**PPIs and Risk for Bone Fractures**

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Abstract

The very large prospective study by Gray, et al., reviewed in this edition of VHJOE, Literature in Review, suggests that post menopausal women taking PPIs, do not have increased risk for hip fracture. However, these researchers did identify chronic PPI use to be associated with increased fracture risk of the wrist, forearm, clinical spine and total bone fractures, see Table 1.

The mechanism of chronic PPI use and increased fracture risk had been presumed to be decreased absorption of calcium caused by PPI inhibition of gastric acid production. However, data from the Women’s Health Initiative examining supplemental calcium and vitamin D showed that it did not appear to mitigate this risk. This finding has further raised doubt about the true cause and association of PPI use and bone fracture risk.

Several recent epidemiologic studies have indicated that the chronic use of PPIs is associated with increased risk for osteoporotic fractures. A British based study suggested a 44% increased hip fracture risk with PPI use for > 1 year, with the fracture risk accelerated among men and with higher doses. Targowink, et al., reported on an extensive case-control review of hip fracture risk in a Canadian province. They found that fracture risk was increased after chronic use of PPIs. More than 7 years of PPI use was associated with a 92% increased risk for any osteoporotic fracture and more than 5 yrs of PPI use associated with 62% increase for hip fracture risk. A summary of chronic PPI use and relation to hip and non-hip fractures is outlined in Table 2.

The majority of these studies on chronic PPI use and risk for bone fracture have been in individuals age 50
yrs or more. It is of great concern that the spiraling obesity epidemic in America has been paralleled by an epidemic of GERD in the young.\(^9\) Institution of PPI therapy among this younger cohort with chronic GERD offers a potentially longer exposure to PPIs and even greater lifetime bone fracture risk.

The recent Food and Drug Administration alert to Consumers, Patients and Healthcare Professionals was reasonable and timely.\(^10\) Although the numerical risk for bone fracture is small with chronic PPI use, the fracture risk is indeed consistently increased for forearm, wrist, and clinical spine. Hopefully, awareness of the association with increased bone fracture risk with chronic PPI use will heighten interest in bone health among all. For clinicians it will be prudent to periodically reevaluate the need for chronic PPI therapy and consider alternative management. For the elderly with requirement for chronic PPI, it may be important to consider prescribing the lowest effective PPI dose, ensuring adequate dietary calcium, and heightened awareness and suspicion for occult osteoporosis.

References:


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<thead>
<tr>
<th>Variable Examined</th>
<th>Number of Studies Supporting</th>
<th>References</th>
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<tbody>
<tr>
<td>Number of studies indicating increased fracture risk from chronic PPI</td>
<td>6 studies</td>
<td>1,2,3,4,6,7</td>
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<td>↑ Duration of PPI exposure until increased fracture risk</td>
<td>5 studies (1-12 yrs)</td>
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<td>PPI related bone fracture risk increased among older persons</td>
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<td>Higher doses of PPI reported to convey increased bone fracture risk</td>
<td>2 studies</td>
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<tr>
<td>Number of studies not finding increased risk for bone fracture among chronic PPI</td>
<td>1 study</td>
<td>5</td>
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