Eye diseases in OI, a Nation-wide, register-based cohort study

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Disclosures

• I have no industry involvement relevant to this study

• I have no industry involvement at all really

• I am part of the OIFE advisory board

• I was part of the organizing committee for this meeting

• MAJOR DISCLOSURE: I AM NOT AN OPHTALMOLOGIST
Background

- Collagen type 1 is found in most parts of the eye.

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- Several studies have shown thinner corneal thickness and lower ocular rigidity in patients with OI
  Dahl Hald, Ost Int 2018

- Case Reports describing patients with OI and glaucoma or retinal detachment have been published
  Rosbach, Der Ophthalmologe 2012
  Fleissig, Retinal Cases and Brief Reports 2014

- Some mutations in COL1A1 may be causative for OI and glaucoma
  Wallace, Molecular Vision 2014

- It is likely that patients OI will have increased risk of eye diseases.
Hypothesis & Aim

• We hypothesise that patients with OI have increased risk of:
  • Glaucoma
  • Refraction abnormalities
  • Retinal Detachment
  • Cataract

• We aimed to use the Danish health registers to evaluate the risk of these diseases in patients with OI compared to a reference population of non-OI inhabitants of Denmark.
Methods - the registers

- National Patient Register
  - Outpatient visits (1995)

- National Patient Register
  - Discharge diagnosis (1977)

- National Prescriptions Register (1995)

Central Persons Register
Methods - Endpoints

• Glaucoma = relevant ICD-8 / ICD-10 diagnosis OR dispensed prescription of drugs used to treat glaucoma

• Refraction abnormalities = relevant ICD-8 / ICD-10 diagnosis

• Retinal Detachment = relevant ICD-8 / ICD-10 diagnosis OR relevant operations code

• Cataract = relevant ICD-8 / ICD-10 diagnosis OR relevant operations code
Methods - Statistics

- Fine and Grey Competing risk regression
- Cumulative incidence plots
- % / n of all endpoints
- All statistics were done via a remote desktop at Statistics Denmark Division of Research using Stata 15
- Sub Hazard Ratios were significant when 95% CI did not include 1.00
Methods - Window of observation

• Identified all OI patients via NPR

• The NPR cover 1977 and onwards, and data was available until the end of 2012

• From 1995 information until the end of 2012, data was available on dispensed prescriptions

• All participants were followed from birth, until they met an endpoint, died or migrated.
Results - Participants

• We identified 687 (379 F) patients with OI

• They were matched 1:5 to persons from the CPR

• Covering 23,152 patient years of observation in the OI group

• Covering 119,338 person years of observation in the reference population
## Results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>OI group % (n)</th>
<th>Reference population % (n)</th>
<th>SHR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaucoma</td>
<td>2.9% (20)</td>
<td>1.3% (45)</td>
<td>2.12</td>
<td>1.25-3.59</td>
</tr>
<tr>
<td>Refraction abnormalities</td>
<td>2.3% (16)</td>
<td>0.5% (17)</td>
<td>4.15</td>
<td>2.11-8.19</td>
</tr>
<tr>
<td>Retinal Detachment</td>
<td>1.2% (8)</td>
<td>0.1% (4)</td>
<td>12.2</td>
<td>3.22-46.25</td>
</tr>
<tr>
<td>Cataract</td>
<td>5.7% (39)</td>
<td>2.4% (82)</td>
<td>2.23</td>
<td>1.50-3.32</td>
</tr>
</tbody>
</table>
Results - Age at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>OI Median age [IQR]</th>
<th>Ref.Pop Median age [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>60 [51-68]</td>
<td>64 [55-77]</td>
</tr>
</tbody>
</table>

[Graph showing cumulative incidence of glaucoma over years of life for Osteogenesis Imperfecta (dashed line) and Reference Population (solid line).]
Results - Age at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>OI</th>
<th>Ref.Pop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>[IQR]</td>
<td>[15-37]</td>
<td>[31-57]</td>
</tr>
</tbody>
</table>

Refraction Abnormalities

Cumulative Incidence

Years of life

Reference Population

Osteogenesis Imperfecta
Results - Age at diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median age [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteogenesis Imperfecta (OI)</td>
<td>60 [34-68]</td>
</tr>
<tr>
<td>Reference Population</td>
<td>45 [38-59]</td>
</tr>
</tbody>
</table>
Results - Age at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>OI Median age [IQR]</th>
<th>Ref.Pop Median age [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>62 [47-69]</td>
<td>73 [64-80]</td>
</tr>
</tbody>
</table>
Discussion

- Little clinical data on OI type
- No information on what bases the eye diseases were diagnosed
- Berkson’s bias
- Low absolute risk of eye disease in both cohorts
Conclusion

There is an association between OI and the risk of glaucoma, retinal detachment, refractional abnormalities and cataract.

Further evaluation of the pathogenesis of this increased risk is warranted.

Based on our data routine ophthalmological evaluation may be indicated in patients with OI.
Thank you for listening

If we did not have time for your question, or I simply do not know the answer please come talk to me at the dinner and let us collaborate!