhancing the potential risk for keratin debris accumulation, allowing the enlargement of the formed sac (46). The epithelial migration theory suggests that tympanic membrane perforations allow squamous epithelium to move into the middle ear (44) (47). The squamous metaplasia theory, proposes that that chronic or recurrent otitis media causes the desquamated epithelium in the middle ear to transform into a keratinizing stratified squamous epithelium, which then develops into a cholesteatoma (48) (49). The basal cell hyperplasia theory propose that papillations, pseudopods or microcysts filled with keratin formed in the basal cell layer of the pars flaccida epithelium, invade the subepithelium of Prussack's space (49). An inflammatory reaction, possibly due to poor ventilation, may then compromise the basal membrane allowing a cord of epithelium to start inward proliferation (44).

A critical aspect of cholesteatoma is its inability to heal on its own. Instead, it tends to progressively expand into the middle or inner ear, or even beyond the temporal bone. Despite its name, cholesteatoma is a benign disease, it is not a tumor and does not metastasize, but if left untreated it can lead to significant morbidity and even mortality, due to its destructive character (44) (49) (45) (3).

To begin with, cholesteatoma destroys the ossicular chain, causing conductive hearing loss. Later, destruction of the bony facial canal wall can result in a slowly progressive facial palsy (10) (45). With constant growth, cholesteatoma can thin out the bone of the labyrinth, resulting in a labyrinthine fistula, which is located most often in the lateral semicircular canal due to its proximity to the middle ear cleft (47). This lesion is associated with vertigo and the characteristic fistula symptoms (10) (44). Further progression of the inflammation may lead to sensory hearing loss too (46). With further advancement the cholesteatoma can reach the brain and if so, it can be the trigger for serious, life-threatening conditions such as meningitis, encephalitis or brain abscesses (10).

Acquired cholesteatoma becomes usually symptomatic with othorrea. The discharge is purulent and may be foul smelling and on clinical examination, the presence of abundant granulation tissue may accompany the drainage (50) (44) (10). Acquired cholesteatoma tends to be more severe in children than in adults for several reasons: it is often more widespread when first detected; the condition of the ossicular chain is usually worse due to greater ossicle degradation; and there is a higher likelihood of recurrence and remaining lesions. This greater severity in pediatric cases is often attributed to unique aspects of the

cholesteatoma matrix in children and/or persisting predisposing factors such as poor ear ventilation (45) (51).
Assessment of cholesteatoma consists of a thorough otologic history and otomicroscopy examination (Figure 14).

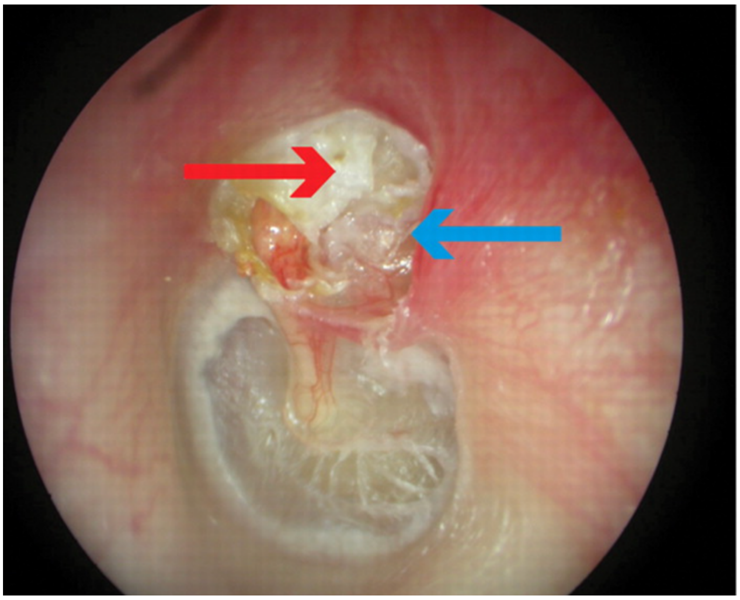


Figure 14: Cholesteatoma (red arrow) arising in the upper part (pars flaccida or "attic") of left tympanic membrane. Note erosion of surrounding bone (blue arrow) (10).

Temporal bone CT assesses cholesteatoma extension, exploring complications and detecting anatomic variants so as to prepare for any difficulties in surgery (47) (44) (10). The prime objective of therapy is to eradicate the disease to restore a healthy aerated ear. Equally important is to restore or improve the ossicular chain functionality. Since no conservative treatment option exists, cholesteatoma must be surgically removed (10). Only if surgery has to be postponed, conservative treatment with meticulous cleaning of the debris and drying the sac, together with microscopic control of the progression, may be an option (50) (52). Given the variability of the local extension of the cholesteatoma, the surgical approach, excision and reconstruction need customized to the anatomy and extent of the disease in each individual patient (45) (44).
Congenital cholesteatoma is typically an expanding cystic mass of keratinized squamous epithelium located medial to the intact tympanic membrane (44). The most popular theory on its formation claims that rests of epithelial cells, otherwise referred to as an epibranchial placode, are located behind an intact tympanic membrane and fail to involute (53). An additional theory of formation, the invagination theory, helps to explain the existence of lesions that are not located in the anterosuperior quadrant of the tympanic

membrane. In fact, it proposes that squamous epithelium from the external canal migrates through the tympanic ring into the middle ear, eventually forming into a congenital cholesteatoma. In utero or during childhood, an inflammatory injury to the tympanic membrane induces invagination leading to development of a congenital lesion (54) (44). In this case, the tympanic membrane is adherent to the malleus or incus and leaves behind a remnant of keratinized epithelium which over time then forms a cholesteatoma (55).

Congenital cholesteatoma often develops subtly, with unilateral hearing loss frequently going unnoticed in children, which allows the growth of larger lesions until they are incidentally detected during routine exams. Hearing impairment becomes noticeable when the cholesteatoma is substantial enough to occupy the middle ear and begin to erode the ossicles (56) (44) (10).

1.3 TYMPANOPLASTY SURGERY

1.3.1 INDICATIONS, GOALS AND CLASSIFICATION

Tympanoplasty is the surgical repair of the tympanic membrane and/or the middle ear ossicles and its main indications in the pediatric population are chronic otitis media, cholesteatoma, iatrogenic perforation in patients with tympanostomy tubes or, rarely, traumatic membrane perforations inflicted by mechanical trauma that did not heal (37) (17) (57).

Tympanoplasty is indeed the gold standard treatment for chronic otitis media with perforation of the tympanic membrane that does not heal with medical treatment (32). The objectives of surgery for chronic otitis media are elimination of disease to produce a safe and dry ear and to prevent recurrent disease, and reconstruction of the middle ear to achieve stable postoperative hearing. This is made possible by restoring sound pressure transformation at the oval window by coupling an intact tympanic membrane with an intact or reconstructed ossicular chain (1) (27).

Depending on the tympanic cavity structures addressed by the surgery, tympanoplasty can be classified into specific subtypes. In Manual of Middle Ear Surgery (1993) M. Tos identifies:

- Myringoplasty: repair of the tympanic membrane alone.
- Type I tympanoplasty: in cases with an intact ossicular chain at the end of the operation. It can involve manoevers to achieve removal of adhesions around the ossicles or the elimination of pockets.

- Type II: ossiculoplasty in cases with a defective ossicular chain but with the stapes present. It includes interposition techniques between the head of the stapes and the malleus handle or the grafted eardrum remnant.
- Type III: ossiculoplasty in cases with absence or severely defective stapes superstructure. Columella techniques are used to go from the footplate to the malleus handle or the grafted eardrum.
- Type IV: it involves protection of the round window in cases with absent ossicles but with an intact and mobile stapes footplate.
- Type VA: fenestration of the lateral semicircular canal in cases with no ossicles and a fixed footplate.
- Type VB: the stapes footplate is removed (platinectomy) in cases with a fixed footplate and no ossicles (2).

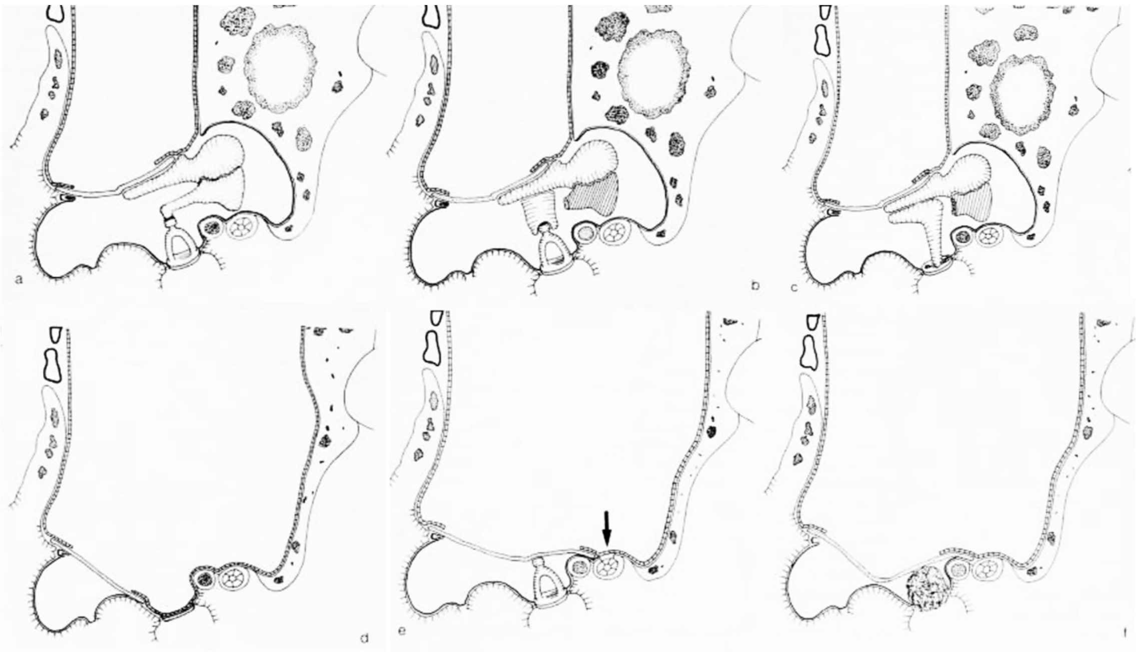


Figure 15: A Type I, B type II, C type III, D type IV, E type VA, F type VB tympanoplasty (2).

However, inflammatory processes in CSOM have the potential to extend beyond the tympanic cavity. Therefore, classification of tympanoplasty should also consider the paratympanic cavities and structures such as the posterior wall of the ear canal, whose integrity or sacrifice becomes an integral part of more extensive tympanoplasty surgeries (58) (2) (59). Zini et al. in 1983 distinguished:

• Open Tympanoplasty or Canal Wall Down Tympanoplasty (CWDT), which requires demolishing the posterior wall of the external auditory canal, thereby externalizing the epitympanum and mastoid. The posterior canal wall of the external auditory canal is the structure that divides the external auditory canal lumen and the mastoid. Therefore, open tympanoplasty require mastoidectomy as part of the surgical steps. This allows part of the middle ear to be aerated and drained through an appropriately enlarged external auditory meatus. A functionally smaller tympanic cavity is reconstructed, drained and aerated through the Eustachian tube, and the tympano-ossicular apparatus is repaired or reconstructed.

• Canal wall Down Tympanoplasty with obliteration: it differs from the open tympanoplasty as it reduces the size of the tympanic cavity by obliterating the attic-mastoid space.

• Closed Tympanoplasty or Intact Canal Wall Tympanoplasty (ICWT), which aims at preserving or reconstructing the posterior wall of the external auditory canal, preserving the tympano-ossicular system in its original position.

1.3.2 SURGICAL APPROACH

Traditionally, tympanoplasty surgery is performed with a microscopic approach, which helps magnifying the small structures of the middle ear, although recently the endoscopic approach has become popular (59). It is less invasive, but it has some disadvantages such as performing with one hand and the potential harm caused by heat production from the endoscope's light source to surrounding structures (14).

With regards to the microscopic approach, most of the tympanic surgery is performed using a postauricular access, which is realized through a semicircular incision roughly 1cm posterior to the auricle skin fold (Figure 16A). The superior portion of the incision is elevated laterally to provide easy access to the temporalis fascia and, after dissecting the subcutaneous soft tissues, an anterior periosteal flap is raised off the mastoid bone. With that, followed by a meatal skin flap, the posterior ear canal lumen becomes visible (59) (60) (2).

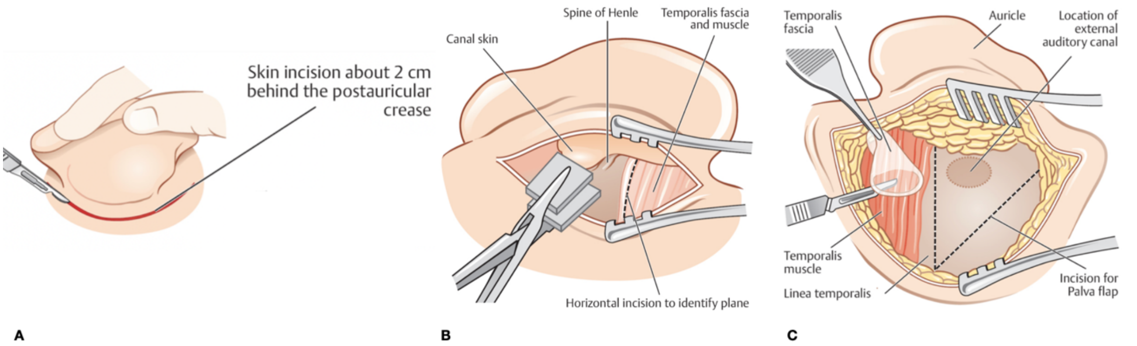


Figure 16: Postauricular approach: A skin incision, B exposure of the temporalis fascia, C Palva flap (60).

Endaural (through the ear canal) and transcanal approaches can also be used. Each technique has advantages as well as limitations; factors that need to be considered when deciding which approach to use include the size of the tympanic membrane perforation, the size of the ear canal, and the preference of the surgeon (37).

The transcanal approach is performed through an ear speculum placed in the external ear canal. Because exposure is one of the limiting factors of this approach, its use is limited to repairing traumatic perforations or in cases where there is a wide ear canal with a posterior perforation (60). The ear canal must be wide enough, and one should be able to visualize the entire margins of the perforation; most often this would apply to posterior perforations. The anterior margin of an anterior perforation may be obscured by an overhanging canal wall (60) (2).

The endaural approach entails making an incision between the tragus and helix; the entrance to the ear canal is then stretched open with endaural retractors. It is a good approach to use for posterior perforations. While the view is better than with a transcanal approach, it is not suited to anterior perforations either (60) (2).

1.3.3 TYMPANOPLASTY: GRAFT MATERIALS AND TECHNIQUES

Autologous materials for tympanic membrane grafting are the most common choice for tympanoplasty surgery as they are biocompatible and cost-effective, offering limited justification for the use of synthetic substitutes. Typically, grafts are derived from the patient's own temporal fascia or tragal/conchal perichondrium. Temporalis fascia is more frequently used by surgeons, showing success rates of 93% to 97% (37) (60). Cartilage is usually a better option when greater stability is needed, for example in case of repeated perforations or surgery in high-risk individuals. Temporalis fascia is obtained during the first steps of tympanoplasty and subsequently flattened to extract the moisture from the graft. Next, it is allowed to dry and cut into shape (61).

Such autologous grafts for reconstructing the tympanic membrane are most inserted using an underlay technique (undermining the limbus, lifting the tympanic membrane, and covering the defect with the graft from the medial side), owing to its relative ease of use and high success rate. While this approach is generally very good for most perforations, limitations include recurrent perforations and perforations located anteriorly, or subtotal in extent. In these instances, some otologists prefer lateral grafting (overlay technique) which places the graft material between the inner middle ear mucosa and outer squamous epithelial layers of the tympanic membrane, thereby replacing the fibrous layer (10) (3). Since no tympanic remnant is required, subtotal perforations seem to be well manageable via lateral grafting.

All these techniques rely on the induction of epithelial migration by excision of the pathologic mucocutaneous junction at the margin of the perforation. In overlay tympanoplasty both epithelial layers migrate across their respective surfaces to re-epithelize the structure and incorporate the graft material to the new tympanic membrane. By contrast, underlay tympanoplasty techniques place the graft material exclusively medial to both the mucosal and outer epithelial surfaces of the membrane, therefore initially relying on the graft material as a scaffolding for outer layer migration. Subsequently, the inner mucosal layer migrates with incorporation of the graft material (60) (10).

To perform the underlay technique, a tympanomeatal flap is needed (59). Firstly, the tympanic perforation is inspected and the mucocutaneous junction of the perforation is excised to encourage vascularization of the graft. Subsequently, a tympanic membrane-ear canal skin flap is elevated, and the middle ear is entered medial to the fibrous tympanic annulus. Irrespective of the materials used, the underlay method requires placement of the graft in direct apposition with the undersurface of the TM remnant and completely covering the perforation (Figure 17). Finally, absorbable collagen sponges or analogous materials are used to keep the graft in place and the ear canal is packed with similar materials too (2) (60) (58).

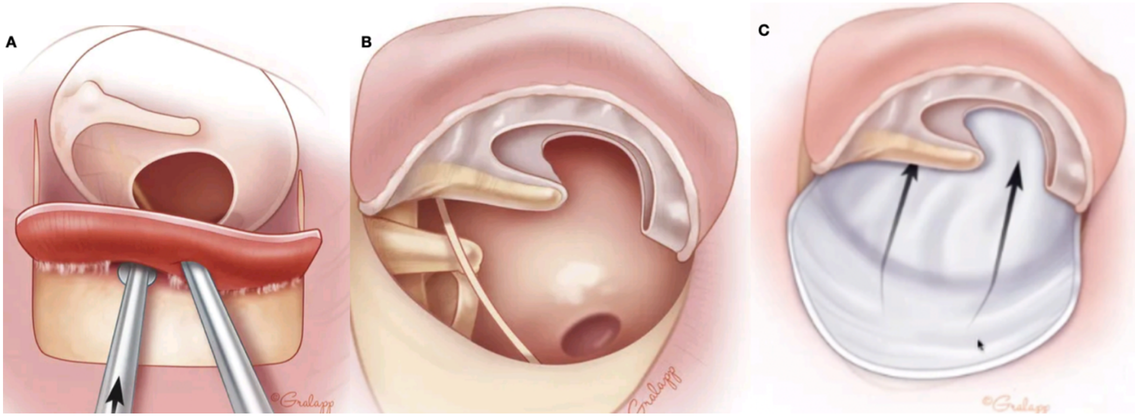


Fig. 17: Underlay technique steps: A Creation of a tympanomeatal flap, B tympanomeatal flap folded forward, C fascia graft positioned under the membrane remnants (60).

The mechanism of tympanic repair is different in lateral grafting. Specifically, a vascular strip flap and a canaloplasty are required, whereas in the underlay technique these steps are not always necessary. A vascular strip is a flap created to move the posterior superior ear canal skin (the vascular strip) laterally into a protected area to provide exposure of the tympanic membrane (2) (56). This flap requires two vertical incisions, one roughly in line with the tympanomastoid suture and one with the tympanosquamous suture. The postauricular approach can then be completed and the previously created canal incisions can be found from behind. Canaloplasty is performed to visualize the entire extent of the tympanic annulus. After harvesting a temporalis fascia graft and removing the anterior canal skin at the tympanic annulus, the entire circumference of the bony ear canal is exposed. Tympanic membrane remnant are deepithelialized to avoid entrapment of squamous debris and subsequent cholesteatoma formation. The fibrous layers of the tympanic annulus and the tympanic membrane can be left in place. Finally, the graft has to be inserted under the malleus handle. To do so, a slit is cut in the fascia to allow for placement medial to the malleus handle (Fig. 18) . Once an adequate position of the graft has been obtained, the anterior canal skin is placed back onto its previous site and tight packing is applied. Lateral grafting typically requires a healing period of several weeks (10) (59) (60).

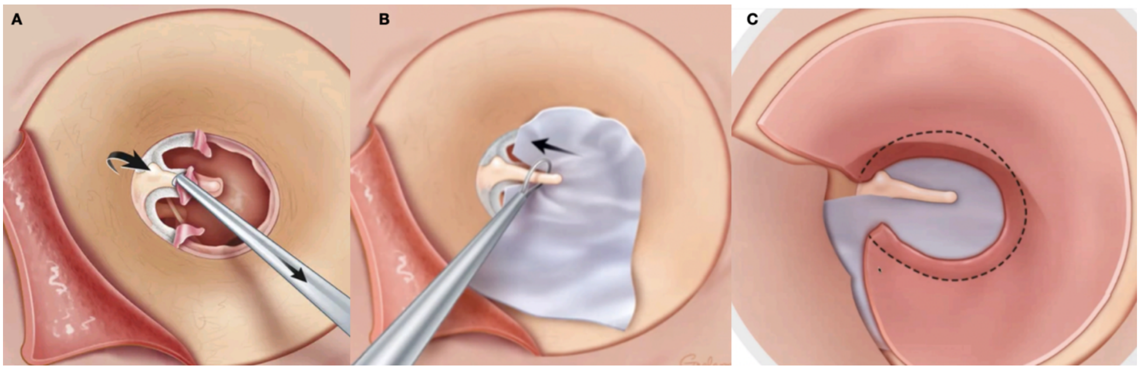


Figure 18: Overlay technique steps: A removing squamous layer from the tympanic remnants, B placement of the fascia lateral to the tympanic membrane but medial to the malleus handle, C replacement of the free graft (60).

1.3.4 OSSICULAR CHAIN RECONSTRUCTION

While it is generally possible to ascertain the need for ossiculoplasty during the preoperative evaluation based on the audiogram and physical exam, one should be prepared for this necessity in every middle ear case (62). The reconstructive measures for the ossicles vary according to the location and extent of the ossicular defect but they all have the same goal which is providing a stable and long term durable sound conduction between the tympanic membrane and the inner ear (59) (60).

The materials currently used are autografts and allografts. Autologous grafs are the most biocompatible and tend to maintain their configuration over time through bone substitution (61). The incus remodeled is used most commonly. Allografts are manufactured in two configurations: a partial ossicular replacement prosthesis (PORP) is used when the stapes superstructure is present, and a total ossicular replacement prosthesis (TORP) when it is absent (2) (59). Many variations are possible in the shape of the prosthesis portion which connects to the tympanic membrane; some contact the undersurface of the membrane, whereas others are designed to conform to the undersurface of the malleus. There are three main groups of allografts: polymers, ceramics and metals. Titanium prostheses are in widespread use; they combine low weight and high rigidity, and it is the closest in mass to the ossicles it tries to replace. These characteristics lead to reduction in acoustic impedance and sound damping, particularly for high frequencies (63) (1).

In type II and III tympanoplasty, the ossicular chain is repaired such that the lever mechanism, which is a normal function of the malleus and incus, is restored. Continuity of the ossicular chain in type II can be restored through mechanisms of interposition, transposition or pexis (57) (2). Interposition means placing an ossicle or any other prosthesis between the stapedial arch and the malleus handle or drum. Transposition refers to procedures in which an ossicle is still partly attached to its origin but is transposed onto the stapes. In pexis, the drum or malleus handle can be connected, without interposition, to the remaining part of the ossicular chain, particularly the head of the stapes. Type III tympanoplasty, which is performed when there is a missing or severely defective stapedial superstructure, involves building a columella between the footplate and the malleus or tympanic membrane (59) (60).

1.3.5 TYMPANOPLASTY OUTCOMES AND PROGNOSTIC FACTORS

Tympanoplasty is a unique surgery because of the constraints imposed by a combination of factors, including the air-bone interface, the complex interconnection of all the middle ear components, and the very small area of the middle ear cavity (37) (64) (65). Moreover, the achievement of a restored middle ear anatomy does not guarantee a good hearing functionality (66) (34).

Surgical success is indeed often measured in terms of both anatomical restoration of middle ear and audiological outcomes. With regards to the first parameter, in the existing literature tympanoplasty shows a broad spectrum of success rates in the pediatric population. The most recent evidence ranges from 76% to 92% (67) (43) (64) (68) (69) (70). In a meta-analysis on tympanoplasty in children, Hardman from University Hospital of Coventry and Warwickshire reported a mean tympanic membrane closure rate (after 12 months) of 83.4% in 2015 (71). The table below shows a literature overview done by Mantsopoulous K. et al. where the anatomical success rates of different papers have been collected.

First author (year)	N	Age (years)	Follow-up (months)	Success rate (%)
Buchwach (1980) [41]	80	9 (3–17)	25.2	66
Kumar et al. (2010) [16]	132	10.6 (6–15)	≥12	67.3
MacDonald et al. (1994) [32]	29	10 (5–16)	15 (2–47)	69
Knapik et al. (2011) [14]	201	11 (3–18)	≥24	70.1
Halim et al. (2009) [27]	218	10 (4–18)	≥7	71.6
Charlett SD et al. (2009) [29]	213	12.1 (4–15)	16 (2–99)	71.8
Duval M et al. (2015) [28]	284	2–13	7.5 (1–106)	72.5
Koch et al. (1990) [31]	64	2–17	23.4 (6–67)	73
S. Barrueco A et al. (2015) [24]	142	10.1 (5–14)	≥12	74.6
Black (1995) [12]	93	10.9 (2–17)	8.8 (6–24)	75.3
Shih et al. (1991) [42]	59	10 (6–16)	11 (1–72)	76
Takahashi-Tatsumi (2013) [43]	67	8.7 (2–16)	40.7 (12–113)	81
Collins et al. (2003) [23]	72	10.3 (3–18)	12.5 (1–74)	82
Lou et al. (2020) [4]	93	15.1 (10–18)	≥24	82.8
Rozendorn et al. (2016) [33]	165	11.7 (4.8–17.9)	≥6	83
Emir et al. (2007) [13]	131	<16	≥12	83.2
Hardmann et al. (2015)	2609	11.4 (2–18)	≥6	83.4
Sckolnick et al. (2008) [22]	777	7.1	5.6	87.3
Umapathy et al. (2003) [44]	89	4–14	34 (12–72)	90
Dursun E et al. (2020) [3]	62	12.7	28.8 (7–78)	91.9
Chandrasekhar et al. (1995) [19]	268	10 (1–19.5)	37 (6–168)	92.5
Bartel R et al. (2019) [2]	54	10.7 (7–16)	≥6	92.6
Denoyelle et al. (1999) [35]	231	10.5 (4–17)	31 (≥12)	93.5
Özdemir et al. (2019) [5]	50	13 (9–17)	≥6	94
Friedmann et al. (2013) [21]	119	4–13	19 (1.5–56)	95

Table 1: Literature overview with information on the size of the patient population, age, follow-up time and anatomical success rate (69).

Conversely, the percentage of cases with a postoperative air-bone gap below 20dB was 76.7% in Hardman's study. A postoperative airborne gap of 20 dB (dB) or less is indeed advocated as a functional success, although in literature there are many inconsistencies in the reported audiological outcomes (28) (34). To mention more recent studies, the results of B. Harsimran (43) and A. Goncalves (70), respectively of 75% and 87% postoperative airborne gap of 20 dB or less, are quite consistent with the result of the previously mentioned meta-analysis.

The reported variability of pediatric tympanoplasty's success underlines how the achievement a functioning middle ear requires more than an intact graft. A good

Eustachian tube functionality is certainly critical, especially for middle ear ventilation, but is usually achieved with advancing age in children. This is one of the reasons why age and tube function are debated as a prognostic factor for the outcome of tympanoplasty. As the Eustachian tube function is thought to be symmetrical, the finding of a pathologic contralateral ear seems to be the best parameter to evaluate tubal function and to predict poor bilateral ear ventilation and a worse outcome (64) (72) (71). However, the results of many papers on the prognostic role of the contralateral ear status are contradictory as shown in the table below (Table 2).

	Significant	**Not significant**	
Age	Raine 1983 Kessler 1994 **Vrabec 1999 (metanalysis)** Trabalzini 2022 Haci 2023	Sadè 1981 Caylan 1998 Carr 2001 Abood 2012 **Hardman 2015 (metanalysis)** Rodrigues 2017	Baklaci 2018 Zhan 2019 Abood 2020 Marquez 2021 Foulon 2022
Contralateral ear status	**Hardman 2015 (metanalysis)** Baklaci 2018 Haci 2023	Pignataro 2001 Abood 2012 Zhan 2019 Marquez 2021	
Previous adenectomy	Foulon 2022 Hamans 1996 Characon 1984	**Vrabec 1999 (metanalysis)** Abood 2012 **Hardman 2015 (metanalysis)**	
Previous ventilation tube insertion	Ophir 1987 Zwierz 2019	**Foulon 2022**	
Middle ear mucosa status	Zwierz 2019 Mantsopoulos 2021 Goncalves 2021	Denoyelle 1998 Vrabec 1999 (**metanalysis**) Albera 2006	

Table 2: The table shows papers in literature that found a significant or non-significant statistical correlation between age, contralateral ear status, adenectomy, mucosa status and tympanoplasty success.

The definition of contralateral ear status in different studies has included all possible abnormalities such as perforations, tympanostomy tubes, atelectasis and effusive otitis media and this explains the variability of the results (71) (34). Besides the immaturity of the Eustachian tube, age is often proposed as a significant parameter to consider for tympanoplasty as younger children have lower immunity and recurrent upper respiratory tract infections, as well as a narrow ear canal. In addition, the rate of spontaneous perforation closures that is not to be disregarded (34) (69). Consequently, timing of surgery is a matter of debate, with opinions divided between delaying surgery to allow for physiological development of the child and choosing earlier intervention to prevent complications. A recent paper on the matter by Abdood A. et al. analyzed 180 pediatric tympanoplasty surgeries to determine whether age had an influence or not on the outcome and did not find a correlation. The image below shows the age distribution related to surgical success rates found in the study (Figure 19) (27).

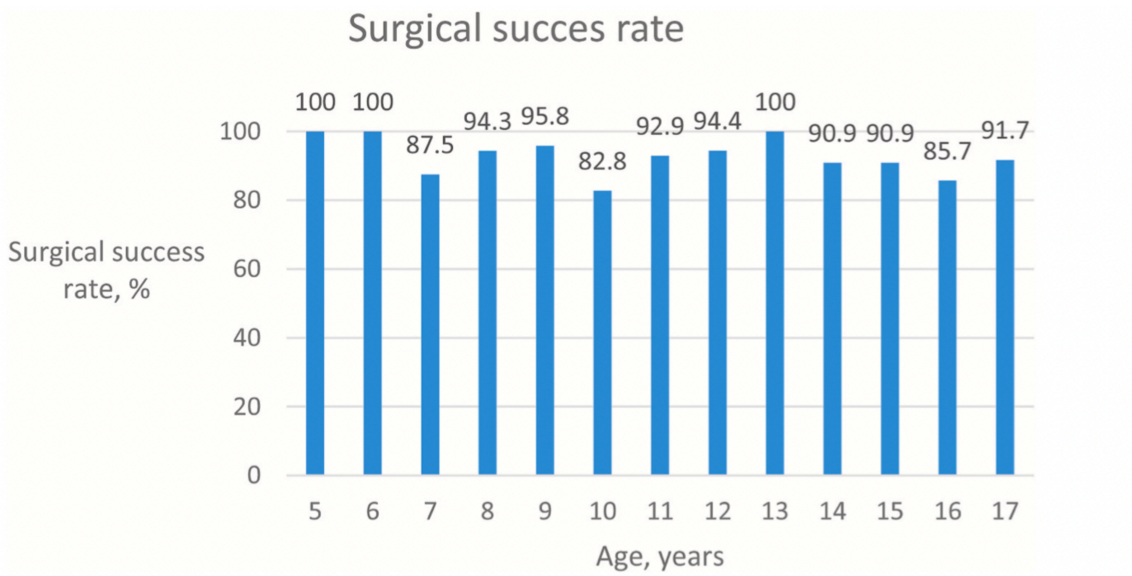


Figure 19: Surgical success rates at different ages. Fisher's exact test was used to test for potential differences among ages. No statistical significance could be found (27).

Other debated prognostic factors mentioned in table 2 are history of adenectomy, and state of middle ear mucosa. A few papers demonstrated that chances of success were higher in children with a history of adenoidectomy, claiming that ears with mechanically obstructed Eustachian tubes due to adenoid hyperplasia have a worse outcome (28) (66). Active middle ear inflammation is often believed to be a contraindication for tympanoplasty because of the longer surgery, greater blood loss and worse operative conditions (66). Denoyelle F. et al. (73) also stated that otorrhea and middle ear inflammation have an impact on middle ear effusion, reperforation rate and retractions. Conversely, many authors reported good results in this group of patients too, and a recent study of R. Caylan even claimed better results in children with otorrhea (74).

Finally, different surgical techniques, in terms of approach, graft materials and underlay versus overlay technique, have also been proposed as prognostic factors. A meta-analysis study conducted by Lyons et al. showed no difference between the cartilage graft and the fascial graft (75). A systematic review by F. Chatelet et al. compared 70 papers on pediatric tympanoplasty surgeries with different techniques, including techniques without elevation of the tympanomeatal flap too, and no significant differences emerged (76). The recent introduction of the endoscopic approach tympanoplasty has made necessary the comparison with the traditional microscopic approach. A study conducted by Sungsu Lee and Hyong-Ho Cho demonstrated that endoscopic approach offers similar surgical results compared to traditional microscopic technique (77).

Overall, despite the many published papers on the subject, there is no universal agreement on surgical prognostic factors (64) (28). The consensus is that the respective ear surgeon should weigh up the benefit of the perforation seal against the risk of possible re-perforation or the future need for a ventilation tube insert due to persistent tube dysfunction in each individual case (69) (34). When surgery is successful it has been demonstrated that quality of life, mental and language skills and children's development are thus positively influenced by the operation. Furthermore, irreversible complications of a chronification of a tympanic perforation such as ossicular erosion and migration of squamous epithelium is prevented (34).

2 THESIS PURPOSE

All the cases of pediatric patients who underwent tympanoplasty, with or without ossiculoplasty, in our department between 2010 and 2023 have been analyzed. The main objective was to evaluate anatomical and functional outcomes of pediatric tympanoplasty and determine the prognostic factors that influence the success of this surgery.

3 MATERIALS AND METHODS

This study was conducted at the Department of Otorhinolaryngology of Ospedale Maggiore della Carita' in Novara.

This is a retrospective study, where all records from a pediatric population, undergoing tympanoplasty between 2010 and 2023, were examined. Patients under 18 years old with chronic otitis media were included in the study. Patients with cholesteatoma and patients with a prior surgery on the same ear were excluded.

Of all patients the following were examined:

- personal data and clinical history: age, sex and comorbidities (craniofacial dysmorphism and other pathologies with Eustachian tube dysfunction)
- previous adenoidectomy or placement of transtympanic ventilation tubes
- characteristics of the pathology: affected side, amplitude of the perforation, duration of ear discharge and contralateral ear status
- clinical examination
- preoperative pure tone audiometry
- technique of the undergone surgery: retro-auricular or endaural approach, graft materials
- follow-up findings.

The clinical examination involved otomicroscopic or endoscopic examination of both the ears, noting the size and site of the TM perforation and the condition of the middle ear mucosa. Nose and throat examinations were done to find out any associated pathology. To assess the functionality of the ears audiometry tests were then performed to know the type & degree of hearing loss and to detect the worse earing cases of bilateral disease. Audiological results were recorded as air-bone (AB) gap (calculated as an average of the difference between air conduction and bone conduction at 500, 1000, 2000 and 4000 Hz.

In the surgeries of our database the retro-auricular approach was adopted for all the patients and all surgical treatment were performed with a microscopic approach. Some patients underwent myringoplasty only, other patients ossiculoplasty too. Two types of graft materials for the tympanic membrane were used: temporalis fascia or cartilage graft.

A short term and a long term follow up were done postoperatively. On each visit, patients were examined otomicroscopically or endoscopically for intactness of tympanic membrane graft and hearing status was assessed by pure tone audiometry.
Anatomical success was defined as the presence of an intact graft without residual perforation. A successful functional result was defined as a postoperative AB gap less of 20 dB (dB). The occurrence of improvement or worsening in the long term compared to the short term was also evaluated.
Among the collected data, the investigated prognostic factors for tympanoplasty were: age at surgery, health status of the contralateral ear, history of adenectomy and tympanostomy tube placement, and type of surgery. They were statistically compared to both the anatomical and functional success.

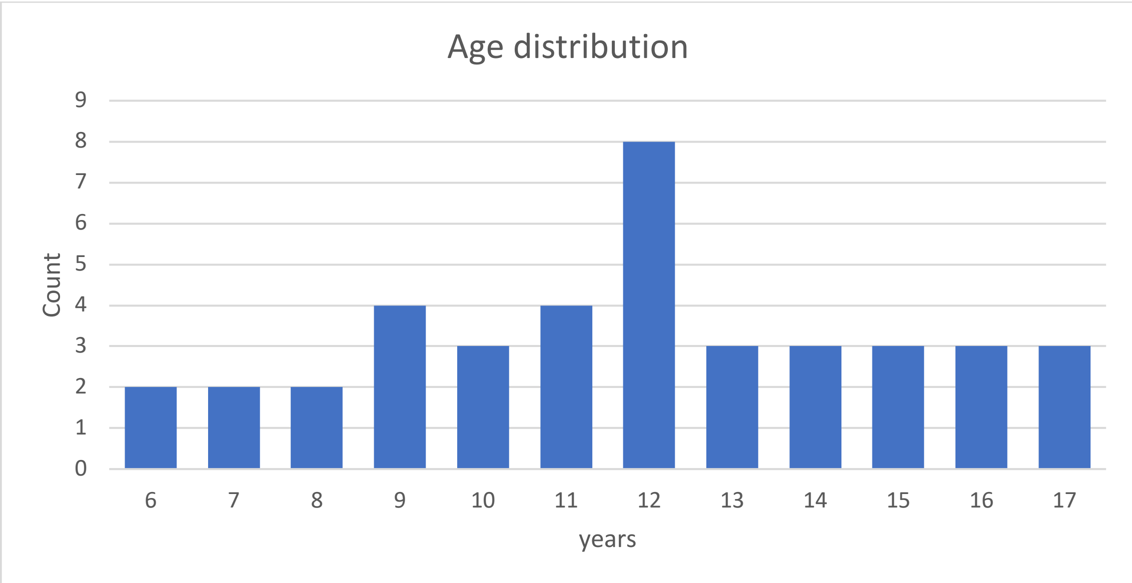
Descriptive statistics are presented as frequencies (n) and percentages (%) for categorical variables and means and standard deviations for continuous variables. To test the relationship between possible prognostic factors on tympanoplasty a Fisher's Exact test was used to compare categorical variables and the Mann-Whitney test for continuous variables. All tests were performed at a significance level of 0.05. The analyses were executed using STATA SE.

4 RESULTS

4.1 PREOPERATIVE RESULTS

From 2010 to 2023 53 pediatric patients underwent tympanoplasty in our department for chronic otitis media. Of these, 4 (7.5%) patients were operated on both ears, resulting in a total of 57 cases. A total of 17 (32%) of the patients who underwent unilateral surgery were lost to follow-up.

A total of 36 patients (40 surgeries) underwent post-operative follow-up and were included in the study. Of these patients the mean age was 11.8 years (SD 3.07). 14 children were between 6 and 11 years of age, while the other 22 were older than 12 years. The age distribution is shown in the graph below:

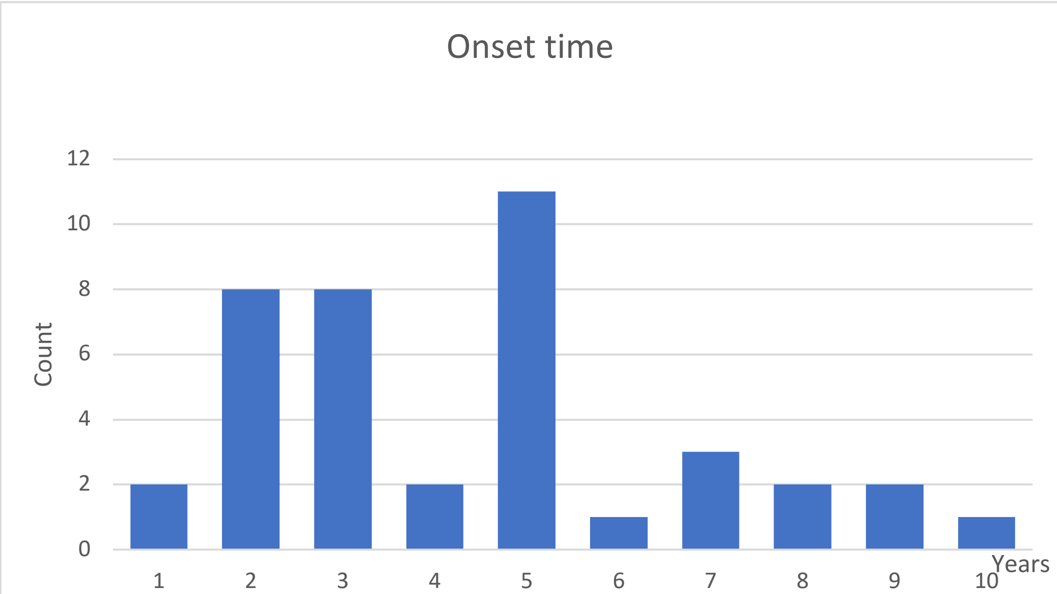


Graph 1: the age distribution of the patients in our study.

The tympanic membrane perforation cause was chronic otitis media in all cases, involving the right side in 19 (48%) cases and the left side in 21 (52%) cases. The perforation was subtotal in all cases and the mean time between surgery and beginning of the pathology was 4.4 years (52.8 months*) (Graph 2)*.

No comorbidities were found in the selected patients. The evaluation of the preoperative prognostic variables shows 13 (32%) cases with a former adenoidectomy and 4 (10%) with a tympanostomy tube placement.

From otoscopic examination a healthy contralateral ear was found in 29 (73%) cases, whereas 11 (27%) patients had a perforation or chronic otitis media in the contralateral ear too *(Table 3)*.



Graph 2: Onset time of pathology.

The surgical approach was identified based on the otologic history, audiologic and microscopic examination, risk of recurrence of the disease and the ossicular chain status. The approach was retro-auricular in all the surgeries. Underlay myringoplasty was performed in 21 (53%) cases, overlay myringoplasty in 15 (37%) cases and closed tympanoplasty in 4 (10%) cases. The graft material used to repair the tympanic membrane was the temporalis fascia in 36 (90%) patients and in the remaining 4 cases (10%) perichondrium cartilage of the tragus was used.

The collected audiometric exams showed a pre-operative AB gap of > 20dB in 24 (60%) cases, <20 and >10 in 10 (25%) cases and <10 in 6 (15%) cases.

Pre operative and intra-operative factors	n	%
Former adenoidectomy		
yes	13	32.50
no	27	67.50
Former tympanostomy tube		
yes	4	10
no	36	90
Healthy contralateral ear		

yes	29	72.50
no	11	27.50
Affected side		
Right	19	47.50
Left	21	52.50
Surgery		
Underlay myringoplasty	21	52.50
Overlay myringoplasty	15	37.50
Closed tympanoplasty	4	10
Graft		
Temporalis fascia	36	90
Pericondrium cartilage	4	10

Table 3: Preoperative and intraoperative factors.

4.2 SURGICAL RESULTS

Postoperatively, the anatomical success, defined as a closed tympanic membrane after surgery, was achieved in 31 (78%) patients. Only 5 (13%) patients had a residual perforation, while epitympanic retraction was found in 3 cases (7%) and blunting in one case (2%) at the microscopic follow up.

Similarly, the functional success was achieved in 30 (75%) cases in the short term, with 20 (50%) <10 dB AB gaps and 10 (25%) <20dB AB gaps. Only 10 (25%) cases did not have an improvement in the AB gap. At the long-term follow-up 3 cases which had not achieved a AB gap <20dB improved, two of which demonstrated a AB gap <10dB. Conversely, 3 cases with a short-term AB gap <20dB worsened in the long-term with an AB gap >20dB. The mean follow up duration was 87.4 months (7.3 years, SD 53.8).

<u>**Post surgical results**</u>	n	%
Anatomical success (closed tympanic membrane)		
yes	31	**78**
no	9	22
Functional success		
yes ABG <20	10	25
yes ABG <10	20	50

yes (Total)	30	**75**
no (ABG >20)	10	25

Table 4: Surgical results.

4.3 PROGNOSTIC FACTORS

The influence of the chosen prognostic factors on success was evaluated by comparing age at surgery, health status of the contralateral ear, history of adenectomy and tympanostomy tube placement, and type of surgery with both anatomical and functional success.

The mean age of children with a closed tympanic membrane after surgery was 11.6 (SD 3.2) years and the mean age of children with a persistent perforation was 12.4 (SD 2.6) years (p value = 0.57). Similarly, the mean age of children with an AB gap <20dB was 11.53 (SD 3.26) years and the mean age of children with AB gap >20dB was 12.7 (SD 2.35, with a p value of 0.30. Although no statistically significant association could be detected, children with a persistent perforation and without AB gap reduction were mostly of the group age 12-17 years.

Children with a history of adenoidectomy did not have a better outcome compared to children who did not have an adenoidectomy. In the anatomical success group 32% cases had a former adenoidectomy and in the functional success group 37%. We could not detect a statistically significant association comparing the success and failure groups (p value of 1 and 0.45).

As regards to prior tympanostomy tube placement, an intact tympanic membrane was observed in all cases, as well as an improvement of the AB gap. The association between success and failure groups with tympanostomy tube was not statistically significant, with a p-value of 0.56 in both cases.

The presence of a healthy contralateral ear was found in 22 (71%) cases of the anatomical success group and in 24 (80%) of the functional success group with a p-value respectively of 1 and 0.10 when compared to the groups with a pathologic contralateral ear.

Lastly, the comparison between type of surgery and functional and anatomical success showed that all surgery techniques had similar success outcomes. In the anatomical success group 45% were underlay myringoplasty, 42% overlay myringoplasty and 13%

closed tympanoplasty surgeries. In the functional success groups 50% were underlay myringoplasty, 40% overlay myringoplasty and 10% closed tympanoplasty surgeries. Conversely, in the anatomical failure group 78% were underlay myringoplasty and 22% overlay myringoplasty surgeries. In the functional failure groups 60% were underlay myringoplasty, 30% overlay myringoplasty and 10% closed tympanoplasty surgeries. The p value was 0.24 for the anatomical success and 0.87 for the functional success.

Comparison of preoperative and intraoperative parameters between anatomical success and anatomical failure groups	Success	Failure	p-value
Age (Mean)	12.4	11.65	0.57
Former adenoidectomy			
Yes	10 (32%)	3 (33%)	1
No	21 (68%)	6 (67%)	
Former tympanostomy tube			
Yes	4 (13%)	0 (0%)	0.56
No	27 (87%)	9 (100%)	
Healthy contralateral ear			1
Yes	22 (71%)	7 (78%)	
No	9 (29%)	2 (22%)	
Surgery			0.24
Underlay myringoplasty	14 (45%)	7 (78%)	
Overlay myringoplasty	13 (42%)	2 (22%)	
Closed tympanoplasty	4 (13%)	0 (0%)	
Comparison of preoperative and intraoperative parameters between functional success and functional failure groups	Success	Failure	p-value
Age (mean)	12.7	11.53	0.30
Former adenoidectomy			
Yes	11 (37%)	2 (20%)	0.45
No	19 (63%)	8 (80%)	

Former tympanostomy tube			
Yes	4 (13%)	0 (0%)	0.56
No	26 (87%)	10 (100%)	
Healthy contralateral ear			
Yes	24 (80%)	5 (50%)	0.10
No	6 (20%)	5 (50%)	
Surgery			0.87
Underlay myringoplasty	15 (50%)	6 (60%)	
Overlay myringoplasty	12 (40%)	3 (30%)	
Closed tympanoplasty	3 (10%)	1 (10%)	

Table 5: Prognostic factors results.

5 DISCUSSION

Chronic otitis media is a common disease in pediatric patients, which reduces quality of life and educational success (27) (64) (28) (34). Tympanoplasty is the standard treatment for chronic otitis media with perforation of the tympanic membrane, with or without ossicular chain disruption, that does not heal with medical treatment (32). The surgical procedure varies according to the severity and examination findings of the patient from simple myringoplasty to tympanoplasty with ossiculoplasty. Tympanoplasty in children remains a matter of debate concerning the optimal age to perform the surgery and the factors thought to influence surgical outcome (78). Identifying factors that have an impact on success is essential for many reasons: informing patients of the expected results, performing a better preoperative patient care, and selecting the proper surgical approach (79).

Hardman's metanalysis of 2015 is the most recent comprehensive literature review on pediatric tympanoplasty which analyzed 564 articles identifying 2,609 cases from 45 eligible studies (71). The conclusion of the study was that tympanoplasty in children is a very successful treatment option, that age does not have an impact on its outcome whereas larger perforations and the presence of an abnormal contralateral ear are relevant negative prognostic factors (71). Consequently, surgery was claimed to be best delayed until the contralateral ear has healed as it can predict poor ear ventilation also in the ear to be operated on. Since then, several new studies have been performed with conflicting results, investigating even more potential prognostic factors and raising more questions on whether it is better to resolve potential negative prognostic factors before surgery or not. The disparity of outcomes in the numerous studies on this surgery can be related to heterogeneity of the patients included, different definition of success and heterogeneity of the patients included and the post-operative follow-up period.

In our study, the anatomical and functional outcomes of pediatric tympanoplasty were compared to some of the most debated prognostic factors and no statistically significant difference was found between the groups with and without the factors.

In specific, age, which is often proposed as a significant parameter to consider for tympanoplasty, did not have a statistically significant effect on success, as the mean age of children with a closed tympanic membrane after surgery and with an AB gap <20dB was very similar to the mean age of the respective anatomical and functional failure groups. This is consistent with Hardman's metanalysis results (71) and with the more recent A. Abdood et al. paper (27) which did not find a correlation between age and surgical success rates in 180 pediatric tympanoplasty surgeries. However, in our series, despite the association not being significant, children of the failure groups were mostly older than 12 years old, suggesting that waiting too long to perform the surgery could lower the chances of success. Conversely, a recent study by C. Bruno et al. (64) found that success chances are higher in children older than 8 years. Also, Koch et al. in 1990 reported that surgery was successful in 81% of children aged 8 or over, while only 30% of the younger patients had satisfactory results (80). Cleary, in younger children, probably for higher susceptibility to upper respiratory tract infections and immaturity of Eustachian tube function and immune system, there is a more or less significant increase in the risk of reperforation, but surgery should not be delayed too much because a long-term tympanic membrane perforation can have very serious consequences on the middle ear integrity and function (34).

Given the critical Eustachian tube middle ear ventilation role, also the finding of a pathologic contralateral ear in literature has often been proposed as a negative prognostic factor and a valid reason to postpone surgery. The finding of an otitis media with effusion in the contralateral ear, seems indeed to be the better parameter to evaluate the tubal function. Pignataro et al., Beklaci et al. and Goyal et al. reported 89% vs 61.5%, 93.2% vs 69.0%, and 80% vs 73% anatomical success rates, respectively for unilateral vs bilateral disease (81) (65) (82). In our study, anatomical success was achieved in 76% cases of the group with unilateral disease and 82% cases of the group with bilateral disease; functional success was achieved in 83% cases of the unilateral disease group and 55% of the bilateral disease group. Statistical analysis showed no significant difference in the outcome, similarly to the studies of N. Verma et al. and J. Marquez (34) (68). However, bilateral ear disease seems to reduce the functional outcome in our cases.

Connected to the Eustachian tube function, history of a prior adenoidectomy and transtympanic ventilation tube also have been debated as prognostic factors, with the former being positive and the second being positive or negative in different studies. In our series, these factors had no statistically significant effect on outcome. In fact, 32% of our patients had a former adenoidectomy and 10% a ventilation tube but this did not have any bearing on the outcome of the surgery. Conversely, according to Zwiertz et al.

children who had previous surgeries, adenoidectomy or tympanostomy tube placement have better outcomes and lower risk or recurrence (66). I. Foulon et al. (28) and Takahashi et al. (83) also claimed that ears with adenoid hyperplasia have a higher chance of recurrence of disease, therefore in case of history of adenoidectomy in their studies success was higher. Also Hamans et al. and Charachon et al. recommended treatment of adenoid hyperplasia (84) (85). On the other side, Pignataro et al (82), N. Verma (34) et al and Abood (27) reported that adenoid hypertrophy did not affect the outcome of surgery. Hardmann et al. (71), stated that graft closure rates were higher in those undergoing adenoid surgery though the result was not statistically significant.

In our study simple myringoplasty was performed in 36 (90%) cases, of which 21 (53%) with an underlay grafting technique and 15 (37%) with an overlay technique, and tympanoplasty with ossiculoplasty in 4 (10%) cases. In literature, the majority of studies on pediatric tympanoplasty included myringoplasty only and just a few compared the surgical outcomes with the presence or absence of ossiculoplasty too. Our cases of tympanoplasty with ossiculoplasty were all (100%) successful in terms of closure of the tympanic membrane, while the AB gap reduction was achieved in 3 (75%) cases only. Conversely, myringoplasty in our series were anatomically and functionally successful in 27 (85%) cases with similar results between underlay and overlay techniques. We could not detect a statistically significant difference between the different types of surgery's success rates. This is consistent with J. Marquez and L. Pignataro results, which showed that surgical outcome was not affected by surgical technique, respectively tympanoplasty with or without ossiculoplasty and overlay or underlay techniques (68) (82). Also F. Chatelet systematic review named a few studies which compared underlay and overlay techniques without significant difference in the closure rates of the tympanic membrane (76). However, many studies support the underlay technique as a the better choice against overlay because of the shorter surgical procedure, easier assessment of mobility of the ossicular chain, faster healing, better hearing results and fewer complications (86) (87) (88).

The limitations of this study are mainly the total number of cases, which is quite small and spread over a long period of time, and the significant number of cases lost at follow-up.

6 CONCLUSION

Tympanoplasty is a successful surgical treatment in children to close a chronic tympanic membrane perforation and obtain favorable hearing results, thus improving the quality of life. Our study highlights how the anatomical and functional outcome of tympanoplasty in children is not significantly dependent on age and other debated prognostic factors, such as previous adenoidectomy or ventilation tube insertion, healthy contralateral ear and surgical technique.

The results of our analysis therefore suggest that surgical treatment should not be postponed when chronic otitis media is not solved with medical treatment in order to prevent severe modifications of the middle ear and negative audiologic consequences. It is not always necessary to wait for the child to grow and develop a more mature Eustachian function nor to perform adenoidectomy sistematically in case of adenoid hypertrophy. All tympanoplasty surgical techniques have shown valid success rates and the most appropriate approach should be searched for each individual case according to the surgeon's experience. Surgical success is mainly influenced by factors inherent to the underlying pathology and surgical needs.

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