The Effects of Hyponatremia on Bone Density and Fractures: A Systematic Review and Meta-analysis

Kalyani Murthy, MD, MS, FACP, FASN, Diplomate of ABOM; Gerard J. Ondrey, BS; Natasha Malkani, MD; Gowri Raman, MD, MS; Mary Beth Hodge, MD; Andrew J. Marcantonio, DO, MBA; Joseph G. Verbalis, MD

Objectives: Hyponatremia decreases bone mineral density and a major risk factor for fragility fractures. Objectives of our systematic review and meta-analysis were to analyze the overall effects of hyponatremia on bone fractures, osteoporosis and mortality.

Methods: We extracted data from MEDLINE®, Cochrane Central, and EMBASE 1960-2017 and conference abstracts from 2007-2017. We included studies with data on serum sodium, fractures, bone density, or diagnoses of osteoporosis. Studies were independently reviewed by two authors and assessed for bias using the Newcastle-Ottawa scale. Random effect models meta-analysis was used when at least three studies reported the same outcome measures. We reported summary odds ratio (OR) and 95% confidence intervals (CI).

Results: We included 26 studies for qualitative analysis. 15 studies were included in the meta-analysis to evaluate the effects of hyponatremia on fractures, 4 studies for bone-mineral density changes and 6 for mortality. Hyponatremia increased the odds of fractures at all sites (summary OR 2.34 [95% CI 1.86, 2.96]. There was an increase in the odds of osteoporosis (summary OR 2.67 [95% CI 2.07, 3.43]). Mortality risk among the included studies remained high (Summary OR 1.31 [95% CI 1.16, 1.47]).

Conclusion: Our meta-analysis confirms a statistically significant association of hyponatremia with bone fractures and osteoporosis along with higher mortality. Long-term prospective studies

evaluating the impact of correcting hyponatremia on bone health, fractures and mortality are required.