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Objectives

• What is Otosclerosis?
  • Definition
  • Prevalence
  • Demographics
  • Etiology
  • Histopathology/Pathophysicsology
• Making the Diagnosis
• Management
  • Non-surgical
  • Surgical
• Conclusion
What is Otosclerosis?

History of Otosclerosis

• 1860 – Toynbee - first described fixation of stapes as a cause of hearing loss
• 1893 – Politzer referred ankylosis of the stapes as otosclerosis
• 1912 – Siebenmann described otospongiosis – microscopic examination of the lesions revealed spongification of the bone
What is Otosclerosis?

- Metabolic bone disease unique to the otic capsule and ossicles
- Abnormal resorption/deposition of bone
- Fixation of stapes
- Conductive hearing loss or mixed hearing loss
  - SNHL in 10% of patients
- Rarely causes pure sensorineural hearing loss
Prevalence

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Prevalence of histological otosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>10%</td>
</tr>
<tr>
<td>Asian</td>
<td>5%</td>
</tr>
<tr>
<td>Black</td>
<td>1%</td>
</tr>
<tr>
<td>Native American</td>
<td>0%</td>
</tr>
</tbody>
</table>

- Vary widely between different populations
  - Prevalence - 2.1%
- More common in white population
  - 10% of white population have histological finding
  - 10% have clinical symptoms
- 1% of white population
Demographics

- 2:1 female:male distribution
  - 1:1 histological distribution
  - May progress during pregnancy
  - 15-45 years of age
    - 3rd decade of life
  - Early as 7 years of age and as late as the 50s
Etiology

• Exact cause is unknown
• Genetic
  • 2/3 of patients with otosclerosis have family history of hearing loss
  • Autosomal dominant with incomplete penetrance
• Infectious
  • Measles
    • Virus RNA sequence found in active otosclerotic lesions
• Autoimmune (type II collagen), metabolic, and endocrine disorders
Histopathology

- 2 forms of otosclerotic lesions
  - Otospongiosis (early phase)
    - Active phase of lesion
    - Osteocytes – most active
    - Amorphous spongy bone
    - Stains blue (basophilic)
  - Otosclerosis (late phase)
    - Dense sclerotic bone
    - Stains red (acidophilic)

Heavy arrow – otospongiosis
* - otosclerotic bone
Distribution of Otosclerotic Lesions

- Anterior to oval window 90%
- Round window 30%
- Cochlear labyrinth 25%
- Stapes footplate 12%
- Posterior to oval window 5-10%
Histopathology

- Most common sites of involvement
  - Fissula ante fenestrum
    - Often non-clinical unless involvement of annular ligament or footplate
Histopathology

- Otosclerotic footplate
Histopathology

• Cochlear Otosclerosis
Objectives

- What is Otosclerosis?
  - Definition
  - Prevalence
  - Demographics
  - Etiology
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- Making the Diagnosis
- Management
  - Non-surgical
  - Surgical
- Conclusion
Making the Diagnosis

Presentation
• Hearing loss of gradual onset/slow progression
  • 70-80% bilateral
  • Asymmetrical
• Low-volume speech
• Paracusis of Willis
• Other otological manifestations
  • Tinnitus – 65-85% patients
  • Vertigo – 24% patients
• Family history
Making the Diagnosis

Physical Exam

- Tympanic Membrane appears normal in majority of cases
  - Schwartze sign
    - 10% OS
    - Increased vascularity associated with otospongiosis
  - Reverses 512Hz fork – 15-20dB loss; 1024-Hz – > 25dB loss
Making the Diagnosis

Audiometry
- Type A/A<sub>s</sub> tympanogram
- Acoustic reflex
  - Absent
  - Diphasic – on-off effect
- Carhart’s notch
- Speech discrimination normal
  - Unless cochlear involvement
Making the Diagnosis

Radiology

• CT Temporal Bone
  • Differentiate from other causes of CHL
  • Areas of bony demineralization
  • Double ring or halo sign
  • Enlarged cochlear aqueduct
Differential Diagnosis

- Cholesteatoma, middle ear effusion, tympanic membrane perforation
- Ossicular discontinuity
  - Hypermobile tympanic membrane ($A_d$)
- Congenital stapes fixation
  - Non-progressive
  - Early hearing loss
- Malleus head fixation
  - Stiff tympanic membrane ($A_s$)

![Graph](image_url)
Differential Diagnosis

- Paget’s disease
  - Elevation of alkaline phosphatase
  - Other skeletal bone involved
- Osteogenesis Imperfecta
  - Blue sclera
  - Multiple fractures
  - Progressive hearing loss
- Superior semicircular canal dehiscence
  - Conductive hearing loss
  - Tullio phenomenon
  - CT scan
  - VEMP
Management

- Non-Surgical Treatment
  - Amplification
  - Medical
- Surgical Treatment
- Advanced Otosclerosis Treatment
Management

• Hearing Aid
  • Alternative to surgery
  • Should be offered as an option
  • Hearing aid even after successful stapedotomy if SNHL component is present
  • Avoids profound hearing loss
  • Higher satisfaction rate in patient who undergo successful surgery
    • Device in ear
    • Difficulty with feedback
  • Most insurances do not cover the cost
Non-Surgical Management

- Sodium Fluoride
  - 1916 – first potential role in resorptive bone disease
    - Decrease in tooth decay in school age children with fluoride present in drinking water
  - 1923 – Escot was the first to suggest the use of calcium fluoride for treatment of otosclerosis
  - 1964 – Shambaugh and Scott – proposed using sodium fluoride for the arrest of otosclerosis
Sodium Fluoride

**Mechanism of action**

- Fluoride ions replace the hydroxyl radical
- Bretlau et al. investigated the morphological and mineral distribution of otosclerotic lesions with/without sodium fluoride therapy
  - 20 stapes – minimum of 12 months of treatment
  - 16 stapes – without treatment
  - Treated group – sclerotic bone dominated
  - Untreated group had mixed lesions present
  - Calcium fluoride ratio mean 2.59 in treated vs 2.05 in untreated (P<0.001)
Sodium Fluoride

• Mechanism of action
  • Potent antagonist of bone remodeling
  • Various enzymes - higher concentrations in perilymph of patients with otosclerosis
    • Action of trypsin
  • Causse et al. measured higher concentrations of trypsin in perilymph of untreated vs sodium fluoride treated patients
    • 7.01 micrograms/ml vs 5.93 micrograms/ml
Sodium Fluoride

- Many studies have been performed evaluating efficacy
- Controversial
- Bretlau et al. performed a prospective double-blinded placebo controlled study
- Treatment group received 20mg sodium fluoride BID, 500 mg of calcium gluconate, and 400 units of Vitamin D
- Some patients may benefit from Sodium Fluoride therapy

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Audiometry (500–1000–2000 Hz)</th>
<th>SRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A*</td>
<td>P†</td>
</tr>
<tr>
<td>Improved</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Unchanged</td>
<td>39</td>
<td>36</td>
</tr>
<tr>
<td>Worse</td>
<td>14</td>
<td>19†</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>52</td>
</tr>
</tbody>
</table>

* A, actively treated patients (40 mg sodium fluoride daily)
† P, patients who received placebo
‡ p < 0.025
§ p < 0.15

Change was indicated by greater than 10dB over the study period.
Sodium Fluoride

• When to use
  • Progressing hearing loss
  • Early stages of otosclerosis
  • Alternative to surgery

• Dosing
  • No exact dosing
  • Bretlau et al. 20 mg twice daily with 500 mg of calcium gluconate and 400 units of vitamin D
  • Colletti et al. 6-16 mg (age adjusted dose)
  • Florical 8 mg TID until hearing loss stabilizes

• Time
  • No study has evaluated treatment length as a primary objective and the studies of efficacy had different treatment lengths
Sodium Fluoride

• Safety/Risk
  • Animal studies have shown that it is not teratogenic and epidemiological studies have shown no increase in birth defects
  • Low dose
    • Few side effects
    • High dose
    • Gastrointestinal issues
      • Decrease by using enteric coated formulations or by buffering with calcium carbonate
  • Arthralgia
  • Ligamentous calcification, intense bone remodeling and bone pain
Sodium Fluoride

- Contraindications
  - Pregnancy or breastfeeding
    - Can pass through the placenta and secreted in milk
  - Renal failure
    - hampers excretion, toxic levels of the drug
  - Children
Sodium Fluoride

• Available formulations
Sodium Fluoride

• Should sodium fluoride be used for otosclerosis?
  • Studies have shown that it can be effective in some patients in combination with calcium supplementation at slowing or halting the progression of the disease
  • Risk factors and contraindications must be taken into account when prescribing the medication
  • Low doses have been given safely with few side effects
  • No clear evidence is available on length of treatment
Bisphosphonates

- Alternative to sodium fluoride
- Analog of organic pyrophosphate that binds Ca\(^{2+}\)
- Blocks osteoclastic activity
- No large studies have been performed on its use specifically for otosclerosis and dosing has not been established

- Adverse events
  - Osteonecrosis of the jaw, renal toxicity, erosive esophagitis
Bisphosphonates

• Recent pilot study from Mass Eye and Ear showed promising results:
  • 10 patients with progressive SNHL due to otosclerosis
  • Treated with 3rd generation bisphosphonates
  • Word discrimination and bone conduction pure tone average stabilized/slowed on follow-up audiogram
Management

• Non-Surgical Treatment
  • Amplification
  • Medical

• Surgical Treatment

• Advanced Otosclerosis Treatment
Surgery

Patient Selection

• CHL of at least 15 dB
• Worse ear
• Good word discrimination
• Work environment
• Other otologic complaints
• Relative contraindications
  • Active OS – Schwartz sign
  • Pregnancy
  • Ear infection
  • TM perforation
  • Meniere’s disease
• Only hearing ear – only absolute contraindication
Surgery

General vs Local Anesthesia

- Surgeon and patient preference
- Local
  - Medical problems not allowing for general anesthesia
  - Immediate feedback on hearing
  - Can inform surgeon of vertigo
  - Risk associated with general anesthesia
- General
  - Teaching Institutions
Surgery

• General vs Local Anesthesia
  • Wegner et al. – meta-analysis evaluating the difference by air-bone gap outcomes
  • No significant difference was present between the two methods of anesthesia
  • No significant difference in postop vertigo
Surgery

- Canal injection
  - 4 quadrant canal injection
    - 1% or 2% lidocaine with 1:100,000 epinephrine
    - Buffer with 7.5% bicarbonate for awake patients
    - Bony-cartilaginous junction
  - Speculum selection
Surgery

- Raising the Tympanomeatal flap
  - Approximately 6 o’clock and 12 o’clock position
  - Extended laterally 6-8 mm
  - Importance of flap size
Surgery

- Raising the Tympanomeatal flap
  - Raised to the bony tympanic annulus
  - Annulus raised from its sulcus
  - Raised inferiorly until visualization of the round window and superiorly until the neck of the malleus is identified
Surgery

• Mobilizing the Chorda Tympani
  • Care must be taken when raising the flap to not damage the chorda tympani
  • Attachment to the bony superior tympanic annulus and the undersurface of the malleus
  • Do not stretch, if necessary cut
Surgery

• Removal of Scutum
  • Posterior bony canal is removed with curettage or microdrill
  • Important: curettage posterior to the scutum – weakening the bone
Surgery

- Removal of Scutum
  - Horizontal portion of Fallopian canal visualized superiorly
  - Pyramidal process visualized posteriorly
  - Adequate exposure of oval window
Surgery

- Middle Ear Examination
  - Evaluate mobility of lateral ossicular chain
  - Confirm stapes fixation
  - Evaluate for middle ear anatomy variants

- Next steps are performed in different orders depending on surgeon preference and technique

Dehiscent facial nerve
Surgery

- Incudostapedial joint
  - Separated with joint knife
  - Side to side motion

- Laser used to remove the stapedial tendon or it can be cut
Surgery

- Posterior Crus Removal
  - Laser used to char the posterior crus
  - Alternatively a diamond bur drill can be used
Surgery

- Stapedial Superstructure Removal
  - Using a rosen needle the stapedial superstructure is down fractured toward the promontory
  - Quick motion
  - Mobilization of footplate – slow motion
  - Can be performed later in the procedure after fenestra creation and piston placement
Surgery

- Measurement for Prosthesis
  - Distance between the footplate and lateral aspect of incus is measured
  - 4.5 mm – most common
  - Measure in a consistent fashion
Surgery

- Prosthesis selection
  - Know your prosthesis and measurements
  - Most prosthesis are measured from the medial portion of the incus, whereas the measurement is taken from the lateral surface
    - Subtract .25 mm from the measurement
  - What diameter prosthesis to use?
Surgery

Influence of prosthesis diameter in stapes surgery

- Laske et al. performed a meta-analysis comparing .4mm and .6mm diameter prosthesis
- Results showed significant better closure of ABG in .6mm group (p=0.05)
Surgery

Influence of prosthesis diameter in stapes surgery

Pooled data was then obtained from 62 studies using individual prosthesis sizes.
Postoperative ABG, BC, AC were evaluated:
- .6mm significantly better ABG closure and AC, no difference in BC
- Conclusion – without interposition, .6mm is associated with better results than .4mm

**TABLE 5. Postoperative air-bone gap in decibels**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases, n (%)</th>
<th>Mean (dB)</th>
<th>No. of studies, n (%)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mm</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>0.4 mm</td>
<td>1,303 (24)</td>
<td>11</td>
<td>14 (35)</td>
<td>(9,11,16,19,22,24,29,31,35,39–41,43)</td>
</tr>
<tr>
<td>0.5 mm</td>
<td>141 (2.6)</td>
<td>8</td>
<td>2 (5)</td>
<td>(8,45)</td>
</tr>
<tr>
<td>0.6 mm</td>
<td>3677 (67.7)</td>
<td>7</td>
<td>22 (55)</td>
<td>(8,9,11,16,19,46,48,51–53,55,58,59,61,62,65–71)</td>
</tr>
<tr>
<td>0.8 mm</td>
<td>311 (5.7)</td>
<td>7</td>
<td>2 (5)</td>
<td>(72,73)</td>
</tr>
<tr>
<td>Total</td>
<td>5,432 (100)</td>
<td>—</td>
<td>40 (100)</td>
<td></td>
</tr>
</tbody>
</table>

*0.4 mm versus 0.6 mm, p < 0.001.

**FIG. 3.** Postoperative ABG at different frequencies. *p < 0.05, **p < 0.001.
Surgery

- Creating the fenestra
  - Laser – a footplate vessel is the initial target, each sequential laser is placed over prior char forming a rosette pattern
    - Char slightly larger than intended fenestra
    - Sizing instrument used to create fenestra
      - 0.6 mm
Surgery

- Creating the fenestra
  - Alternatively a microdrill can be used with a 0.7mm diamond burr
  - No pressure is exerted on the footplate
  - Combination of laser and microdrill
Surgery

Laser vs Conventional Fenestration

- Laser
  - High precision
  - No touch principle
  - Low risk of footplate mobilization
  - KTP and Argon – more favorable hemostasis – potential to damage structures medial to the footplate
  - CO2 – rapid vaporization of bone and collagen– increased risk of thermal injury
  - No statistical difference in outcomes
Surgery

Laser vs Conventional Fenestration

• Microdrill
  • Precise
  • Avoids excess heat production
  • Thickened footplates

• Risk
  • Can startle awake patients
  • Footplate fracture
  • SNHL
All but one study had higher air-bone gap closure (<10dB) in the laser group
Risk of SNHL was higher in microdrill group
Risk of tinnitus was higher in the laser group
No footplate fracture in the laser group
Surgery

- Prosthesis placement
  - Placed into the oval window
  - The shepherd's hook is maneuvered into position over the incus
  - The wire is crimped with crimping forceps or if using newer prosthesis heated with the laser resulting in self crimping
Surgery

• Seal
  • Venous blood is applied to the oval window
  • 3 ml syringe with 20 gauge suction tip

• Other Seals
  • Fascia
  • Perichondrium
  • Vein
  • Fat
  • Gelfoam
Surgery

- Stapedectomy vs Stapedotomy
  - Proponents of stapedectomy
    - Less chance of recurrence
    - No increased risk in a skilled surgeons hands
  - Proponents of Stapedotomy
    - Smaller opening of vestibule – less risk to damage to inner ear and SNHL
    - Less incidence of prosthesis migration
    - Better closure of air-bone gaps in higher frequencies
    - Better speech discrimination scores
Surgery

- **Stapedectomy vs Stapedotomy**
  - 209 ears - 145 patients
  - No significant difference in early or post PTA air-bone gap
  - Mean of 10.4 ABG in stapedectomy group / 8.0 in stapedotomy group (late)
  - No difference in speech discrimination
  - 4kHz closure was significantly better early postop and was better late postop but no significant

House et al.
Surgery

• Stapedectomy vs Stapedotomy
  • 42 patients had stapedectomy in one ear and stapedotomy in the opposite ear
  • Results were similar with no statistical difference between the two surgical techniques in closure of pure tone average air-bone gap

| TABLE III.  
<table>
<thead>
<tr>
<th>Audiometric Results and Statistical Comparison for Paired Cases (n = 42).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>--------------</td>
</tr>
<tr>
<td>Length of follow-up</td>
</tr>
<tr>
<td>Early post (mo)</td>
</tr>
<tr>
<td>Late post (y)</td>
</tr>
<tr>
<td>PTA (dB HL)</td>
</tr>
<tr>
<td>Pre</td>
</tr>
<tr>
<td>Early post</td>
</tr>
<tr>
<td>PTA air-bone gap (dB HL)</td>
</tr>
<tr>
<td>Pre</td>
</tr>
<tr>
<td>Early post</td>
</tr>
<tr>
<td>Late post</td>
</tr>
<tr>
<td>4 kHz air-bone gap (dB HL)</td>
</tr>
<tr>
<td>Pre</td>
</tr>
<tr>
<td>Early post</td>
</tr>
<tr>
<td>Late post</td>
</tr>
<tr>
<td>Δ PTA air-bone gap (dB HL)</td>
</tr>
<tr>
<td>Pre to early post</td>
</tr>
<tr>
<td>Δ SNHL (dB HL)</td>
</tr>
<tr>
<td>Pre to early post</td>
</tr>
</tbody>
</table>

PTA = pure-tone average; SNHL = sensorineural hearing level (average bone thresholds at 1 kHz, 2 kHz, and 4 kHz); dB HL = decibel hearing level; Δ = change; pre = preoperative; post = postoperative.
Surgery

• Stapedectomy vs Stapedotomy
  • No statistical difference in SNHL
    • 9.8%(stapedectomy) vs 5.9%(stapedotomy) had worse than 10dB hearing loss
    • No ears in the study had profound SNHL but one ear had greater than 20dB SNHL in the stapedectomy group
  • Concluded that technique used should depend on the experience and comfort level of the surgeon
Postoperative Complications

- SNHL
- Taste disturbance
- Tinnitus
- Vertigo
- Facial paralysis
- Perilymph fistula
- Reparative granuloma
Management

• Far Advanced Otosclerosis
  • 1961 - AC pure tone average of greater than 85dB an no measurable bone conduction
  • Word discrimination - commonly used
  • No standard guidelines
    1. No intervention and continue hearing aids
    2. Stapedotomy and hearing aid use
    3. Cochlear implantation
Management

- Mercus et al. proposed an algorithm for management of advanced disease
  - CT grading
    - Grade 1 – solely fenestral
    - Grade 2A – retrofenestral – halo effect
    - Grade 2B – narrowed basal turn
    - Grade 2C – both 2A and 2B
    - Grade 3 – diffuse confluent retrofenestral
  - Speech discrimination
  - Air-Bone Gap
Management

- Another study looking specifically at cochlear implantation for far advanced otosclerosis
  - Suggested stapedotomy with hearing aid as first line treatment
    - Cost
    - Better sound quality of acoustic transmission
    - Previous stapedotomy does not negatively affect the outcome of subsequent cochlear implantation
  - If basal turn narrowing is present, cochlear implantation should be offered as a first option because further narrowing would complicate electrode insertion

Kabbara et. al
Conclusion – Page 1

• Otosclerosis is a disease primarily associated with CHL but mixed hearing loss can be present
• Primarily a disease of white population with 2:1 female:male distribution
• Presents as gradual onset/progressive hearing loss, usually bilateral, and asymmetrical
• Diagnosis made by clinical, audiological, and CT findings
• Hearing aid should always be offered as an option of treatment
• Medical therapy may benefit some patients in halting disease progression but no definitive recommendations have been made on use of medical therapy
• Several surgical techniques exist for stapes fixation and outcomes widely depend on surgeon skill and comfort level with the surgical technique
• No definitive guideline has been established for treatment of far advanced otosclerosis
Dr. Smith, that was a good discussion. It was very thorough and covered a lot of questions that come up in treatment. One of the things I want to highlight is the differential diagnosis in the patient with a normal looking ear and a conductive hearing loss. It’s important to consider the differential diagnosis. A lot of things you would diagnosis in the surgical exploration of the middle ear, but the notable one is the superior semicircular canal dehiscence, because that will present as a normal ear with a conductive hearing loss.

When you operate, however, assuming that you don’t realize that the patient isn’t sick and you take it out and fix it and put a prosthesis in you’re going to find that it makes no difference in the conductive hearing loss and in fact that syndrome, superior semicircular canal dehiscence was identified not that many years ago, in fact I think I was in residency when Lloyd Minor published on that. Subsequently they’ve gone back and looked at a bunch of patients who had conductive hearing loss and found that many of these patients who did not get better after the stapedectomy had the syndrome.

Sodium fluoride. It’s controversial. Some surgeons use it; some don’t. I don’t know where the variability comes from. I use it inconsistently. The big part about it is that the dosage has never been established. So you worry about the problems, the GI problems, the arthritis. Most people who give fluoride use the vitamin supplement FluoroCal.
The expected outcome of surgery for otosclerosis. Typically, across the board the result that people get is about a ten decibel air bone gap closure. So with a patient with less than a fifteen decibel air bone gap, it doesn’t make much sense to offer him an operation. You’re just putting him at risk for complications, namely, sensorineural hearing loss.

Most surgeons will want to verify the air bone gap themselves. The way we do that is by going through the 250, then the 500 then the 1000 then the 2000 and the adage that we go by is if they flip on the 512 then they’re probably a good candidate. If they flip on the 1024 then they are a great candidate.

**Laser vs. drill.** There may not be a whole lot of difference in a primary case. I think that in a revision you have a very good reason for choosing a laser over a drill. In a revision case where you already have a prosthesis in place there’s a chance there may be some scarring around the prosthesis even down to some of the delicate structures underneath. You then have a higher risk of causing sensorineural hearing loss in a revision case and that’s possibly the reason why. In a revision case the laser is safer in that situation because it is atraumatic in doing this.
References

MANAGEMENT OF OTOSCLEROSIS

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Faculty Mentor/Reviewer: Tomoko Makishima, MD, PhD
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Grand Rounds Presentation
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