Cobb angle, vertebral deformity and fractures in alcoholic patients

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Summary

Background: Hypercyphosis and vertebral deformity are related to vertebral fractures. There are no studies in chronic alcoholics.

Objective: To analyse the relationship which exists between the Cobb angle and different degrees of vertebral deformity, and bone mass and various variables related to bone metabolism in chronic alcoholic patients.

Material and methods: 57 alcoholic males aged 52 ± 12 years were included. The Cobb angle was calculated and the degree of vertebral deformity of T7, T8, T9 and T10 was measured using MorphoXpress® and thoracic X-ray. The bone mass in the spine and hip were determined using a DXA Hologic Walthan 2000, and exiting clinical fractures with the clinical history. In addition, the nutritional state, the degree of alcoholism, variables of hepatic function, the presence of hepatic cirrhosis, and bone metabolism, were analysed. The results were also studied in 20 controls of similar age and of the same sex.

Results: The patients had a greater Cobb angle in comparison with the controls (30 ± 9° vs 17 ± 5°, respectively, p<0.001). Those with cirrhosis had lower bone mass than those without in the lumbar vertebrae (p<0.01) and femoral neck (p=0.02). The deformities in T7, T8, T9 and T10 were associated with a greater cyphosis, longer period of consumption and with existing vertebral fractures (p<0.01), non-vertebral fractures (p<0.002) and hip fractures (p<0.001). There were 65 existing fractures, 46 in the rib, 12 vertebral and 7 in the hip. The patients with a higher Cobb angle had more vertebral (p<0.01) and non-vertebral (p<0.004) fractures, as well as a longer period of alcohol consumption (p=0.02).

Conclusions: Chronic alcoholics have greater cyphosis than the controls. Wedge or biconcave vertebral deformities are related with a greater cyphosis, higher consumption of alcohol and existing fractures. In this series a higher Cobb angle is related to existing vertebral fractures. The most intensive drinkers had a higher Cobb angle and more fractures.

Key words: hypercyphosis, Cobb angle, vertebral fractures, alcoholism.
**Introduction**

The chronic alcoholic patient, in the fourth or fifth decade of their life, has a reduced bone mineral density (BMD) comparable with an old person. This decrease in BMD, combined with an irregular lifestyle, with a propensity to traumas due to accidental falls or to aggressive attacks led Oppenheim (1977) to coin the term “battered alcoholic syndrome” to designate those alcoholic patients with three or more fractures in different stages of development.

The bone pathology of the chronic alcoholic consists essentially in osteoporosis of low turnover in which malnutrition, chronic hepatopathy, changes in the pancreas and hormonal changes, and life style (unemployment, marginalisation, little exercise) play an essential role.

In men, the frequency of an osteoporotic vertebral compression fracture is estimated at approximately 5%, which results in a loss of vertebral height and/or angulation, with the progressive development of thoracic kyphosis.

In chronic alcoholics, the relationship between bone mass and fractures has been little studied. The prevalence of fractures diagnosed though thoracic radiography in alcoholics has varied in different series analysed from 8.7 to 36%. Earlier studies have described in alcoholic patients an association between vertebral fractures and peripheral fractures in spite of a BMD above the fracture threshold, suggesting the use of conventional X-ray imaging techniques combined with bone densitometry for the diagnosis of osteoporosis in these patients.

The changes in curvature of the thoracic kyphosis may be related to the intensity and type of vertebral or non-vertebral deformity or fracture which exist in alcoholic patients. Therefore, the objectives of this study were to compare the Cobb angle of alcoholic patients with those of a control population and to analyse the relationship which exists between this angle and the vertebral deformity measured with the use of a MorphoXpress®, with the BMD, variables of bone metabolism, hepatic function, degree of alcoholism and previous vertebral and non-vertebral fractures.

**Material and method**

We designed a prospective unicentric study in which we included 57 male alcoholic patients admitted to the internal medicine service of the University Hospital of the Canary Islands between May 2005 and June 2007 consecutively, due to alcoholism-related organic complications, alcoholic abstention syndrome or decompensation of hepatic cirrhosis. We classified the patients into cirrhotic or non-cirrhotic as a function of clinical, analytical and imaging variables.

Excluded from the study were those patients with neoplastic diseases, chronic hepatopathies of a different origin, or those with HIV infection, in order to avoid confusion at the time of the study, as well as those who were taking drugs which may interfere with calcium metabolism. The control group was composed of 20 healthy males who drank less than 10g/ day of alcohol.

Once the informed consent had been given, the clinical history was reviewed and the history and locations of earlier fractures, degree of the alcoholism, organic and clinical repercussions of the alcoholic disease, hepatic cirrhosis (ascites and encephalopathy) and nutritional state were obtained.

- In addition, general and routine analyses were carried out to determine the following:
  1. Hormones related to bone metabolism: IGF-1, thyroid hormones (free T4), parathormone (PTH), vitamin D, cortisol, estradiol, testosterone.
  2. Variables related to bone turnover: osteocalcin, telopeptide, osteoprotegerin (OPG) and RANKL.
  3. Hepatic function evaluated through prothrombin activity, albumin and blood bilirubin.

An analysis of the nutritional status of the patients was made by calculating the subjective global nutritional assessment (SGNA) where:

- Well nourished: 0-2 points
- Moderate malnutrition: 3-4 points
- Severe malnutrition: 5-10 points

For this assessment an anthropometric evaluation was carried out using dynamometry, tricipital cutaneous fold, and brachial perimeter.

- Posterior-anterior and lateral X-rays of the thorax: with the lateral thoracic X-ray the degree of thoracic curvature was determined by calculating the Cobb angle between T1 and T12, and the morphology of the vertebral bodies were studied for the diagnosis of existing vertebral fractures. Existing vertebral fractures were defined at the time of inclusion in the study as a reduction of - at least - 20% in the anterior medial or posterior height of the vertebral body, according to the Genant criteria, or the presence of visible vertebral wedging or crushing.

- MorphoXpress® (deformity and fracture): the vertebral morphometry was evaluated in T7, T8, T9 and T10. Both evaluations were carried out by a single observer. The MorphoXpress® system is a digitised method of reading of standard or digital X-rays of the dorso-lumbar spinal column in their lateral projection. After the digitisation of the X-ray image it is compared by a system expert with a database internal to the system which contains more than 3,000 images, with the aim of identifying tridimensionally the different vertebrae analysed. After this tridimensional study, the equipment positions six points in each vertebra analysed, allowing the operator to modify these points to adjust them for a better view. In evaluating the image thus obtained, the software calculates the different vertebral heights from the positioned points, and detects the existence and severity of vertebral deformity and fracture. This method has shown a high level of precision and little inter-observer variability.

- Densitometry: we determined the bone mass in the spinal column (L2, L3, L2-L4), femoral neck of the hip, the extremities, rib cage, dorso-lumbar spine and pelvis, using DEXA with HOLOGIC® QDR-2000 (Waltham, MA, USA).

This study was approved by the ethics committee of our centre (2009/23) and complies with the 1975 Helsinki Declaration.
Statistical analysis
Firstly, it was determined if the variables had a normal distribution using the Kolmogorov-Smirnov test. Even though they mostly showed a parametric distribution, in some, such as fracture, IGF-1, PTH, osteocalcin and RANK, it was non-parametric. Therefore, for the univariate inferential statistics, in the case of parametric variables the Student-t test was used to compare a variable between two groups, the VARIANZA analysis (in the case of three or more groups) and, subsequently, the Student-Newman-Keuls (SNK) test to discern between which groups differences were established, and the Pearson correlation test to analyse the relationships between two quantitative parameters. Given the relationship with bone mass to age, a covariant study was conducted with these parameters.

In the case of non-parametric distributions, the Mann-Whitney U test to analyse differences between 2 groups, and Kruskall-Wallis to analyse differences between 3 or more groups, as well as Spearman’s correlation, were used.

Results
The 57 alcoholic patients studied had an average age of 52 ± 12 years and were all drinkers up until the time of admission, with a consumption of more than 201 ± 79 g/day of alcohol. The average period of consumption was 28 ± 11 years. The total accumulated dose of alcohol was 29 kg – alcohol/kg (Table 1).

53% of the patients were cirrhotic (29 patients) and 47% non-cirrhotic (28 patients). There were no differences between the ages of the two groups (p=0.27).

The average Cobb angle between T1 and T2 in the group of patients was 30 ± 9º and in the controls, 17 ± 5º (p<0.0001).

The deformities of the vertebrae studied are expressed as a percentage of the loss of height in the anterior wall (wedging), central height (biconcave) and global (crushing).

The averages of wedging in T7 were 16 ± 9%, of biconcave deformity 15 ± 7% and of crushing 3 ± 4%.

The wedging of T8 was an average of 13 ± 8%, while the biconcave deformity and crushing were 13 ± 9% and 10 ± 8% respectively. The vertebral wedging of T9 was an average of 14 ± 9%, the biconcave deformity 15 ± 8% and the crushing 7 ± 6%. The wedge deformity in T10 was an average of 14 ± 9%, biconcave 15 ± 9% and crushing 2 ± 5%.

In the group of patients a total of 65 fractures were detected: 46 costal fractures, 12 vertebral fractures and 7 fractures of the hip. The number of fractures was similar in the cirrhotic and non-cirrhotic patients (vertebral, non-vertebral and costal).

66% of the patient were smokers with a packets/year index (PYI) averaging 29 ± 22. There were no differences in the Cobb angle (p=0.6) or in vertebral morphometry (p=0.2) between smokers and non-smokers.

The cirrhotic patients had less bone mass than the non-cirrhotic in the different areas analysed (Table 2). The Cobb angle in cirrhotic patients (29 ± 9°) and non-cirrhotic (28 ± 8°) was similar (p=0.6). The intensity of the thoracic kyphosis was not related to the Child-Pugh stage, nor to other clinical variables (ascitis and encephalopathy) or analyses of liver function (prothrombin, albumin and bilirubin). In the group of patients the wedging of T7 (p<0.01) and the biconcave deformity of T8 were related to a greater Cobb angle.

Table 1. General characteristics of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=57)</th>
<th>Controls (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 ± 12</td>
<td>50 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>24.1 ± 3.1</td>
<td>25.6 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Subjective nutritional assessment</td>
<td>30/12/15</td>
<td>20/0/0</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Consumption of alcohol (g)</td>
<td>201 ± 79</td>
<td>&lt;10</td>
<td></td>
</tr>
<tr>
<td>Cobb angle (degrees)</td>
<td>30 ± 9</td>
<td>17 ± 5</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Osteocalcin (ng/ml)</td>
<td>3.3 ± 3.1</td>
<td>7.0 ± 2.5</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Telopeptide (ng/ml)</td>
<td>0.59 ± 0.40</td>
<td>0.19 ± 0.10</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Vitamin D (pg/ml)</td>
<td>29.1 ± 15.2</td>
<td>82.5 ± 27.6</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IGF-1 (ng/ml)</td>
<td>95.9 ± 101.1</td>
<td>179.32 ± 97.25</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Serum PTH (pg/ml)</td>
<td>77.2 ± 136.4</td>
<td>75.2 ± 105.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant
In terms of the deformities, we found that the crushing of T7 was related to the presence of ascites (p=0.009) and high values of PTH (p=0.02) and free T4 (p=0.01), while the wedging was related to a smaller tricipital skin fold (p=0.04). The wedging of T8 was related to a reduction in prothrombin activity (p=0.01) and the biconcave deformity with a reduction of osteocalcin (p=0.03). The wedging of T9 was related to the presence of ascites (p=0.04), low values of IGF -1 (p=0.01) and raised levels of cortisol (p=0.005) while the biconcave deformity of T10 was related to free T4 (p=0.01).

In terms of the patients’ existing vertebral fractures, the fractured patients had a greater degree of kyphosis and, therefore, a greater Cobb angle in comparison with those who were not fractured (p<0.01) (Figure 1).

Those patients with vertebral fracture had a greater biconcave deformity of T7 (p=0.002) and T8 (p<0.01), as well as wedging of T8 (p=0.04). However, by introducing the amount of daily intake in grams and the period of consumption as covariables, we see that, with respect to the biconcave deformity of T7, the relationship is dependent on the period of consumption. This is not the case with T8. An existing fracture of any type was related to the biconcave deformity of T7 (p=0.02) and T10 (p=0.009), while in both cases this relationship depended on the period of consumption. The wedging of T10 was related to fracture of the hip (p=0.0001) and to costal fracture (p=0.002), although in this case the quantity of daily alcohol intake replaces vertebral deformity.

We found no relationship between the Cobb angle and hip or costal fractures.

Patients with a longer period of consumption had a higher Cobb angle (p=0.002) (Figure2) and greater T7 wedging (p=0.03) and T8 biconcavity (p=0.03).

Those patients with a fracture had a longer period of consumption in comparison with those with no fracture (p=0.04), and the intake was heavier, with a higher total accumulated dose (p=0.02).

Those patients with costal fractures consumed more alcohol daily (228 ± 96 g/day, p=0.03) in comparison with those with no fractures (163 ± 64 g/day, p=0.012) (Figure 3).

In this series we found no relationship between the Cobb angle and the variables relating to nutritional state, parameters and hormones of the calcium-phosphorus metabolism, or with the markers for bone synthesis or resorption.

### Discussion

In alcoholic patients a decrease in bone mass is common, the effect being more intense in those with cirrhosis. Our patients had less bone mass in the lumbar spine, pelvis, extremities and hip; data in accord with earlier studies9-11. Osteopathy in the alcoholic is multifactorial. The alcohol exerts a double lesive effect on the bone; on the one hand, it affects bone synthesis due to osteoblast toxicity12, while on the other, it increases bone resorption by stimulating osteoclast activity and osteoclastogenesis through IL-6 and the induction of RANKL13. In addition, its toxic effects on muscle and the nervous system appear to be related to a higher risk of falls. Finally, other factors related to a propensity to traumatism, falls, social marginalisation, and irregular meals, among others, contribute to bone loss and fractures in alcoholics14-15.

### Table 2. Bone mineral density in cirrhotic and non-cirrhotic

<table>
<thead>
<tr>
<th></th>
<th>Cirrhotic (n=29)</th>
<th>Non-cirrhotic (n=28)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal column</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>0.9 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>p=0.01</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>0.8 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Total hip</td>
<td>0.8 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>p=0.05</td>
</tr>
<tr>
<td>Pelvis</td>
<td>0.9 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>p=0.008</td>
</tr>
<tr>
<td>Right leg</td>
<td>1.1 ± 0.1</td>
<td>1.2 ± 0.2</td>
<td>p=0.01</td>
</tr>
<tr>
<td>Left leg</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Right arm</td>
<td>0.7 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Left arm</td>
<td>0.7 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Right rib cage</td>
<td>0.5 ± 0.1</td>
<td>0.6 ± 0.1</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Left rib cage</td>
<td>0.5 ± 0.1</td>
<td>0.5 ± 0.1</td>
<td>p=0.001</td>
</tr>
</tbody>
</table>
The angle of thoracic kyphosis increases with age and is related with underlying osteoporosis and/or the presence of vertebral fractures. Hyperkyphotic posture and postural changes offer the capacity for clinical prediction which the markers for osteoporosis do not. Epidemiological studies have shown that hyperkyphotic posture is associated with a deterioration in pulmonary function, physical state, falls, fractures and mortality.

It is known that one of the effects of the consumption of alcohol on the metabolism is a 2.4-fold increase in the relative risk of vertebral fracture. This study also underlines the importance of tobacco in vertebral fracture, observing that the concomitance of both factors in the same patient multiplied the risk of vertebral fracture. In our study the alcoholics had a greater Cobb angle in comparison with the controls, but smoking did not significantly increase it. In classifying the patients as cirrhotic or non-cirrhotic we found no differences, and the angle of kyphosis was not related to the degree of the underlying hepatopathy, nor with the nutritional state. However, the presence of ascites was related with various degrees of deformities of the dorsal vertebrae. As is it logical to expect, those patients with greater vertebral deformity and with vertebral fractures had a higher Cobb angle, and, therefore, greater kyphosis. The different types of deformities in the vertebrae analysed were significantly related to existing vertebral, non-vertebral, and hip fractures. However, greater kyphosis was not associated with either non-vertebral or hip fractures.

The Cobb angle was not related to bone mass determined in the dorso-lumbar spine, pelvis, hip, rib cage or limbs, or with non-vertebral or hip fractures.

From a biomechanical point of view the square of the BMD is proportional to the resistance to compression of the trabecular bone, which means that small reductions in BMD would be associated with significant decrements in bone resistance. In vivo, a high BMD does not necessarily imply a greater biomechanical resistance, which indicates that other factors independent of BMD are related to bone resistance.

These results concur with those of a study carried out with 76 chronic alcoholics with 27 vertebral fractures, in which no significant differences were found in the BMD in the lumbar spine in patients with or without vertebral fractures, although those patients with vertebral fractures actually had more peripheral fractures.

The intensity of the alcoholism is a factor related to the osteopathy of these patients. In our study we included patients with significant alcohol intake, higher than 200 g of alcohol a day for more than 20 years, and we have observed a significant relationship between the quantity of consumption and vertebral deformity and an increase in the Cobb angle; there is also a relationship between the period of consumption and the angle of kyphosis (dose- and time-dependent). Hence, in the heaviest drinkers we find more episodes of fracture.
The direct effect of alcohol on the osteoblasts is already an old observation. There are studies which describe a dose-dependent effect with an anti-proliferative action on the osteoblasts. The quantity of bone mineral present in the skeleton depends on the quantity acquired during the skeleton's development and maturation phases, and which reaches its maximum value (peak bone mass) in adulthood. Genetic, nutritional, environmental and hormonal factors contribute negatively to the achievement of an adequate reserve of bone. One of the greatest risks of developing osteoporosis is the attainment of a lower peak bone mass in youth. The consumption of alcohol, common in adolescents and young people, tends to occur at this stage, which compromises the attainment of an adequate peak bone mass. Many of our patients started to drink at an early age and have continued, which results in structural and functional changes in the bone in the medium and long term. The consumption of alcohol can affect different parts of the skeleton in different ways, and the vertebrae appear to be the most sensitive to damage after chronic consumption, and their recuperation after abstinence slower, which would result in skeletal changes which may persist, increase fragility and cause osteoporosis, deformity and fracture.

The use of MorphoXpress allows the early diagnosis of deformity and vertebral fracture through the use of conventional X-rays, reducing the time needed for morphometry, increasing the accuracy of the process, with little intra- and inter-observer variability, and facilitating a sensitive following of its development vertebra by vertebra.

In this disease there is a high incidence of complications during the treatment of fractures. Studies in rats suggest that alcohol exerts direct, dose-dependent biological effects on the process of consolidation of the fracture, essentially an anti-proliferative effect, and an inhibition of osteoblast function. Experimentally, in alcoholic rats subject to femoral ostectomy, a total absence of bone callusing compared with the controls in which the consolidation was complete, has been confirmed. Chakkalakal et al. described a defective bone repair, poor rigidity and demineralised bone matrix, with deficient mechanical properties, effects which improve with abstinence. Other studies found that ethanol inhibits rapid "intramembranous" bone formation which characterises normal consolidation in fractures, and promotes fibrosis instead of osteogenesis at the point of repair, by which the osteoid and fibrous tissue ossify, resulting in dysmorphic mineralisation, originating new tissue with poor biomechanical properties independently of the bone mineral content. The essential differences are in the rigidity of curvature, strength and ash density of the tissue which forms the bone callus. Thus, these data reinforce even more the leseive effect which alcohol exerts on the skeleton. What is notable in this series is the absence of a relationship between vertebral deformity and fractures and markers for bone and mineral metabolism. It is possible this is related to the irregular lifestyle of these patients with a propensity to falls and traumatisms which change bone morphology and increase the risk of fractures.

Conclusions

Chronic alcoholics show a decrease in BMD and a greater degree of kyphosis compared with the controls. Vertebral deformity - wedge or biconcave - are related with a greater kyphosis, higher consumption of alcohol and the presence of existing fractures. A greater Cobb angle is related with a higher prevalence of vertebral fractures in our patients, independently of BMD, hepatic function, nutritional state and bone metabolism. The most intensive drinkers had a greater Cobb angle and more existing fractures.

Bibliography


