Differences in proximal femur bone density over two centuries

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Summary

The incidence of osteoporotic hip fractures in Northern Europe has been increasing over the past few decades faster than the rate adjusted for increased life expectancy. One important factor that determines osteoporotic fracture risk is bone density. The restoration of a London church, during which skeletal material dating from 1729 to 1852 was recovered, gave us the opportunity to compare the rate of bone loss in the femora of these samples with that of present-day women.

The rate of bone loss, as judged by dual energy X-ray absorptiometry, was significantly greater in modern-day women than in the women from two centuries ago, both pre-menopausally ($p<005$) and post-menopausally ($p<0.01$). The difference in bone loss in the Ward's triangle region between the Spitalfields samples and present-day women remained even when the assumed age at menopause was increased to 48 years or decreased to 42 years.

The results suggest that differences in rates of bone loss over two centuries may partly account for the increasing incidence of hip fracture in modern day women. Reasons for these differences are unclear, but one factor may be a lower degree of physical activity in present-day women.

Introduction

Although many factors contribute to osteoporotic fractures, reduced bone density[] and falls[] are especially important. In several countries, incidence of hip fracture has been increasing over the past few decades much faster than would be expected for be increased population growth due to a greater life expectancy.[] The reasons for this increase in incidence have not been established, but one possibility is that women of the present day have lower bone density than those from the past. As part of a restoration programme, the crypt of Christ Church, Spitalfields, London, was recently cleared. The crypt was unique in that it contained a collection of human skeletal material of known age at death and about whom a great deal of information on their environment, lifestyle, occupation, and families could be gathered. These individuals had been buried between 1729 and 1852; mostly born in England, they were often of Huguenot ancestry and all were white. This historic finding gave us the opportunity to compare the female subjects born in the 18th and 19th centuries with those of present-day women.

Subjects and methods

Only well-preserved dry femora with undamaged femoral necks were selected for inclusion in this study (fig 1). All the femora underwent radiography to establish the presence of previous fracture, and any femur with evidence of disease, such as Paget's disease of the bone, was excluded.

TABLE I – DEMOGRAPHIC DATA OF FEMALE SUBJECTS

	No	Age (yr)	Height (cm)*
Spitalfields			
Pre-menopause	25	31.7 (9.0)	155.1 (6.1)
Post-menopause	62	65.0 (11.9)	157.5 (5.5)
Modern day			
Pre-menopause	62	34.2 (6.1)	160.8 (3.5)
Post-menopause	232	55.1 (5.0)	161.4 (5.3)

*Estimate only in Spitalfields group· Data are mean (SD).

TABLE II—BONE DENSITY MEASUREMENTS

			Bone density (g/cm^2)	
	Age(yr)	Height(cm)	Femoral neck	Ward's triangle
Spitalfields (male n=30)	53 (15)	168 (6.4)	1.017 (0.168)	0.869 (0.178)
Spitalfields (female n=87)	55 (19)	157 (5.7)*	0.821 (0.183)*	0.693 (0.210)*

*$p < 0.001$ male vs female subjects. Data are mean (SD).

The Spitalfields sample consisted of 87 left femora from female subjects (age range 15-89 years) and 30 from male subjects (25-88). Although body weights were unknown, heights were estimated with a regression formula,[] in which overall height is calculated from the dimensions of the long bones in the skeleton.

The femora were placed in a plastic box containing 15 cm water, which acted as a soft-tissue equivalent. The bones were positioned so that the femoral head was flat. Bone density was measured in the femoral neck and Ward's triangle regions of the proximal femur by dual-energy X-ray absorptiometry[] (Lunar DPX, Lunar Corporation, Madison, Wisconsin). The precision of measurement of these femora was assessed by scanning 3 femora five times each. The bones were removed from the water bath between each scan. Femoral neck precision was 1.24% and Ward's triangle was 1.70% . Bone density was expressed in g/cm^2 (an area density derived from bone mineral content [g] divided by the area [cm^3]).

The Spitalfields subjects were matched as a group for age and height with a group of 294 healthy white British women of known menopausal status, selected from our existing database of proximal femur bone density measurements (table 1). We estimated that the menopause in the 18th and 19th centuries would have occurred around the age of 45 years.[] Therefore, the Spitalfields cohort was divided into pre-menopausal (≤45 years) and post-menopausal (>45 years) groups. Likewise, the present-day women were also divided into two groups on the basis of this menopausal age.

Comparisons of dead and living bone may be invalid since living bone includes fat and marrow elements. Thus, rather than using the actual bone density measurements, we expressed results as a percentage of the mean value found in young normal subjects (age 15-30 years) for each group.

Two-tailed unpaired Student's t-test was used to compare sex differences in the ancient bones. Linear regression analyses were used to assess associations between bone density and age. Regression coefficients were compared by the large sample chi-squared method.[]

After completion of all studies on these samples, they will be returned to the church.

Results

Mean bone density of the Spitalfields sample was significantly higher ($p < 0.001$) in male than in female subjects in both the femoral neck and the Ward's triangle regions (table II). In the ancient femora there was no significant loss of bone density pre-menopausally in either region, in striking contrast to modern-day women (fig 2, table III). Even after varying the assumed age at menopause between 42 and 48 years, there was still no significant pre-menopausal bone loss. However, post-menopausally there was a significant loss of bone density with age in both the femoral neck and Ward's triangle in both the ancient ($p<0.005$) and the modern-day women ($p < 0.001$).

When the regression coefficients were compared, the modern-day women had lost femoral neck bone density pre-menopausally significantly faster than did the Spitalfields women ($p<0.05$), although for the Ward's triangle region this difference did not reach significance. Post-menopausally, bone loss in the Ward's triangle region was significantly greater in the modern-day women than the Spitalfields female bones ($p<0.01$), although the differences were not significant for the femoral neck region. This difference in bone loss in the Ward's triangle region between Spitalfields and modern-day women remained even when the assumed age at menopause was increased to 48 years or decreased to 42 years.

TABLE III - REGRESSION RELATION BETWEEN BONE DENSITY & AGE

	Intercept (c)		Slope (age) (mx)		r		SEE (%)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Spitalfields								
Femoral Neck	93.93	119.27	0.197	-0.622	0.132	-0.424*	13.69	15.87
Ward's Triangle	102.85	108.41	-0.162	-0.643	-0.09	-0.405*	16.45	17.39
Modern-day								
Femoral Neck	119.45	142.04	-0.658	-1.006	-0.374*	-0.377†	9.98	12.29
Ward's Triangle	126.58	155.24	-0.921	-1.402	-0.361*	-0.418†	14.54	15.11

Regression equation: $y = c + mx$.

SEE = standard error of the estimate;

Pre = pre-menopause; Post = post-menopause.

* $p < 0.005$, † $p < 0.001$

Discussion

Healthy women attain peak bone mass at or soon after the end of linear skeletal growth.[] Before the menopause, bone density undergoes little change in the vertebrae but starts to decline in the proximal femur with an accelerated loss after the menopause.[] In our study we saw the typical decline in pre-menopausal bone density in the present-day women but found no significant loss in the Spitalfield samples. That post menopausally there was a significantly greater rate of bone loss in the Ward's triangle region of present-day women than in the Spitalfields females suggests that a modern-day 70-year-old woman would have a lower bone density than a 70-year-old woman living two centuries ago.

These differences could be due to many factors. One of the most important might be in physical activity. The individuals buried in the crypt at Spitalfields had various occupations, but by far the most important industry in the area was that of silk-weaving.[] The weavers worked long hours at their looms, often 14-16 hours a day. Although their activity at work would have varied considerably, overall the amount would probably have been far greater than that nowadays. Similarly, it is likely that the Spitalfields women would have undertaken more exercise outside of work than women of today since we know that walking was an important feature of their everyday lives. Our previous studies have shown that exercise, especially of the weight bearing type, can influence bone density in the proximal femur,[] especially in the Ward's triangle region.

Other lifestyle factors that may influence bone mass are parity, smoking, alcohol consumption, and diet. We have suggested that parity may conserve bone density.[] Parity was certainly greater in the 18th and l9th centuries than it is today. Average parity among these women was 3.4, although some women had 15 children. Cigarette smoking cannot be regarded a risk factor because cigarettes were unknown in the 18th and early l9th centuries, although records show that the men smoked pipes. Alcohol was consumed by the men, but it is not known to what extent, if at all, the women indulged.

The dietary intakes of the Spitalfields women would have almost certainly differed from that of modern-day women. It is known that milk was taken mainly in the form of puddings. Meat consumption was very high, and green vegetables were available. Even if the Spitalfields women had a greater calcium intake than that of today, there is no convincing evidence that a high calcium intake will substantially affect bone loss.[] Dietary factors alone, therefore, are an unlikely explanation for why the Spitalfields women lost less bone than the modern-day women. Falls are important in the occurrence of hip fractures, but we do not know whether incidence off falls has changed since two centuries ago. The use of medications, especially hypnotics and tranquillisers, could be responsible for an increase in falls today. Poor street lighting and uneven floors and pavements could have predisposed people to more falls two centuries ago. Thus, there is no obvious reason to suspect that there has been a change in the frequency of falls sufficient to explain the change in hip fracture incidence. Interestingly, out of the total of 1000 femora excavated only 1 had evidence of previous capsular fracture.

We suggest that the increasing incidence of hip fracture is due to a greater loss of bone density, both pre-menopausally and post-menopausally. The reasons for this remain unclear, but one factor may be less physical activity now. However, other as yet unidentified environmental factors cannot be excluded.

Questions

a *"The precision of measurement"* was 1.24% [3rd paragraph of Subjects and Methods]?

It is not clear if the 1.24% is an average (or other summary) of three SD's or 3 CV's (Coefficient of Variation). The latter is more general, since it is independent of units. Suppose that for <u>one</u> of the three femora, the five measurements at one site were 0.84, 0.86, 0.86, 0.88, 0.81. Calculate the coefficient of variation (CV) as
CV = 100 x SD[5 measurements] / mean[5 measurements].

b What does the "SEE (standard error of the estimate)" measure? Explain how it is calculated. Under what other name is it found in the output of other statistical packages?

c Put the "slope=0.197" in Table III into plain words.

d *"in the ancient femora, there was no significant loss of bone density premenopausally in either region"* [1st half 2nd sentence Results]

(i) Superimpose onto Fig 2 the fitted regression line for the ancient femora, femoral neck, premenopausal women.

(ii) One way to test for a non-zero slope is via the statistic: slope/SE[slope], vs. t-distrn..

What information is needed to calculate the SE of the slope?

What 3 factors influence the magnitude of the SE of the slope?

[the alternative form for the SE of a slope, in my notes for M&M Ch 2/9 or for G&S Ch 2, might help]

(iii) Use the information in Tables I and III to reconstruct the SE of the slope [for the ancient femora, femoral neck, premenopausal women] and calculate the test statistic. Interpret the result.

[Another way is to test for a non-zero correlation -- since in simple linear regression there is a 1:1 relation between the slope and correlation]

(iv) Calculate a 95% CI for the slope. In view of this, can we take the statement about "no significant loss" above as a definitive statement about the absence of premenopausal loss?

d *"in striking contrast to modern women"* refers to the slope of 0.197 vs. that of –0.658 (neck) and –0.162 vs. –0.921 (triangle).

Calculate a SE for the –0.658. Use it and the one for the 0.197 to verify that this "striking difference" was indeed statistically significant. [see G&S p27-28].

If you were an editor, and -- for space reasons -- it was a choice in Table III between showing the column of "SEE's" and showing "SE's" for selected slopes, which would you choose? Why?

e The answer from the test involving r=0.424 was " * p<0.005"; upon what null hypothesis is the p value calculated?