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ORIGINAL ARTICLE

Bone mineral density assessed by dual-energy X-ray absorptiometry in patients with viral or alcoholic compensated cirrhosis. A prospective study

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Summary
Background/aim: Cirrhosis is considered as a risk factor for osteoporosis whose prevalence is poorly known. The aim was to assess prospectively bone mineral density (BMD) in patients with alcoholic or viral compensated cirrhosis.
Methods: From 2006 to 2008, patients with viral or alcoholic compensated cirrhosis had BMD assessment by dual-energy X-ray absorptiometry. The prevalence of osteopenia (-2.5 SD < T-score < -1 SD) and osteoporosis (T-score ≤ -2.5 SD), and the influence of age, gender and aetiology of cirrhosis were assessed using univariate and multiple regression analysis.
Results: One hundred and nine patients were studied (72 men, 55.3 ± 11.4 years and 37 women, 65.2 ± 11.0); with HBV ($n = 35$), HCV ($n = 43$), or alcoholic cirrhosis ($n = 31$). At the lumbar spine, 25 patients had osteopenia and 12 had osteoporosis. At the femoral site, 23 had osteopenia and 4 had osteoporosis. Female gender had an independent decreased effect on the total BMD.
Conclusions: The prevalence of osteoporosis was up to 11% at the lumbar spine, greater in women independently of age, without significant difference according to the aetiology of cirrhosis.

Abbreviations: BMD, Bone mineral density; DXA, Dual-energy X-ray absorptiometry; WHO, World Health Organization; HCV, Hepatitis C virus; HBV, Hepatitis B virus; SD, Standard deviation.

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Osteoporosis is a major public health problem because of the ageing of the population and the risk of bone fracture that is a source of morbidity and mortality [1]. The association between chronic liver diseases and osteoporosis has been suggested by clinical and more recently physiopathological studies. The physiopathology of osteoporosis is now focused on:

- osteoclastogenic proinflammatory cytokines (interleukin-1 and tumor necrosis alpha) implicated in hepatic inflammation and fibrosis [2];
- osteoprotegerin, that promote osteoclastic bone resorption in addition to the receptor activator of NF kappa beta (RANK) and the receptor activator of NF kappa beta ligand (RANKL) [3].

These main osteoclastic proteins are produced in part by the liver. Their serum levels have been assayed in patients suffering from chronic liver diseases but ranges are very large [4]. Moreover, during chronic liver diseases, there is a decreased activity of osteoblasts under the influence of various factors such as low level of Insulin-Growth Factor-1, cholestasis or alcohol [5].

Due to recent improvements in the management of cirrhosis, patients with cirrhosis have an increased life expectancy and are potentially exposed to an increase in bone complications. Several studies have assessed bone mineral density (BMD) during chronic liver diseases [5,6]. However, methodological disparities exist regarding radiological techniques and sites of measurement and definition of osteoporosis. Considering only the studies using both the reference technique (dual-energy X-ray absorptiometry, DXA) and the World Health Organization (WHO's) criteria for the definition of osteoporosis [1], there is a large heterogeneity of the studied populations with regard to risk factors of osteoporosis such as gender, age, cause of liver disease, level of hepatic fibrosis and degree of liver failure. The vast majority of studies enrolled subjects with chronic cholestasis such as primary biliary cirrhosis [7]. Studies on non-cholestatic chronic liver diseases, particularly viral hepatitis [3,8—13] and alcoholic liver disease [14] are much fewer. Some have included patients free of cirrhosis, who are probably at low risk of osteopenia [8,15]. Among the main studies evaluating BMD in virus related-cirrhosis [3,8—13], the number of patients was low and the severity of cirrhosis was marked, with only a minority of patients with compensated disease and no liver failure. Three studies [3,9,11] have determined the prevalence of osteoporosis in the sub-group of patients with Child-Pugh class A viral cirrhosis, but only 34 patients were enrolled, the prevalence of osteoporosis ranging from 0 to 37.5%.

The aim of this prospective study was to describe the prevalence of osteopenia and osteoporosis assessed by the reference method (DXA) and defined according to WHO's criteria, in a large number of patients with viral and/or alcoholic Child-Pugh class A cirrhosis.

Patients and methods

Patients

Between November 2006 and May 2008, all consecutive patients fulfilling the following criteria were included:

- age greater or equal to 18 years;
- histologically proven cirrhosis, whatever the date or method of liver biopsy;
- viral or alcoholic cause of cirrhosis, defined by the presence of serum HBsAg and/or antibodies against hepatitis C virus (HCV), or excessive consumption of alcohol (more than 21 and 28 glasses of alcohol per week or 30 and 40 g/day in women and men respectively for over 5 years);
- absence of human immunodeficiency virus co-infection and/or other severe life-threatening affection;
- compensated liver disease (Child-Pugh class A) and absence of detectable hepatocellular carcinoma;
- absence of ongoing pregnancy;
- signed informed consent.

The following clinical items were collected at enrolment for each patient: date of birth, gender, height, weight, body mass index (BMI,) daily consumption of alcohol at enrolment and in the past years, overall consumption of tobacco, personal or family history of fracture, age of menopause, associated medical conditions, treatments that could affect BMD (corticosteroids, substitutive hormone therapy, calcium and vitamin supplementation, anti-osteoporotic drugs, beta blockers, HBV or HCV anti-viral treatment) either current or in the last 24 months.

The results of recent blood tests (less than 3 months) were also collected: serum bilirubin, ALT and AST activities, alkaline phosphatase, gamma-glutamyl transferase, platelets count, prothrombin time, albumin, total cholesterol with HDL and LDL fractions, triglycerides, fasting glucose, calcium, phosphorus, HBsAg status and in case of positivity serum DNA level, HBeAg/anti-HBe status and hepatitis delta serology, HCV serology and in case of positivity serum level of HCV RNA.

Measurement of serum 25 OH vitamin D

25 OH vitamin D serum level was measured using a commercial test (Kit RIA/DIASORIN) on available frozen serum collected at the time of DXA and conserved at −20 °C.

Measurement of bone mineral density

All procedures were performed and interpreted by the same operator (NS) blindly to the biological and clinical data. For women of childbearing age, pregnancy was ruled out before DXA both by the date of the last menstrual period and urinary ßHCG level.

BMD was measured at the femoral neck and the lumbar spine (L1-L4) in the absence of osteoarthritis, by DXA with a direct digital conversion device (Lunar Prodigy Advance, Paris, France) integrating the French reference curves for subjects older than 20 years and the European reference curves for subjects younger than 20 years, taking into account gender, ethnicity, and the exam site. T-scores (difference in standard deviation [SD] between the patient's measured BMD value and the maximum mean BMD of young adult of same gender obtained from reference curve) and Z-scores (difference in SD between the patient's measured BMD value compared to normal reference for age and gender) were calculated. According to the WHO's