ABSENCE OF METABOLIC BONE DISEASE IN THE PROXIMAL FEMUR IN PATIENTS WITH FRACTURE OF THE FEMORAL NECK

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A clinical, radiological and histopathological study of femoral heads from 125 patients with fracture of the neck of the femur and from 30 cadavers was carried out to identify various risk factors. The findings showed that the Singh index was unreliable as a radiological indicator of the bone content of the femoral heads; that the bone content of the femoral head in patients sustaining a fracture of the femoral neck did not differ from that of the controls; that osteomalacia was not found in any of the heads examined; and that the distribution of trabecular microfractures did not support the hypothesis that fracture of the neck was the result of progressive fatigue. It was concluded that the single most important factor leading to fracture in this Australian population was injury caused by falls and that such injury was frequently associated with other disease processes.

Intracapsular fracture of the neck of the femur is a common orthopaedic problem. Despite the many papers which have been published on the subject, it remains uncertain whether a specific population is at risk of sustaining this type of fracture.

The lack of agreement on the relative importance of various pathological processes in the aetiology has arisen largely from the manner in which the evidence has been adduced. While senile osteoporosis has been incriminated most frequently as the major causative factor (Stevens et al. 1962; Newton-John and Morgan 1970; Dalén, Hellström and Jacobson 1976; Lender et al. 1976), some studies have suggested that osteomalacia may be a contributory factor in a significant proportion of cases (Chalmers et al. 1967; Jenkins et al. 1973; Aaron et al. 1974; Faccini, Exton-Smith and Boyd 1976; Sokoloff 1978). The majority of studies supporting such pathogenetic concepts have been based upon radiographic indices of bone loss from the upper femur or metacarpal, or upon histoquantitation of biopsies taken from the iliac crest. These studies, therefore, have assumed that the radiograph is a reliable indicator of bone status in the proximal femur, and that the findings in a biopsy from the iliac crest may be directly extrapolated to the bone of the proximal femur. The possibility that mechanical fatigue may play a pathogenetic role has received support from studies of trabecular microfractures in the proximal femur (Freeman, Todd and Pirie 1974).

We have undertaken a clinical, radiological and histopathological study to try to establish whether patients with a fracture of the femoral neck form part of an identifiable and discrete population; whether osteoporosis or osteomalacia are commonly associated risk factors; whether radiographic findings correlate with the bone content of the proximal femur; and whether studies of trabecular microfractures in the neck of the femur support the hypothesis that its failure may, in part, be due to mechanical fatigue.

MATERIALS AND METHODS

One hundred and twenty-five patients suffering from fracture of the femoral neck were studied as the test group, after the exclusion of patients with conditions known to affect bone structure (malignant disease, chronic renal failure, gastro-intestinal disease, and steroid or other hormone therapy). Details of age, sex, and medical conditions which might have been associated with a fall were recorded. Radiographs of the hips were available for 108 test subjects and the trabecular pattern of each was graded to give a Singh index value (Singh, Nagrath and Maini 1970). Ninety-five femoral heads removed at operation from these 125 patients were available for pathological examination.

A control group was provided by 30 femoral heads removed at necropsy from subjects who had died within three days of admission to hospital and had not suffered from any disease or received any treatment known to affect bone structure; this avoided the possibility of disuse osteoporosis.

Pathological examination. From each of the freshly excised femoral heads, four coronal slices four millimetres thick were made from the central portion and were fixed in 10 per cent formal saline for 24 hours. The four slices were then subjected to the following procedures and assessments.
Slice 1. This was decalcified until all calcium had been removed as assessed by radiographic examination using a Faxitron X-ray cabinet (Hewlett-Packard). The slice was then embedded in paraffin wax, sections eight micrometres thick were made with a Jung K motorised heavy-duty microtome and stained with haematoxylin and eosin. These sections were used for microscopic examination to exclude malignancy, Paget's disease of bone or other abnormality, and for an assessment of the percentage volume of total bone (mineralised and unmineralised osteoid) by point-counting analysis using an integrating eyepiece graticule (Garner and Ball 1966).

Slice 2. A 3 x 10 x 25 millimetre portion of bone having the 10-millimetre margin based on the subchondral bone plate and the long axis aligned on the centre of head of the femur was excised from each slice (Fig. 1). These portions were not subjected to decalcification and were embedded in Araldite. Multiple eight-micrometre sections were cut, and stained by the von Kossa technique which stains calcified bone black, and counterstained by the von Gieson technique which stains non-mineralised bone matrix (osteoid) pink. The sections were examined using a Quantimet 720 image-analysing computer (Cambridge Instruments Ltd, U.K.), which measured the percentage of total bone, mineralised bone and unmineralised osteoid by scanning 100 to 150 fields per section in four sections (Faccini et al. 1976).

Slice 3. One slice was macerated to remove all soft tissue by immersion in four per cent sodium hydroxide at 80 degrees Celsius for 30 minutes, followed by washing and drying, and then bleaching in 10 volume hydrogen peroxide for two hours. The dried slices were examined with a stereoscopic microscope to plot the distribution of trabecular microfractures (Darracott and Vernon-Roberts 1971) of the nodular and fusiform types (Vernon-Roberts and Pirie 1973).

Slice 4. To assist in determining the degree of calcification of the bone, a macerated slice was weighed and placed in an oven at 650 degrees Celsius for 24 hours. The weight of ash was then recorded. The percentage calcification = \[ \frac{\text{ash weight}}{\text{pre-ashing weight}} \times 100 \]

RESULTS

Clinical features. As expected, the 125 patients were in the older age group, with ages ranging from 52 to 95 years (mean age 79.3 years). There were 105 women (84 per cent) of mean age 79.7 years, and 20 men (16 per cent) of mean age 76.5 years. The left femur was fractured in 66 subjects, and the right femur in 59. The operation was performed within 24 hours of the fall in 88 patients, while the remaining 37 underwent operation from 26 hours to five weeks after the injury. The majority of the patients (73 per cent) were found to have medical conditions which could have caused a fall (Table I). The conditions included Parkinson's disease or stroke associated with significant immobility (25 per cent), confusion or dementia (23 per cent), cataracts or other eye disease necessitating recent attendance at an ophthalmic clinic other than for refraction (18 per cent), and severe diabetes mellitus with peripheral neuropathy (seven per cent). After operation, nine patients died, six were not able to walk, and 110 walked from the hospital with or without assistance.

The 30 control specimens were taken from subjects whose ages ranged from 16 to 81 years (mean age 61.5 years); 13 were female (mean age 65.8 years) and 17 male (mean age 58.6 years).

Radiological assessment. The quality of the radiographs of the hips was regarded as suitable for assessment of the Singh index (Singh et al. 1970) in 108 patients. Using the full range of Singh indices from 1 to 6, the mean index for the whole group was 3.2 ± 1.5. There was no significant correlation between Singh index and age or number of microfractures, but there was a significant \( r = -0.22, P < 0.05 \) negative correlation between the Singh index and bone volume in the head of the femur (Fig. 2).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson's disease or stroke</td>
<td>31</td>
</tr>
<tr>
<td>Confusion or dementia</td>
<td>29</td>
</tr>
<tr>
<td>Cataracts or eye disease</td>
<td>23</td>
</tr>
<tr>
<td>Diabetic peripheral neuropathy</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>92</td>
</tr>
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Graph showing significant negative correlation between the percentage of trabecular bone (by volume) in the head of femur and radiological assessment by the Singh index.
Despite $\chi^2$ tests showing that inter-observer and intra-observer agreements in assigning the indices exceeded the 90 per cent confidence limits, the Singh index proved to be misleading in predicting the true density of bone in the femoral head.

**Bone density.** The percentage volume of trabecular bone in the central region of the femoral head assessed by the image analyser (on Slice 2) showed correlation with the point-counting analysis (on Slice 1) of the whole femoral head ($r=0.40$, $P<0.01$). The percentage volume of trabecular bone (calcified and uncalcified) in the central zone of femoral head did not differ significantly between the fracture group (17.6 ± 4.6 per cent) and the control group (22.7 ± 5.9 per cent) despite the control group having a significantly lower mean age than the test group.

There was a significant correlation between declining bone density and increasing age ($r=-0.26$, $P<0.01$), confirming the progressive loss of bone from the proximal femur with advancing age.

**Bone mineralisation.** There was no evidence of osteomalacia in the form of defective mineralisation since, in both the fracture and control groups, the amount of unmineralised bone matrix (osteoid) was less than 0.1 per cent and the calcification front exceeded 70 per cent in all cases. The ashing studies confirmed the lack of significant difference in percentage calcification between the bone of the fracture group (65.8 ± 7.3 per cent) and that of the control group (64.4 ± 3.0 per cent).

**Trabecular microfracture.** There was no significant difference between the number of trabecular microfractures in the fracture group (mean 10.3 ± 9.9, range 1–50) and control group (mean 4.3 ± 5.3, range 0–13). While there was a significant correlation ($r=0.33$, $P<0.05$) between increasing numbers of microfractures and age in the fracture group, there was no significant correlation between the number of microfractures and bone density. A composite plot was made of the trabecular microfracture distribution in the femoral head of both groups (Fig. 3). This revealed that, apart from some slight tendency for clustering to occur in the subfoveal region in the fracture group, the microfractures were fairly evenly distributed throughout the femoral head. There was no evidence of an increase in density of microfractures near the site of fracture, and the controls did not show any evidence of increased density in the region of the junction of the head and neck.

**DISCUSSION**

While this study confirmed the commonly held concept of the patient with a fractured neck of femur as being typically a frail elderly lady, it was of interest that three-quarters of the patients had a medical or visual problem of such severity that it could have played a significant role in the fall which led to the hospital admission. This finding called into question the validity of another commonly held belief, namely whether these patients are, as a group, more susceptible to fracture because their bones are "weaker" than those of persons of the same age who do not experience fracture. The weakness of the bone could be due to excessive loss of bone (osteoporosis) or lack of mineralisation of the bone matrix (osteomalacia), and evidence has been published previously which suggests that both of these processes may have a significant role.

We used the Singh index to try to assess the degree of bone loss from the head and neck of femur, but found an overall lack of correlation between the Singh index and the bone content of the proximal femur assessed by a variety of quantitative methods. This should not be interpreted as indicating that the Singh index is unrelated to bone change in the upper femur, but rather that the majority of radiographs taken under clinical conditions (often in an emergency and at night) are not suitable for the purpose of evaluating this index and are an unreliable indicator of the bone content of the proximal femur.

Despite the fact that our control specimens came from a group of subjects with a greater proportion of males and a lower mean age than the fracture group, there was no significant difference between the amount of bone in the head of femur in the two groups. Although the number of cases in the control group was not large, this finding tells against the concept of these fracture patients being a group who, during ageing, lose bone more rapidly than their non-fracture cohorts. This observation is in agreement with one of the findings in the study of Faccini et al. (1976) who showed that there was little difference in the proportion of bone in the biopsies of the iliac crest from 51 patients with fractured femoral necks compared with those from 54 cadavers.

Even more significant in the present study was that examination of the femoral heads failed to reveal a single case of osteomalacia. In this respect our findings are in agreement with the study of 35 heads of femur from fracture cases examined in the United Kingdom by Hodgkinson (1971). By contrast, in an American study, Sokoloff (1978) found that 26 per cent of patients had "low-grade osteomalacia" evidenced by a slight increase
in the volume of unmineralised osteoid compared with that of controls. In both of these studies no assessments of calcification fronts were performed and the absence or presence respectively of osteomalacia was therefore not confirmed in either study. Further support for our Australian findings comes from another recent study of iliac crest biopsies in 36 patients with fractured femoral necks in which there was no evidence of osteomalacia apart from three patients with a mild form from clearly identifiable causes (Evans, Ashwell and Dunstan 1981). In marked contrast are the studies carried out in the United Kingdom in which biopsies have revealed osteomalacia in over one-quarter of patients with fractured femoral necks (Gallagher et al. 1972; Jenkins et al. 1973; Aaron et al. 1974). While it would appear, therefore, that over one-quarter of these patients in the United Kingdom have osteomalacia (and this may also be the case in at least one area of North America), this does not appear to be a feature in Australia.

It has been postulated that healing trabecular microfractures in bone are evidence of fatigue failure (Radin, Paul and Rose 1972; Todd, Freeman and Pirie 1972). Freeman et al. (1974) reported that the number of microfractures in the femoral head was roughly proportional to the degree of osteoporosis; and also that they were most numerous in the fracture region examined in control (non-osteoporotic) femoral heads from 16 cadavers. Therefore, from their study of 10 femoral heads excised from patients with fractured femoral necks, they considered that senile subcapital fractures in osteoporotic patients were due to fatigue and not to the impact of a fall. Our findings in much larger groups of fracture and control patients show that microfractures are distributed evenly through the femoral head. Our evidence indicates that they do not have a relationship to osteoporosis in the femoral head but accumulate with increasing age. Microfractures do not increase in density as the neck region is approached. Thus, our findings support the concept that fracture of the neck of the femur is more frequently the result of the traumatic impact of a fall rather than the terminal event culminating from progressive fatigue of trabecular bone in the subcapital region.

In conclusion, this study of an Australian population showed that patients with fractured neck of femur did not have less bone in the proximal femur than non-fractured control specimens taken from subjects in a slightly younger age range; that osteomalacia was not a feature of the proximal femur in these patients, and that the distribution of trabecular microfractures in the head of femur did not support the hypothesis that a fracture of the neck is the end-result of the cumulative effects of trabecular fatigue. We suggest that the most important factor in this condition is injury causing the sudden failure of a region of the skeleton which is fracture-prone by virtue of mechanical factors and the loss of bone from that site during the ageing process.

The authors thank the orthopaedic surgeons of the Royal Adelaide Hospital for their co-operation in this study.

REFERENCES


