Does bone quality predict loosening of cemented total hip replacements?

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We matched 78 patients with a loose cemented Charnley Elite Plus total hip replacement (THR) by age, gender, race, prosthesis and time from surgery with 49 patients with a well-fixed stable hip replacement, to determine if poor bone quality predisposes to loosening. Clinical, radiological, biomechanical and bone mineral density indicators of bone quality were assessed.

Patients with loose replacements had more pain, were more likely to have presented with atrophic arthritis and to have a history of fragility fracture, narrower femoral cortices and lower peri-prosthetic or lumbar spine bone mineral density (all *t*-test, $p < 0.01$). They also tended to be smokers (chi-squared test, $p = 0.08$). Vitamin-D deficiency was common, but not significantly different between the two groups (*t*-test, $p = 0.31$)

In this series of cemented hip replacements performed between 1994 and 1998, aseptic loosening was associated with poor bone quality. Patients with a THR should be screened for osteoporosis and have regular radiological surveillance.

Loosening of either the femoral or acetabular component has been reported to occur in up to 29% of patients at 20 years[1] after total hip replacement (THR). Signs of loosening may occur much earlier.[2] Overall, 8% of all hip replacements require revision for aseptic loosening, which itself is the cause of 70% of revision procedures.[3] The outcome following revision is not as good as that following primary replacement and the operative complication rate is higher.[4] The last concern is important since revision surgery is often performed in older, frailer patients.

Osteoporosis is a common condition predisposing to low-energy fragility fractures. Osteoporosis and osteoarthritis (OA) are not mutually exclusive conditions, and many patients undergoing hip replacement also have unrecognised osteoporosis or deficiency of vitamin D.[5] Although patients with OA have a higher bone mineral density (BMD) at the hip, they also have an increased prevalence of osteoporotic fractures.[6,7] Both osteoporosis and aseptic loosening of implants are mediated by increased bone remodelling, characterised by over-activity of osteoclasts.[8,9] There are a number of treatments for osteoporosis, which reduce osteoclastic activity, increase the BMD and lower the incidence of fragility fractures.[10] Bisphosphonates are the principal pharmaceutical agents for managing osteoporosis by the inhibition of osteoclasts.[11]

Relatively few studies have investigated interventions for biologically-mediated aseptic loosening. However, some have suggested that bisphosphonates may be used to prevent or treat aseptic loosening,[12-14] or to prevent the decrease in proximal femoral BMD usually seen after hip replacement.[15] However, others have shown these effects may not be long lasting.[16]

Our aim was to determine if there was a difference in the quality of the bone in patients with and without loosening of a hip replacement and to establish if there were any simple methods for predicting those hips which were likely to develop loosening.

Patients and Methods

The approval of the local ethical committee was obtained for the study. We reviewed 127 patients (127 hips) at a mean of 7.7 years (6 to 10) after THR. Bone quality was assessed either by analysis of pre-operative radiographs, clinical review, serological analysis or dual-energy X-ray absorptiometry (DEXA). Table I shows the number of patients available for each method.

Patient selection and matching. The patients were carefully selected to minimise potentially confounding factors which may have influenced

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doi:10.1302/0301-620X.89B10.19038 $2.00

J Bone Joint Surg [Br] 2007;89-B:1303-8.
Received 14 December 2006; Accepted after revision 22 May 2007

Table I. Methods of assessing bone quality and the number of patients involved

Assessment	Number of patients
Post-operative radiographs	127
Pre-operative radiographs	109
Clinical review	100
Bone mineral density (DEXA*)	75
Vitamin D/PTH†/alkaline phosphatase/ calcium	80

* DEXA, dual-energy x-ray absorptiometry
† PTH, parathyroid hormone

Table II. Clinical details of the loose or stable implants

	Loose (n = 78)	Stable (n = 49)	p-value
Mean follow-up (yrs)	7.6 (6 to 10)	7.8 (6 to 10)	0.71*
Mean age (yrs)	68.9 (39 to 93)	67.3 (39 to 93)	0.34*
Male:female	1:2.1	1:1.3	0.24†
Caucasian (%)	77 of 78 (*99*)	48 of 49 (*98*)	0.73†

* *t*-test
† chi-squared test

either the development of aseptic loosening or bone quality. All patients had the same design of cemented Charnley Elite Plus implant (DePuy International, Leeds, United Kingdom) and all the operations were performed by several surgeons (including GT and WH) at the University Hospitals of Leicester between 1994 and 1998.

In order to minimise variables known to influence bone metabolism,[17] patients with loosening were matched to those with stable implants by gender, race and time since surgery. Minor modifications to the matching had to be made as repeat radiographs after recruitment showed that some patients had developed radiological evidence of loosening in the intervening time. Subsequent analysis revealed that these modifications did not affect the overall matching (Table II).

All 127 patients had their most recent radiograph compared with their post-operative films; for 100 patients (78%) this was within one year of this study. This was performed by the first author (MN) to allow classification into loose or stable THRs using the method described by Dall, Learmonth and Solomon.[18] This involved using a digital calliper to measure the amount of cement-bone radiolucency, prosthetic subsidence and cortical thinning around the femoral and acetabular components. Those scoring below ten Dall points were further classified as having mild loosening. Those with ten points or more, or who had their prosthesis revised because of loosening were classified as having severe loosening.

Pre-operative radiological assessment. This was performed by the first author (MN) and a consultant radiologist (not an author). All measurements were taken in a standardised fashion using digital callipers. Of the 127 patients, 109 (86%) had pre-operative pelvic anteroposterior (AP) radiographs available for analysis, on which three indicators of bone quality were assessed:

1) The cortex ratio was calculated by dividing the thickness of the medial femoral cortex 50 mm below the lesser trochanter by the thickness of the entire shaft.

2) The Bombelli[19] biological classification of OA which assesses the degree of formation osteophytes (atrophic, normotrophic and hypertrophic).

3) The canal ratio which assesses whether the morphology is related to loosening[20] and it is calculated by dividing the thickness of the intramedullary canal at the level of the greater trochanter by that at the isthmus.

Clinical assessment. In total, 100 patients (79%) attended for clinical review. The end-point of follow-up was the latest radiograph and where possible, this was within 12 months. Of the 27 (21%) who did not attend, ten refused to participate, four were medically unfit and 13 had been lost to follow-up. These patients still had their radiographs reviewed, but were not part of the rest of the study. Pain was assessed using a visual analogue scale (VAS) between 0 and 10 points in which 0 denoted the least pain and 10 the most severe. The function was determined by the Oxford hip score[21] (OHS) between 12 to 60 points. Patients were asked about previous fragility fractures, smoking history, and age at the menopause. The body mass index (BMI) was also calculated.

Bone mineral density (BMD). The DEXA scanning was performed on 75 patients (59%); 25 patients did not want to attend for a second appointment to have bone densitometry. This was carried out at a different hospital (the Leicester Royal Infirmary) and many of the 25 were not prepared or were not able to travel. The BMD was calculated in the seven zones of Gruen, McNeice and Amstutz[22]

Table III. Results of the tests for both groups

	Loose	Stable	p-value
Pre-operative radiograph (n = 109)			
Atrophic arthritis (%)	*40 (24 of 60)*	*15* (6 of 40)	< 0.01*
Hypertrophic arthritis (%)	*9 (6 of 69)*	*23* (9 of 40)	< 0.01*
Mean cortex ratio (range)	0.26 (0.15 to 0.43)	0.29 (0.2 to 0.41)	< 0.01†
Mean canal ratio (range)	3.8 (2.7 to 6.0)	4.1 (2.5 to 6.0)	0.25†
Clinical review (n = 100)			
Mean VAS‡ for pain (range)	3 (0 to 9)	1.6 (0 to 9)	< 0.01§
Mean Oxford hip score (range)	24 (12 to 51)	20 (12 to 47)	0.14†
History of fragility fracture (%)	*25* (15 of 59)	*8* (3 of 36)	< 0.05*
Active smoker (%)	*15* (8 of 53)	*3* (1 of 32)	0.08*
Mean body mass index (range) (kg/m^2)	29 (18 to 42)	29 (22 to 41)	0.82†
Mean age at menopause (range) (yrs)	46.9 (31 to 57)	49.6 (37 to 58)	0.11†
Bone mineral density (n = 75)			
Mean peri-prosthetic (range) (g/cm^2)	1.79 (1.12 to 2.48)	1.95 (1.4 to 2.5)	< 0.01†
Mean lumbar spine Z score (range)	0.6 (-2.4 to 5.8)	1.8 (-0.6 to 5.4)	< 0.01†
Mean distal radius Z score (range)	1.11 (-2.8 to 4.3)	1.81 (-1.7 to 6.4)	0.08†
Biochemical tests (n = 80)			
Mean serum calcium level (range)	2.34 (2.15 to 2.50)	2.35 (2.10 to 2.56)	0.65†
Mean alkaline phosphatase (range)	90 (44 to 272)	88 (59 to 169)	0.40§
Mean vitamin D (range)	54 (15 to 149)	47 (15 to 190)	0.31§
Mean PTH¶ (range)	3.2 (0.4 to 8.1)	3.6 (1.0 to 12.3)	0.71§

* chi-squared test
† *t*-test
‡ VAS, visual analogue scale
§ Mann-Whitney U test
¶ PTH, parathyroid hormone

around the femoral component, at the L1 to L4 lumbar region, the distal radius and in the contralateral hip. To allow standardised measurements in patients with prosthetic subsidence, the Gruen zone I was modified slightly in that it was measured from the tip of the greater trochanter rather than the shoulder of the prosthesis. The mean peri-prosthetic BMD for all zones was also calculated. Because all the prostheses were cemented no adjustment was made for the cement.

Measurement of the BMD at sites distant to the prosthesis allowed estimation of the global bone quality. Both the T score (standard deviations below the mean bone mass for healthy young adults) and Z score (standard deviations below the mean bone mass for age and gender-matched controls) were calculated, with adjustments made for lumbar scoliosis and sclerosis.[23] If bilateral replacements were present, the BMD was calculated in the contralateral Gruen zones. A total of 40 of the patients attending for bone densitometry had a contralateral THR, and the BMD in the Gruen zones of this prosthesis was also calculated.

Biochemical analysis. In 80 patients (63%) a serum sample was obtained which was analysed for calcium, alkaline phosphatase, vitamin D and parathyroid hormone.

Statistical analysis. Statistical analysis using appropriate tests (chi-squared, *t*-test, Mann Whitney U test and analysis of variance (ANOVA)) was performed under the guidance of a medical statistician at the University of Leicester using Microsoft Excel (Microsoft Corporation, Redmond, Washington) and SPSS software (SPSS Inc., Chicago, Illinois). A p-value ≤ 0.05 was considered to be statistically significant.

Results

Of the 127 patients reviewed, 49 (38%) had no radiological evidence of loosening, 43 (34%) had mild and 35 (28%) severe loosening. There was no statistical difference in the demographic details between patients with loose or stable implants (Table II). Table III summarises the findings.

Clinical assessment. Those patients with severe loosening had a significantly higher VAS score for pain with a mean of 3.8 (0 to 9) than those patients with stable implants in whom the mean score was 1.6 (0 to 9) (Mann-Whitney U test, p = 0.003), but not than those with mild loosening who had a mean score of 2.2 (0 to 9) Mann-Whitney U test, p = 0.30). The mean OHS was not significantly different in those with no loosening (mean 20; 12 to 47) or mild (mean 22; 12 to 46) or severe loosening (mean 25; 12 to 51; Kruskal-Wallis test, p = 0.12).

Risk factors. A total of 15 (25%) of the 59 patients with loosening that responded to the questionnaire had a history of fragility fracture compared with three (8%) of 36 respondents with stable implants (chi-squared test,

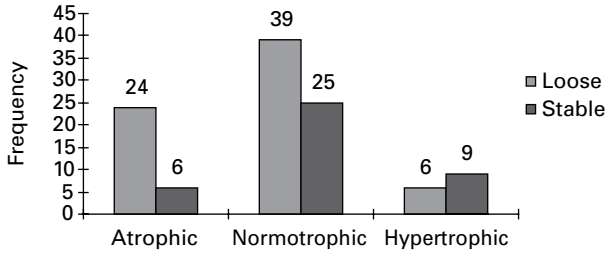

Fig. 1

The incidence of loosening according to the Bombelli[19] classification of osteoarthritis.

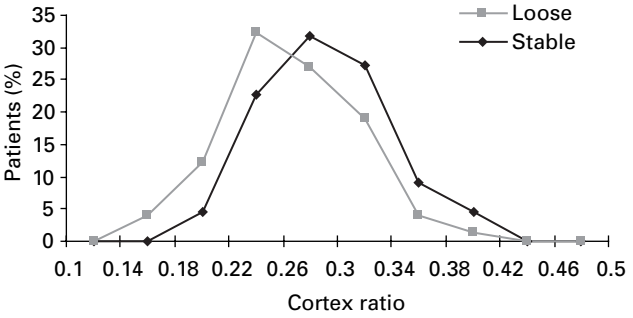

Fig. 2

Line graph showing distribution of the cortex ratio.

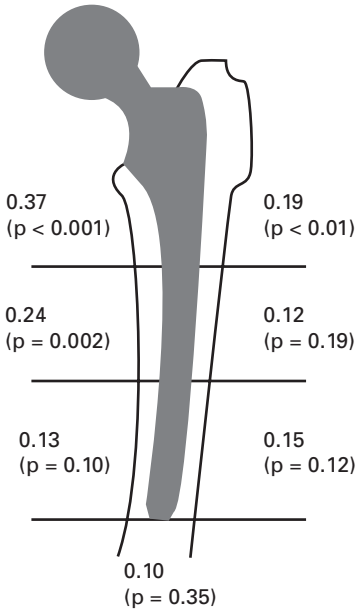

Fig. 3

Drawing showing the difference in bone mineral density in each Gruen zone between patients with loose or stable implants. (values given are the difference in means; all p-values were calculated using the *t*-test).

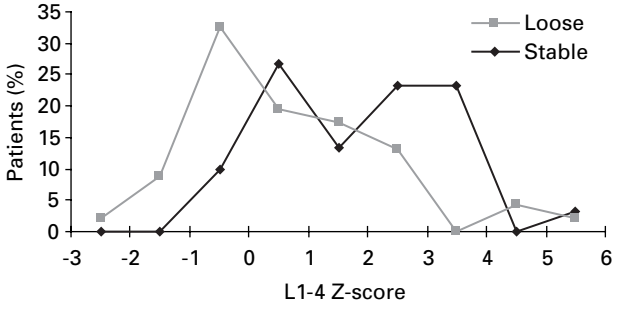

Fig. 4

Line graph showing the incidence of lumbar Z scores in patients with and without loosening.

p = 0.039, odds ratio (OR) 3.75, 95% confidence interval (CI), 2.2 to 13.2). They also tended to be active smokers (eight of the 59 questionnaire respondents with loosening compared with one of the 26 questionnaire respondents with stable implants; chi-squared test, p = 0.08, OR 5.5 95% CI, 0.8 to 38). However, we found no link between the age at which female patients reached the menopause and the development of aseptic loosening with mean ages of 49.6 years (37 to 58), 47 (31 to 57) for those with no, mild or severe loosening, respectively (ANOVA, p = 0.426). No association was found between the mean BMI with values of 29 kg/m^2 (22 to 41), 30 (18 to 42) and 29 (22 to 41) for those with no, mild or severe loosening respectively (ANOVA, p = 0.845).

Classification of osteoarthritis. Of 109 patients with preoperative radiographs available 30 (28%) had atrophic, 64 (58%), normotrophic and 15 (14%) hypertrophic OA. This was a good predictor of the development of aseptic loosening with 24 patients with atrophic OA (80%) progressing to loosening compared with six with hypertrophic OA (40%) (chi-squared test, p = 0.0073, OR 6, 95% CI 1.6 to 22, Fig. 1).

Cortex ratio. This was significantly less in those with loosening compared with those with a stable THR (*t*-test, p = 0.0023, Fig. 2). However, because of the extensive overlap between the two groups, it could not be used to predict future loosening. We found no significant statistical differences in the canal ratio between those with and those without loosening (*t*-test, p = 0.25).

Peri-prosthetic BMD. The mean peri-prosthetic BMD was significantly lower in patients with signs of loosening (*t*-test, p = 0.0049). This finding was also true for each Gruen zone, with the greatest differences seen in the proximal and medial femur (Fig. 3).

Distant assessment of BMD. Osteoporosis with a lumbar T score < 2 was found in nine of the 75 patients who underwent DEXA scanning and this was more likely to be identified in those patients with loosening. Eight (17%) of the 46 patients with loosening who had a DEXA scan had a T score < 2, compared with one (3%) of the 30 with stable implants (chi-squared test, p = 0.06, OR 6.1, 95% CI 0.9 to 41). The mean Z score at the lumbar vertebrae for those with loosening was 0.65 (-2.4 to 5.8), compared with 2.8 (-0.6 to 5.4) for those with no loosening (*t*-test, p = 0.003) (Fig. 4). At the radius there was a less strong association. The patients with loosening had a mean Z score of 1.11 (-2.8 to 4.3) and those without a mean Z score of 1.83 (-1.7 to 6.4; *t*-test, p = 0.081).

We found a weak, butsignificantcorrelation between the cortex ratio and the BMD at the wrist (Pearson's correlation, r = 0.48, p < 0.001), the lumbar spine (Pearson's correlation, r = 0.46, p < 0.001) and the operated hip (Pearson's correlation, r = 0.45, p < 0.001). This implied that pre-operative radiological measurement was a reasonable assessor of bone strength.

There was no correlation between the mean VAS for pain or the mean OHS and either the mean peri-prosthetic BMD (Pearson's correlation, both r = -0.3, p = 0.99) or the mean lumbar spine Z score (Pearson's correlation, r = -0.03, p = 0.60 and r = -0.05, p = 0.68, respectively). This suggested that the lower BMD seen in patients with loose THRs was not a result of disuse osteoporosis.

Biochemical analysis. The results of assays for serum calcium, alkaline phosphatase, parathyroid hormone and vitamin D are detailed in Table III. There was no significant difference between the two groups, despite vitamin-D deficiency, defined as < 25 mmol/l, being found in 15 of 80 patients (19%), or insufficiency defined as < 50 mmol/l in 33 (41%).

Discussion

Our study has shown that there are significant differences in bone quality in those patients with and without signs of radiological loosening, and that osteoporosis is a commonly found co-morbidity.

The simple VAS score for pain was better than the self-administered OHS in detecting loosening, but only identified patients with advanced radiological changes. This is probably because aseptic loosening is initially a pain-free phenomenon, with little effect on function. Because of the 'silent' nature of loosening we advocate the use of regular radiological surveillance, particularly in those patients with risk factors for failure. This has also been recently recommended by others.[24]

Loosening of the femoral component was first described in 1976,[25] and has since been found to have many causes. Particulate wear debris activates osteoclasts which mediate bone resorption, with polyethylene particles below the size of 1 μm being thought to be particularly important.[26,27]

The stress shielding produced by a femoral component may result in up to 50% of the bone mineral content of the proximal femur being lost,[28,29] and as in our study, the degree of bone loss is related to bone quality distal to the prosthesis.[30] Other important factors include micromovement of the prosthesis[31] and the failure to protect the prosthesis-bone interface from the ingress of particulate debris.[32] High intra-articular fluid pressures can also damage bone by preventing adequate tissue oxygenation and by activating macrophages.[33-35]

As previously described, we found that atrophic OA was a risk factor for early failure,[20] and also that cortical thickness and a history of smoking or fragility fracture were other risk factors. Additionally, patients with loosening of the femoral component had a lower peri-prosthetic BMD, although we acknowledge that this was measured after loosening had already developed. This is a weakness of our study since it is possible that the lower BMD was caused by disuse osteoporosis.[36] We tried to address this problem by measuring the BMD at sites not involved in the surgery, such as the lumbar spine and the radius. We found that the BMD was also lower at these sites and that there was no correlation between pain or level of function and the peri-prosthetic BMD. However, the 'stovepipe' morphology of the femur did not influence the outcome.

Several other studies have suggested that bone metabolism affects loosening and that bisphosphonates may play a role in preventing or treating aseptic loosening.[12-15] Our study has shown a high prevalence of abnormal bone metabolism, particularly in patients with aseptic loosening, which appears to be generalised and present before they had their initial surgery. Accordingly, we recommend DEXA scanning for patients with risk factors for osteoporosis or adverse radiological features before THR.

In conclusion patients with risk factors for loosening should be warned about the increased risk of loosening and encouraged to attend for radiological surveillance. Further investigation is required to determine whether the treatment of osteoporosis and modification of risk factors may prolong the lifespan of their THR.

The authors acknowledge the ability to follow up patients under the care of other consultants for this study, Dr K. Jeyapalan for his help assessing the radiographs, and N. Taub, medical statistician at the University of Leicester.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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