Association between bone mineral density and hearing loss in Osteogenesis Imperfecta

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I. Introduction

Osteogenesis Imperfecta (OI) - Hearing loss

- 50 % of OI patients
- OI types I, III, IV
- Mild to profound hearing loss, progressive
- Intrafamilial variability
- Hearing loss type:

  - Conductive hearing loss
  - Mixed hearing loss
  - Pure high-frequency sensorineural hearing loss
  - Pure sensorineural hearing loss
I. Introduction

OI - Hearing loss (2)

Mixed hearing loss

Conductive hearing loss

Sensorineural hearing loss

Outer or external ear

Middle ear

Inner ear

Semi-circular canals (labyrinth)

Auditory nerve

Cochlea

Eustachian tube

Malleus

Incus

Stapes

Oval window

Pinna

External Auditory Canal

Ear lobe

Eardrum (tympanic membrane)
## I. Introduction

### OI - Hearing loss (3)

<table>
<thead>
<tr>
<th>Conductive – Mixed</th>
<th>Pure sensorineural loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Otosclerosis-like lesions: stapes footplate fixation (and pericochlear lesions)</td>
<td>- Cochlear hair cell atrophy</td>
</tr>
<tr>
<td>- Ossicular discontinuity (fractured/atrophic ossicles)</td>
<td>- Atrophy stria vascularis</td>
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<tr>
<td></td>
<td>- Perilymphe hemorrhage</td>
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</tbody>
</table>
I. Introduction

Computed tomography temporal bones

Bilaterally severely progressed mixed hearing loss in a 67-year old OI-patient: severe pericochlear demineralization of bone
1. Introduction

Research aim

- Relationship between occurrence/type of hearing loss and generalized bone disease?
- Heterogeneity of hearing loss explained by variability in bone characteristics?
II. Methods

Patients and materials

- 56 adult OI patients (F: 34   M: 22) with identified mutation in \textit{COL1A1} or \textit{COL1A2}
  - Mean age: 43 y. (SD 13.7)
  - Bisphosphonates administration excluded

- Audiological evaluation
  - Pure-tone audiometry
  - Admittance measurements
  - Stapedius reflex measurements

- Bone mineral density (BMD) measurements
II. Methods
Bone mineral density measurements

- Dual X-ray absorptiometry (DXA): areal BMD (aBMD)
  - Lumbar spine
    - **trabecular bone aBMD**
  - Whole body
    - **cortical bone aBMD**

- Peripheral quantitative computed tomography (pQCT): volumetric BMD (vBMD)
  - Radial metaphysis (4%)
    - **trabecular bone vBMD**
  - Radial diaphysis (66%)
    - **cortical bone vBMD**

Bone geometry parameters: **cortical thickness, periosteal circumference, endosteal circumference**
III. Results

Audiological phenotype

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>40%</td>
<td>44</td>
</tr>
<tr>
<td>Conductive</td>
<td>46%</td>
<td>24</td>
</tr>
<tr>
<td>Mixed</td>
<td>14%</td>
<td>12</td>
</tr>
<tr>
<td>Stapes surgery</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Sensorineural</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>High-frequency sensorineural</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>
III. Results

Hearing loss as a function of OI type and genotype in 56 OI patients

No association between hearing loss and mutated gene, type I collagen defect or OI type
III. Results

Hearing loss as a function of aBMD (DXA)

- Mean z-scores < 0 (except sensorineural losses)
- ANCOVA (gender, weight, type I collagen defect):
  - sensorineural hearing loss > conductive/mixed hearing loss and normal hearing (P<0.05)
III. Results
Hearing loss as a function of vBMD (pQCT)

- ANCOVA [gender, age, type I collagen defect] for (trabecular vBMD z-score * hearing):
  - conductive/mixed hearing loss < normal and sensorineural hearing loss
- Radial diaphysis: no differences in cortical vBMD or bone geometry parameters
OI patients with conductive/mixed hearing loss have lower BMD compared to their normal hearing relatives with OI.
IV. Discussion

- OI patients with **conductive/mixed** hearing loss have **lower** BMD than patients with normal hearing or pure sensorineural loss.

- OI patients with **pure sensorineural hearing** loss have **higher** aBMD than patients with normal hearing or conductive/mixed hearing loss (small sample + highest mean age).

- No differences in volumetric cortical bone mineral density or bone geometry parameters measured at radial diaphysis:
  - Cortical vBMD: unreliable parameter when cortical thickness < 2.0 mm (spatial resolution too low).
V. Discussion

- Temporal bone:
  - Cortical bone
  - Bone formation complete at age 1 year
  - Bone remodeling is minimal

- Association conductive/mixed hearing loss and lower BMD: accumulating microfractures and fatigue microdamage destruct the osteoprotegerin (OPG) pathways which regulate temporal bone remodeling inhibition?

- Future perspectives:
  - Replication in large population
  - Histological investigations of OI temporal bones
  - Effects of bisphosphonates on hearing in OI