High Prevalence of Osteoporosis in Patients With Chronic Pancreatitis: A Systematic Review and Meta-analysis

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BACKGROUND & AIMS: **Patients with chronic pancreatitis may be at high risk for osteoporosis and osteopenia. We performed a systematic review and meta-analysis to determine the prevalence of osteoporosis and osteopenia in patients with chronic pancreatitis.**

METHODS: **Articles were identified from MEDLINE, EMBASE, and SCOPUS databases (through October 2012) and a manual search of the literature. The primary outcome measure was bone density, measured by dual-energy X-ray absorptiometry (T-score or Z-score). When available, data on the prevalence of osteopenia, bone mineral density, and bone mineral content also were recorded.**

RESULTS: **Ten studies including 513 patients were eligible for inclusion. Based on a random-effects model, the pooled prevalence rate for osteoporosis among patients with chronic pancreatitis was 23.4% (95% confidence interval, 16.6–32.0). The pooled prevalence for osteopenia was 39.8% (95% confidence interval, 29.1–51.6). The pooled prevalence rate for either osteoporosis or osteopenia was 65% (95% confidence interval, 54.7–74.0).**

CONCLUSIONS: **Based on meta-analysis, almost 1 of 4 patients with chronic pancreatitis have osteoporosis, and almost two-thirds of patients have either osteoporosis or osteopenia. Osteoporosis and osteopenia are underappreciated sources of morbidity in patients with chronic pancreatitis. Bone health management guidelines are urgently required in patients with chronic pancreatitis.**

Keywords: Bone Disease, Metabolic; Demineralization; Risk Factor.

Osteoporosis is characterized by structural deterioration of bone tissue and low bone mass, leading to bone fragility and increased risk of fracture. Osteoporosis is a major public health problem because of its potentially severe consequences for both patients and the health care system.[1] Chronic pancreatitis is a progressive inflammatory condition resulting in exocrine and endocrine dysfunction. Exocrine dysfunction leads to reduced production of pancreatic digestive enzymes, and the resultant maldigestion and malabsorption of ingested nutrients leads to malnutrition and nutrient deficiency. Osteoporosis has been described in chronic pancreatitis, with 21% of chronic pancreatitis patients having osteoporosis in the earliest study published in 1997.[2] Since then, a number of studies have shown a varied prevalence of osteoporosis from 5% to 39%.[3–5] From these studies and others, it is reasonable to assume that patients with chronic pancreatitis may be at risk for osteoporosis and osteopenia (termed *osteopathy*). However, to date, no international consensus guidelines have recommended the assessment or monitoring of bone health in chronic pancreatitis. To address this uncertainty, we conducted a systematic review of the literature and a meta-analysis of the data to estimate the prevalence of osteoporosis and osteopenia in chronic pancreatitis.

Methods

Criteria for Consideration of Studies

Observational studies that reported data on the prevalence of osteoporosis in patients with chronic

Abbreviations used in this paper: **BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; DXA, dual-energy X-ray absorptiometry.**

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pancreatitis were included. The search was not limited by sex, geographic location, or publication status. Studies that were limited solely to pediatric patients (age, <18 y) were excluded. The primary outcome measure of interest was the prevalence of osteoporosis or osteopenia based on bone density measured by dual-energy X-ray absorptiometry (DXA) (T-scores or Z-scores), and, where available, bone mineral density (BMD) (g/cm^2) and bone mineral content (BMC) (g/cm).

Literature Search

The following bibliographic databases were searched for studies on chronic pancreatitis and osteoporosis: Ovid MEDLINE (1946 to October 31, 2012), Elsevier EMBASE (1980 to October 31, 2012), and SciVerse SCOPUS (1966 to October 31, 2012).

No date or language restrictions were used, but searches were limited to human beings. Searches were conducted during October of 2012, and search updates were set-up to send updates to the authors automatically from MEDLINE, EMBASE, and SCOPUS. The last update considered for inclusion was sent at the end of October 2012.

The search strategy was developed for Ovid Medline and translated for use on EMBASE and SCOPUS. We searched for articles with combinations of subject headings and key words relating to "Pancreatitis, Chronic" or "exocrine Pancreatic Insufficiency" and "Bone Density" or "Absorptiometry, Photon" or "Bone Diseases, Metabolic." Further searches were performed by scanning the reference lists of the primary and review articles to identify studies not found by the electronic search. We also conducted searches of conference proceedings. Last, we searched the Cochrane central register of controlled trials (The Cochrane Library) but did not find any randomized studies that provided data for our analysis. Both independent reviewers (S.N.D. and N.D.S.) were supported in developing search terms by medical librarians (D.M. and A.M.) in separate institutions.

Study Selection Criteria

All citations identified by literature search were screened independently by 2 reviewers (S.N.D. and N.D.S.) using article titles and abstracts. The full texts of potentially relevant articles were sought and the selection criteria were applied. Conference proceedings were considered for inclusion if they contained adequate relevant information for review. Reviewers were not blinded to author names or institutions. Studies were selected according to predefined criteria. For both conference proceedings and full-text articles in which there were missing data or a requirement for clarity, the study authors were contacted by e-mail. In the case of non–English language articles, translations were performed by Corporate Translation Services in Dublin, Ireland (ISO 9001:2008 certified).

Assessment of the Quality of Individual Studies

The quality of the studies was evaluated independently by the 2 reviewers using the Newcastle–Ottawa Scale, which uses a star rating system to judge the quality of observational studies.[6] This scale awards a maximum of 9 stars to each study: up to 4 stars for selection of participants, 2 stars for comparability of participants on the basis of the design or analysis, and 3 stars for ascertainment of exposure. We assigned scores of 0 to 3, 4 to 6, and 7 to 9 for low-, moderate-, and high-quality studies, respectively.

Data Extraction and Statistical Analyses

Data extraction was performed independently (by S.N.D. and N.D.S.) using a predefined data extraction form. Osteoporosis and osteopenia rates (osteopathy rates) were recorded. BMD and BMC were recorded where available for patients and controls. Additional data sought included the following: study design, sex, age, etiology, DXA scanner used, sites assessed, exocrine function, disease severity, and body mass index (BMI). Studies that reported the rate of osteoporosis were deemed eligible for meta-analysis. If studies also reported the rate of osteopenia, the overall prevalence of osteopathy also was calculated by meta-analysis. Data were meta-analyzed using Comprehensive Meta-Analysis software (version 2.2.064; Englewood, NJ) and Forest plots were constructed using Excel (Microsoft Office 2007; Microsoft, Redmond, WA) as described by Neyeloff et al.[7] Data were presented as prevalence rates (with percentages) and corresponding 95% confidence intervals. A pooled estimation was computed using a random-effects model to provide a more conservative estimate of the prevalence, allowing for variations between studies. Statistical heterogeneity between studies was calculated as I^2 (values ranged between 0% and 100%, with values closer to 0% indicating less heterogeneity). The I^2 quantity describes the percentage of total variation across studies that is caused by heterogeneity rather than chance. Details on reported statistical associations with age, sex, smoking, exocrine function, BMI, disease duration, duration of symptoms, smoking, vitamin D level, diabetes, and bone biochemistry within individual studies were recorded and described qualitatively. The Meta-analysis of Observational Studies in Epidemiology guidelines[8] were adhered to where appropriate. P values less than .05 were considered statistically significant.

Results

Search Results

The search and selection process is summarized in Figure 1. Manual searches of the reference sections of relevant articles and reviews did not provide any further