Current aspects of etiology, diagnosis and therapy of otosclerosis

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SUMMARY
The presented article shows the current scientific concept including diagnostics and therapy of otosclerosis with an emphasis on surgical treatment options. The three main proposed causes for otosclerosis are viral and hormonal origin as well as a genetic predisposition. In 25 to 50% a familiar accumulation can be seen. Usually patients become aware of clinical problems by a progressive middle ear hearing loss in the young adulthood. In up to 80% of cases both ear become affected during lifetime. Surgical options of therapy are the stapedotomy, stapedectomy and the laser-assisted stapedotomy. In every case the alternative use of a hearing aid must be offered during the consultation. Typical surgical complications are rare but can be persistent vertigo, secondary facial palsy and a sensorineural hearing loss up to complete single-sided deafness in up to 1% of the cases. The most common finding which necessitates stapes revision surgery is the necrosis of the long incus process with dislocation of the stapes piston.

Pathogenesis
Otosclerosis is a circumscribed disease of the enchondral bone of the otic capsule. It is characterized by alternating phases of bone resorption followed by replacement with dense sclerotic bone. The first identification of this disease was made by Valsalva in 1704 in a description of the bony obliteration of the oval window in a patient with an acquired deafness [64]. The term otosclerosis was introduced by Anton von Tröltsch in 1872, remarkably no difference was made between otosclerosis and tympanosclerosis [66]. Politzer introduced the term otosclerosis as a separate entity in 1894 as the final stage of the disease with sclerotic plaques in the otic capsule [44].

Otosclerosis is a disease with a pathologic remodeling of the bone at a place where remodeling is uncommon in adults. Up to present knowledge usually there is no activity of osteoblasts and osteoclasts in the healthy otic capsule. However in otosclerosis there is pathologic bone resorption of the enchondral bone by osteoclasts in the first stage of the disease (otospongiosis) followed by bony formation made by osteoblasts (otosclerosis in the actual sense). Mosty otosclerotic plaques are found in the anterior part of the oval window (fissula ante fenestram). E.g. Schuknecht and Barber showed a fixation the footplate in the anterior part in 96% of their patients [50]. The term “obliterative otosclerosis” is used in cases with a complete ossification of the oval window accompanied by a severe conductive hearing loss. Otosclerosis is a disease limited to the temporal bone and never found in any other bone of humans [68].

The “malignant otosclerosis” is a term of the otosclerotic remodeling which is not restricted only to the oval and round window but the complete temporal bone including the inner ear which can be followed by a progressive combined severe hearing loss up to nearly complete deafness [52].

The etiology of otosclerosis is not definitely clarified up to now. Currently different hypotheses are discussed:

Genetics
In 1998 Tomek et al. could localize a gene responsible for otosclerosis on chromosome 15q25-q26 by examining the genome of multiple generations of a family with clinical otosclerosis [63]. Recently a second accountable gene was found on chromosome 7q34-36 [65]. Up to now 9 possible genetic loci have been identified, e.g. genes for collagen type I, aggrecan and genes for immunoproteins [30].

Controversial views exist regarding the influence of the degree of the pneumatization of the mastoid on the development of otosclerosis. Sade et al. could demonstrate a close linkage between a distinct pneu-
matization of the mastoid cells in patients with otosclerosis [48].

**Hormonal balance**

For a long time endocrine reasons have been described for manifestation and/or deterioration of an otosclerosis [18]. Many authors noticed a deterioration of the hearing in 30 to 60% of female patients with otosclerosis with at least one pregnancy [33]. The reason seems to be an increased estrogen level during pregnancy with stimulation of osteoblasts and consecutive ossification of otosclerotic plaques. Gristwood and Venables estimate a 33% risk of a deterioration of the hearing by one pregnancy, after six pregnancies this risk enhanced up to 63% [14].

**Calcium metabolism**

Abnormal function of the parathyroid glands with pathologic calcium and phosphate levels are discussed as an additional potential cause of otosclerosis. Jensen et al. compared the calcium and phosphate serum levels and the mineral content of the bone in 63 patients with otosclerosis as well as in 206 healthy adults and did not find any differences in the examined parameters [22]. This supports the hypothesis of an isolated disease of the temporal bone.

**Viral genesis**

A further cause of otosclerosis seems to be an immunological reaction after an infection with measles. Because of similarities between Paget’s disease and otosclerosis studies are performed to investigate a possible viral pathogenesis. Arnold et al. could demonstrate rubella and measles antigens in active otosclerotic plaques by immunochemistry [1, 2]. By using PCR (“polymerase chain reaction”) RNA-sequences of measles could be shown in otosclerotic plaques but not in other tissues of the same patient as well as in a control group without otosclerosis [38]. These results suggest that in a hereditary predisposition a persistent infection with measles could lead to an apparent otosclerosis.

**Epidemiology, diagnosis and clinical symptoms**

A familiar accumulation of otosclerosis is described in 25 to 50% of cases [17]. An autosomal dominant heredity with incomplete penetrance by about 40% is postulated by epidemiological studies as well as by studies with monozygotic twins [10]. The grade of the penetrance depends on the pattern of the otosclerotic plaques in the capsule of the inner ear. Some plaques appear in section areas with no clinical consequence. About 10% of the white population has histological signs of otosclerosis.

Only 10% of these patients have clinical symptoms, so the incidence of otosclerosis in the white population adds up to 1%. In Native Americans, Africans and Asian people the incidence is much lower [13].

The typical sign of otosclerosis is a progresident conductive hearing loss starting in the young adulthood and appears on one or both (up to 80%) ears [46]. About 50% of the patients with otosclerosis complain of tinnitus. The incidence of vestibular symptoms is quoted very differently in the literature [12, 18, 61]. Usually the otoscopy in patients with otosclerosis is inconspicuous, sometimes the “Schwartze sign” a red dot in the area of the posterior inferior section of the tympanic membrane caused by a hypervascularization of the mucosa on the promontory can be seen.

The typical pure tone audiogram of a patient with otosclerosis shows a moderate conductive hearing loss of about 40 dB in the lower frequencies. The conductive hearing loss decreases in the higher frequencies. This is explained by the particular effect of the impaired decreased vibrancy of the footplate in the lower frequencies [32]. A maximal conductive hearing loss especially in the lower frequencies is seen in patients with obliterative otosclerosis [11]. A typical audiological sign of otosclerosis is the “Carhart notch” a lowering of the bone hearing level up to 25 dB at 2 kHz [28]. This artificial sensorineural component is caused by the missing resonance of the middle ear whose maximum is located by 2 kHz [67]. Therefore the “Carhart notch” disappears postoperatively. In an early stage the stapedial reflex shows an on-off-phenomenon with a biphaseal course of the reflex. In the further stage the stapedial reflex is missing completely.

Patients with osteogenesis imperfecta sometimes first present with a progressive conductive hearing loss caused by bone reconstruction and consecutive fixation of the footplate. The therapy is the stapedoplasty in accordance with the otosclerosis.

The aplasia of the anular ligament as a minor middle ear malformation comes along with the fixation of a stapes footplate. This diagnosis should be considered in young patients with clinical symptoms of otosclerosis. In these cases the stapedoplasty is also the preferred therapy.

**Therapy**

**Drugs**

Shambough [54] showed a conservative therapy approach with sodium fluoride. The effect of sodium fluoride is explained by a stabilization of the otosclerotic plaques because sodium fluoride leads to an enhanced resistance against osteoclasts. Histological examinations showed a blocking of the bony depletion and an enhanced calcification of the bone. A daily dose of 6 up to 16 mg was recommended [4, 18, 54]. The
tablets were added with vitamin D (0.3-0.8 mg) and calcium (150-400 mg) which were supposed to lead to an increased calcification of the bone. No studies exist regarding this conservative therapy approach so usually the sodium fluoride therapy is not recommended any longer.

**Hearing aids**

The use of a hearing aid is an alternative therapy of the otosclerosis without many side effects. Before planning surgery every patient has to be informed about this alternative, although up to our experience only few patients decide for hearing aids. In cases of a single sided deafness and an otosclerosis on the contralateral side the supply of the remaining functioning ear can be carried out by a bone anchored hearing aid.

**Stapes surgery**

Originally stapes surgery was founded by Kessler in 1876. By animal studies he described the
mobilization of the stapes as well as the stapedectomy for hearing improvement in otosclerosis [24]. Because of the short duration, only days to weeks, of hearing improvement after surgery, as well as labyrinthitis with fatal endocranial complications stapes surgery was abandoned quickly in the pre-antibiotic-era.

In the 1950s the surgical microscope caused an enormous improvement in the microsurgery of the middle ear and lead to a new era of stapes surgery. Shea and Treace developed a stapes prosthesis of Teflon and performed the first successful stapedoplasty in 1956 with a stapedectomy (removal of the complete stapes) [55, 56, 57]. In this technique the oval window was covered by a vein transplant.

The further development of the stapedectomy was carried out by the removal of the posterior third of the footplate [43]. A modification of this method was performed by Shea and Marquet. They created a small opening in the middle of the footplate and inserted the prosthesis directly into this opening (stapedotomy) [31, 56]. The platinectomy [71] did not find recognition. In this technique, described by Farrior [8], the footplate as well as the posterior crus of the stapes were resected and the anterior crus was placed into the oval window which was covered by fascia [37].

**Indications**

Typical indications for the stapedoplasty are:
- Otosclerosis with fixation of the stapes footplate
- Imperfect osteogenesis
- Severe tympanosclerosis
- Some types of middle ear malformations with conductive hearing loss from 15 dB upward and a negative result in the Rinne tuning fork test

In cases of bilateral otosclerosis the ear with the more extensive hearing impairment should be opera-

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**Fig. 6. The separated suprastructure of the stapes**
**Ryc. 6. Usunięcie suprastruktury strzemiączka**

**Fig. 7. The opened vestibulum after removal of the posterior third of the stapes footplate**
**Ryc. 7. Otwarcie przedsiomka po usunięciu jednej trzeciej tylnej płytki strzemiączka**

**Fig. 8. Insertion of a titanium piston**
**Ryc. 8. Założenie protezy tytanowej typu piston**

**Fig. 9. Cramping of the loop of the prosthesis by a McGee forceps**
**Ryc. 9. Zaciśnięcie zaczepu protezy za pomocą kleszczyków McGee**

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Surgical techniques

Generally a stapedoplasty can be performed in local anaesthesia. Usually the local anaesthetic (e.g. Xylocain 2% with adrenaline 1:200000 additionally) is injected subperiostally with a fine needle (26 gauge) retroauricular in every quadrant of the auditory canal and in the region of the endaural incision. In cases of anxious patients, patients with lack of understanding or disabled patients a general anaesthesia is preferred.

The endaural incision (Heermann) is performed about 2 to 3 mm medial of the border of the cartilaginous to the bony part of the auricular canal (Fig. 1). Then the tympanomeatal flap is performed with an incision on the floor as well as the roof of the canal with a size 15 scalpel. With immediate contact to the bone the flap is dissected with the straight and angled Plester knife up to the fibrous annulus (Fig. 2). After incision of the mucosa of the middle ear the tympanomeatal flap is folded towards the anterior wall of the auditory canal.

After the identification of the chorda tympani nerve and the placement to the handle of the malleus the lateral attic wall is resected with the House curette (Fig. 3) up to the visibility of the pyramidal process. In cases of thick bone this can be performed by a diamond burr too. By gently touching the long process of the incus as well as the handle of the malleus with a sickle knife the mobility of the ossicle chain is tested. In cases of a fixed footplate no movement of the stapes but an adequate movement of the malleus and the incus can be seen.

Afterwards the incustapedial joint is opened by a fine 90° hook (Fig. 4) and the stapedial tendon is cut by a Belucci scissor (Fig. 5). In case of a stapedotomy the perforation of the footplate is performed in the posterior third by a 0.4 mm perforator, microdrill or laser. The posterior and anterior crus is separated by a hook from the footplate and the suprastructure is removed (Fig. 6). Then the perforation is widened by a 0.6 perforator (Fig. 7) and an adaquate prosthesis is inserted (Fig. 8). In our department usually a 4.5 x 0.4 mm titanium implant is used, the loop of the prosthesis is clamped to the long process of the incus with a McGee forceps (Fig. 9).

Other surgeons perform measurements of the distance between the footplate and the long process of the incus. Usually implants with a length of 4.25 up to 4.75 mm are recommended [17, 18, 21]. The loop of the prosthesis should have close contact without putting pressure on the incus. The space of the oval niche around the prosthesis is closed by small pieces of connective tissue which are harvested in the region of the endaural incision. Additionally some surgeons put a further piece of connective tissue onto the loop at the long process of the incus to avoid a necrosis in this part [36, 42, 55]. Afterwards the tympanomeatal flap is replaced, silicon sheets are put onto the incisions and the auricular canal is packed by a sponge soaked with antibiotic (e.g. Merocel). The endaural incision is be closed by 2 to 3 sutures. The removal of the sutures and the package is performed about one week after surgery.

In partial stapedectomy a perforation is created in the region between the posterior and the middle third of the footplate. Afterwards the posterior third of the footplate is removed and the prosthesis is inserted. The risk of an injury of the utricle is minimized because in this area the largest distance to the utriculus (about 1.2 mm) can be found.

Only a few cases require a total stapedectomy. In this procedure the entire footplate is removed, the prosthesis is inserted and the opened vestibulum is closed with connective tissue.

Intraoperative specifics

In cases of an obliterative otosclerosis with extensive thickening of the footplate a fine diamond burr (e.g. skeeter drill) is used for the perforation of the footplate to achieve a small opening to the vestibulum.

The free floating footplate is a dreaded complication of the stapedoplasty. In cases of a floating footplate a small perforation on the promotorial side of the vestibulum is made by a fine diamond burr. the footplate is lifted and removed carefully by a small hook [51].

Sometimes a dehiscent or abnormal low running facial nerve can occlude the access to the oval niche. In such cases some authors recommend the termination of the intervention [69]. In our department a windowing of the promontory is performed in such cases [17]. Häussler published data of 39 patients with stapedectomies and abnormal running of the facial nerve, in 82% of these patients a postoperative conductive hearing loss of less than 20 dB could be achieved [17]. There was no case with a facial palsy or a deafness after surgery.

A further specific is the gusher-phenomenon which can occur after perforation of the footplate In cases of a heavy gusher the break of the stapesplasty and the "waterproof" closure of the oval window by fat or connective tissue is recommended [53]. The oozer is the milder type of the gusher phenomenon and can often be controlled by a quick insertion of the prosthesis and sealing with connective tissue. In cases of a more extensive discharge of cerebrospinal fluid a lumbar drainage can be helpful to reduce the pressure of the cerebrospinal fluid.

In 1:1000 of all otosurgical interventions a persistent stapedial artery can be seen [29]. In the stapesplasty insertion of the prosthesis after removal of the stapes suprastructure and anterior dislocation of the artery is recommended by Schuknecht [51]. Some
otosurgeons recommend the coagulation of the artery and to proceed with the surgery in the usual manner [17]. Other surgeons advise against the coagulation of the stapedial artery and recommend the termination of the surgery in case it is impossible to dislocate the vessel [62].

**Stapedotomy versus stapedectomy**

The different techniques of stapedectomy versus stapedotomy are discussed controversially in literature. Whereas some surgeons report on better hearing improvement especially in the higher frequencies after stapedotomy [9, 34, 40] other surgeons prefer the stapedotomy because of better hearing results especially in the lower and middle frequencies [39, 44]. Most studies depict the risk of inner ear damage lower in stapedotomy than in stapedectomy. However House et al. demonstrate no differences of the two different techniques regarding the postoperative hearing results as well as risks for the inner ear by performing a study of 42 patients with stapedectomy on one ear and stapedotomy on the contralateral side [20].

**Stapes replacement prosthesis**

Nowadays usually commercially available stapes pistons are used in stapes surgery. In our department the titanium K-piston with loop (Kurz company, Düsslingen, Germany) has proved to be of value. This piston is available in two diameters (0.4 and 0.6 mm) and different lengths (3.5-10 mm).

In the titanium Clip-piston aWengen (Kurz company) the head of the prosthesis can be snapped around the long process of the incus without pressure.

The Softclip-prosthesis (Kurz company) is an advancement of this piston though long-term results are not yet available.

A new stapes replacement prosthesis on the market is the smart-stapes-piston by Gyrus ENT company, Tuttlingen, Germany. The loop of the piston consists of a nickel-titanium-alloy awarding a memory effect of 45°C (by laser or bipolar forceps) onto the loop. After insertion of the prosthesis and putting the loop around the long process of the incus the self-contained closure of the loop is induced by putting heat of 45°C (by laser or bipolar forceps) onto the loop. First field reports with this prosthesis are promising [15, 19].

Another frequently used prosthesis is the platinum- teflon-prosthesis (Spiggle&Theis, Oeverrath, Germany) which consists of a platinum loop and a piston of teflon.

**Intricacies**

Immediate postoperative vertigo can be caused by a loss of perilymphatic fluid, mechanically induced irritation of the inner ear or a serous labyrinthitis [17]. Symptoms usually fade after a few days. In suspicion of a intricacy a high dosage application of corticosteroids (1000 mg prednisone i.v. once daily on three consecutive days) is recommended [7, 53].

Little vertigo combined with a fluctuating hearing can be the characteristic symptom of a perilymphatic fistula. In the suspicion of such a fistula the immediate revision and closure of the oval niche by connective tissue should be carried out. Also an inner ear diminution and persisting vertigo despite conservative therapy (high dosage corticosteroids and antibiotics) necessitate an immediate surgical revision [5]. For the early detection of these complications it is necessary to do a daily examination of the patient with the tuning fork and the glasses of Frenzel. To prevent an inflammation of the auricular canal the patient has to be advised to leave away hearing aids one week prior to surgery. In cases of an infection with herpes or other infection of the upper airway the highly elective stapes surgery should be postponed.

The most serious complication after stapes surgery is deafness of the operated ear. Most authors put this risk at 1% but there is a big variation in the incidence of this complication in different studies [17]. In most cases the definite reason for the postoperative deafness stays unclear [28]. Some surgical techniques which came along with an increased risk for the inner ear were abandoned. E. g. the coverage of the oval niche with gelfoam was accompanied by an increased risk of inner ear fistulas [58]. In the suspicion of an inner ear complication a high dose therapy with corticosteroids as well as antibiotics has to be initiated [7]. Before performing stapes surgery every patient has to be informed about an alternative therapy in terms of hearing aids if nothing else but because of medicolegal aspects.

Persisting vertigo for months mostly are a sign of a prosthesis which extends to much into the vestibulum. In such cases the revision and replacement of the prosthesis against a shorter piston is necessary.

A facial nerve palsy secondary to stapes surgery is very rare. A viral inflammation particularly with herpes simplex in the geniculate ganglion is assumed [49].

**New techniques in stapes surgery**

In 1980 Di Bartolomeo and Perkins introduced the argon laser into stapes surgery [6, 39]. Further developments comprised the use of the CO2 and the erbium laser [16, 25, 34]. Especially the very precise windowing of the stapes footplate is an advantage of the use of a laser equipment. Several authors have published promising data concerning the use of argon as well as CO2 laser in stapedotomy [3, 23].

The “one shot stapedotomy” is a modification of the CO2 laser by using a scanner system which leads to a
windowing of the footplate by a single laser pulse [23]. Because of pressure waves which can be induced by the use of an erbium laser this type of laser has been abandoned in stapes surgery to prevent an acoustic trauma [17].

In 1998 Silverstein described the so called laser-STAMP (laser stapedotomy minus prosthesis) as a minimal invasive surgery in early stages of otosclerosis in which only the anterior part of the footplate is fixed [59]. In these cases the anterior crus and the anterior part of the footplate will be divided by the use of an argon laser and the vestibulum will be covered by fatty tissue. According to the study of Silverstein et al. the results of the laser-STAMP are comparable to conventional laser stapedotomy [60]. Especially in higher frequencies an excellent hearing result can be achieved but up to now long term results are not available.

**Revision stapes surgery**

Indications of an immediate surgical revision after stapesplasty are a relevant inner ear depression as well as a persisting vertigo inspite of maximal conservative treatment (corticosteroids, antibiotics). Sometimes loosening of the packing of the ear canal can already improve the symptoms. If granulation tissue is detected during revision surgery the prosthesis should be removed carefully and the vestibulum should be covered by connective tissue. A secondary attempt of hearing improvement can be undertaken after 6 months. Persisting vertigo can be caused by a piston which extends too much into the vestibulum. In this case the prosthesis should be replaced by a shorter one [5].

Another indication for revision surgery is a persisting or a new conductive hearing loss of 20 dB or more [26]. The use of a high resolution multi-slice-CT can be helpful for discussion of a revision stapes surgery [47]. In most cases a necrosis of the long process of the incus is the reason for a dislocation of the prosthesis [21]. For the most part the fixing of the prosthesis further proximal on the long process is successful. If this is not possible a malleovestibulopexie will be necessary. Usually the postoperative hearing results after revision surgery are not as favourable as after primary stapesplasty [17]. In the mean a postoperative conductive hearing loss of less 20 dB can be achieved in 45% after revision surgery. On the other side after primary stapedoplasty about 90% of all patients achieve a reduction of the air-bone-gap. The risk of a damage of the inner ear after revision surgery is estimated of about 2.2%.

**References**