Fusion mass bone quality after uninstrumented spinal fusion in older patients

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Abstract Older people are at increased risk of non-union after spinal fusion, but little is known about the factors determining the quality of the fusion mass in this patient group. The aim of this study was to investigate fusion mass bone quality after uninstrumented spinal fusion and to evaluate if it could be improved by additional direct current (DC) electrical stimulation. A multicenter RCT compared 40 and 100 μA DC stimulation with a control group of

uninstrumented posterolateral fusion in patients older than 60 years. This report comprised 80 patients who underwent DEXA scanning at the 1 year follow-up. The study population consisted of 29 men with a mean age of 72 years (range 62–85) and 51 women with a mean age of 72 years (range 61–84). All patients underwent DEXA scanning of their fusion mass. Fusion rate was assessed at the 2 year follow-up using thin slice CT scanning. DC electrical stimulation did not improve fusion mass bone quality. Smokers had lower fusion mass BMD (0.447 g/cm^2) compared to non-smokers (0.517 g/cm^2) ($P = 0.086$). Women had lower fusion mass BMD (0.460 g/cm^2) compared to men (0.552 g/cm^2) ($P = 0.057$). Using linear regression, fusion mass bone quality, measured as BMD, was significantly influenced by gender, age of the patient, bone density of the remaining part of the lumbar spine, amount of bone graft applied and smoking. Fusion rates in this cohort was 34% in the control group and 33 and 43% in the 40 and 100 μA groups, respectively (not significant). Patients classified as fused after 2 years had significant higher fusion mass BMD at 1 year (0.592 vs. 0.466 g/cm^2 , $P = 0.0001$). Fusion mass bone quality in older patients depends on several factors. Special attention should be given to women with manifest or borderline osteoporosis. Furthermore, bone graft materials with inductive potential might be considered for this patient population.

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Introduction

One of the main goals when performing posterolateral spinal fusion is the achievement of bridging bone between

the transverse processes. The most common method for assessment of this is plain radiographs, followed by CT scanning. Previous studies have shown the fusion rate to be dependent on several factors: age [5, 36], smoking [5, 16], use of instrumentation [14] and also the amount of bone graft used [26]. The majority of fusion studies have focused on fusion rates, some have used semi-quantitative scoring techniques to describe the quality of the fusion mass, but few have investigated the quality beyond this. Microscopically, the fusion mass in humans have been investigated by Kleiner et al. [23] who performed a large study where they took biopsies from the fusion mass in connection with surgery for hardware removal or pseudoarthrosis. They found instrumented fusions to have significant higher mineralised volume and trabecular thickness as compared to uninstrumented fusions. Using a radiographic microdensitometry technique, An et al. [1] compared fusion qualities of various allografts with autografts. The same techniques were applied by Jenis et al. [18] in a comparison of direct current electrical stimulation (DC stimulation) and pulsed electromagnetic fields (PEMF) as an adjunct to instrumented posterolateral fusion with autograft. They demonstrated a small decrease in fusion mass bone density from 3 to 12 months in the control group who received no stimulation, compared to the two stimulated groups who both had an increase in bone density in the period. Using dual energy X-ray absorptiometry (DEXA), Lipscomb et al. [28] reported that the density of the grafted area increased in a cyclical pattern after uninstrumented fusion. In experimental studies, bone density of healing fractures has been shown to correlate well with measures of mechanical strength [9]. Also, the bone mineral density (BMD) of tricortical iliac crest bone grafts has been shown to correlate with biomechanical strength [2]. Thus, DEXA scanning might be one method to investigate fusion mass quality in posterolateral spinal fusion.

In the study by Jenis et al. [18] DC stimulation was shown to prevent loss of bone density of the fusion mass. DC stimulation has been shown to increase fusion rates in posterolateral fusion, both with and without instrumentation, as well as in “high-risk” patients [20, 25, 39, 41]. However, these studies investigated fusions using autograft. Only one study demonstrated a positive effect on fusion rates using allograft in interbody fusions [34].

Aim

The aim of the present study was to investigate fusion mass bone quality 1 year after uninstrumented spinal fusion performed in patients above 60 years and to investigate the effect of DC stimulation on fusion mass bone density.

Materials and methods

Study design

The patient cohort in this study was taken from a Danish multicenter randomised trial on the effect of DC electrical stimulation in adjunct to uninstrumented spinal fusion. The main results of the study are reported elsewhere [3, 4]. The study included patients of 60 years or above, eligible for spinal fusion. The main indication for surgery was spinal stenosis, where additional fusion was deemed necessary due to instability or the need for extensive decompression, or a significant degree of back pain indicating that additional fusion could be beneficial. The patients were randomised to posterolateral spinal fusion using fresh frozen allograft with or without 40 μ A DC electrical stimulation in a 1:1 fashion. The electrical stimulation was delivered by the SpF-XL IIB spinal fusion stimulator (former EBI, now BiometSpine). The study was initiated in 2001. In 2004, the manufacturer launched a more powerful new device delivering 100 μ A stimulation, as the number of patients already included was acceptable. This new device was incorporated into the study as a third arm with a 1:1:2 randomisation between control, 40 and 100 μ A. In 2005, the manufacturer stopped producing the 100 μ A device and the study was discontinued. The study and subsequent changes were approved by the regional ethical committees.

Patient population

The original study included 98 patients. Three patients died before the 1 year control leaving 95 patients accessible for the 1 year follow-up. This study included 80 patients (84% follow-up) who underwent bone densitometry of their fusion mass 1 year post-operatively. Patient demographics are seen in Table 1. Characteristics of the patients missing in the study are seen in Table 2. Surgery was a standard posterolateral spinal fusion. The allograft used was a fresh frozen femoral head obtained during total hip replacement; it was milled and mixed with any local bone obtained from the decompression procedure, just prior to insertion. Before insertion, the amount of graft was quantified by weighing. The properties of the femoral head are very similar to those described by Gibson et al. [15]. Battery life in the stimulator was at least 6 months and the stimulator battery (not the electrodes) was removed with local anaesthesia within 6 months to 1 year after the primary operation. To allow for blinded evaluation in all radiographic evaluations, dummy electrodes were utilised in the control group. They were completely identical to those coming with the stimulator device and were provided by the manufacturer of the stimulator. They were placed in a similar fashion as in the intervention groups, but were not coupled to a stimulator

Table 1 Baseline characteristics according to study group

	PLF	PLF + 40 μ A	PLF + 100 μ A	
Sex (male/female)	12/24	13/23	4/4	NS
Age at DEXA scanning (years)	73.7 (62–85)	69.7 (60–81)	72.6 (64–80)	$P = 0.0139^a$
Diagnosis				NS
Degenerative	1	5	0	
Spinal stenosis	25	23	8	
Stenosis + deg. olisthesis	9	8	0	
Stenosis + deg. scoliosis	1	0	0	
Number of fused level(s)				$P = 0.001^b$
One level	10	12	0	
Two levels	19	18	1	
Three levels	6	5	7	
Four levels	1	1	0	
Additional neural decompression				NS
No	1	4	0	
Segmental	5	10	0	
Central	31	25	8	
Previous spine surgery	5	6	2	NS
Smokers	9	13	5	NS

Previous spine surgery was either a partial laminectomy (five cases) or a discectomy (eight cases)

No significant differences between the PLF and the PLF + 40 μ A group

Values are mean (range) or number

NS Not significant

^a PLF + 40 μ A group significantly younger than the PLF group ($P = 0.0079$)

^b Significant difference due to the distribution of patients in the PLF + 100 μ A group

Table 2 Baseline characteristics of patients who completed 1 year clinical control, but missed 1 year DEXA scanning

Dropout patients	
Treatment group (PLF/40 μ A/100 μ A)	6/6/3
Sex (male/female)	4/11
Age at inclusion (years)	67.6 (59–77)
Diagnosis	
Degenerative	1
Spinal stenosis	10
Stenosis + deg. olisthesis	3
Stenosis + deg. scoliosis	1
Number of fused level(s)	
One level	4
Two levels	6
Three levels	4
Four levels	1
Additional neural decompression	
No	1
Segmental	1
Central	13
Previous spine surgery	5
Smokers	7

Values are mean (range) or number

battery. As the control patients did not need to be scheduled for battery removal, they were aware that they did not get active stimulation. All patients were braced postoperatively for 3 months in a BOB brace.

Eight patients missed the weight of the bone graft (five in the control group, two in the 40 μ A group and one in the 100 μ A group). In 54 patients, weight of any used local bone as well as used allograft was measured separately and could be combined into the total weight of the graft used.

Bone densitometry

Bone mineral density (BMD, g/cm^2) and bone mineral content (BMC, g) were measured by dual energy X-ray absorptiometry (DEXA) using a Hologic QDR-2000 densitometer (Hologic Inc., Waltham, MA, USA). BMC and BMD of the fusion mass were assessed with an antero-posterior regional scan using the scanner's "subregion forearm" programme. A region of interest was placed over the posterolateral fusion mass at each side of the spine and the values calculated by the scanner (Fig. 1). This was done both by the technician performing the scan and by the first author (TA), and a mean of these two measurements was used for the statistical analysis. Lumbar spine BMD

Fig. 1 A Lumbar AP DEXA scanning showing the selected vertebrae above the fusion used for lumbar spine BMD measurements. B Fusion mass subregion scanning with regions of interest placed at each side over the fusion mass area

and BMC were assessed using a standard anteroposterior L1–L4 scanning including only the lumbar vertebrae above the fused levels, e.g. L1–L3 in a patient with an L4–S1 fusion.

Radiology

To correlate DEXA scanning results with the final fusion status, data obtained by thin slice CT scanning at the 2 year follow-up was used. All CT scans were performed using 0.8 mm slice thickness and a 0.4 mm overlap and reviewed blinded to the treatment group. Classification of fusion was based on the study by Carreon et al. [11]. For a segment to be categorised as fused, there had to be a continuous bony bridge between the transverse processes or at the lateral side of the facet joints on at least one side or a bilateral fusion of the facet joints. If there was only unilateral facet joint fusion, questionable bilateral facet fusion or possible presence of a cleft in the bony bridge, the fusion was categorised as doubtfully fused. Segments with a clearly definable cleft in the bony bridge, questionable fusion in one facet joint and none in the contralateral or with resorption of most of the fusion mass were classified as non-unions. For the patients to be categorised as fused, fusion had to be achieved at all intended levels. A total of five patients (four in the control group and one in the 100 μ A group) had missing CT scan data.

Functional outcome

Functional outcome was assessed using the Dallas pain questionnaire (DPQ) [27], which assesses the functional

impact of chronic spinal pain in four categories: daily activities, work–leisure activities, anxiety and depression and social concerns. A high score indicates a high influence of back pain on the daily life of the patient and thus a poor outcome. Pain was assessed using the pain assessment index from the low back pain rating scale (LBPRS) [29]. It is measured using 11-box numerical rating scales ranging from 0 representing no pain to 10 representing worst possible pain. It comprises three scales for back and leg pain separately (pain now, worst and average pain in the last 14 days). Each response scale is added giving a scale ranging from 0 to 60. General health was assessed using the SF-36 [7]. The SF-36 yields a profile of scores in eight scales, covering different physical and mental components of health [42]. The score in each scale ranges from 0 (poorest health) to 100 (best health). Additionally, two summary measures are produced: a physical component summary (PCS) and a mental component summary (MCS).

Statistics

Between-group comparisons of continuous variables were done using non-parametric testing (Mann–Whitney rank-sum test or Kruskal–Wallis test without correction for ties). Significance of proportions was calculated using χ^2 test. The level of significance was set to 0.05 (two-sided testing). Correlations were assessed by linear regression. Applicability of the linear regression procedure was tested using Lowess regression and analysis of Studentised residuals. Coefficient of variation (CV) was calculated both for the fusion mass BMC and BMD measurements using the method proposed by Bland and Altman [8]. Stata

Table 3 Fusion mass parameters according to study group

	PLF	PLF + 40 μ A	PLF + 100 μ A	
Fusion mass BMD (g/cm^2)	0.512 (0.161)	0.483 (0.162)	0.458 (0.214)	NS
One-level fusion	0.428 (0.075)	0.440 (0.101)	NA	NS
Two-level fusion	0.559 (0.189)	0.458 (0.135)	0.523 (NA)	NS
Three-level fusion	0.530 (0.146)	0.680 (0.253)	0.449 (0.230)	NS
Four-level fusion	0.451 (NA)	0.440 (NA)	NA	NA
Fusion mass BMC (g)	6.26 (5.82)	5.89 (4.86)	5.94 (3.12)	NS
One-level fusion	2.89 (2.20)	3.27 (2.22)	NA	NS
Two-level fusion	6.83 (5.86)	5.40 (3.78)	6.79 (NA)	NS
Three-level fusion	11.49 (7.91)	13.27 (6.41)	5.82 (3.35)	NS
Four-level fusion	6.46 (NA)	4.84 (NA)	NA	NA
Total graft amount (g)	77.6 (28.3)	81.4 (36.6)	112.7 (40.2)	$P = 0.0654$
Allograft (g)	60.5 (28.0)	63.3 (31.9)	NA	NS
Local bone (g)	16.5 (10.2)	11.9 (9.0)	NA	$P = 0.0970$
Graft/level (g)	45.9 (17.7)	44.8 (19.1)	40.7 (17.3)	NS

Differences in graft amount is due to more graft used in the 100 μ A group

Values are mean (SD) or number

NS not significant

NA not applicable

Intercooled version 9.2 was the software used for the statistical analysis.

Results

Coefficient of variation (CV) for the graft BMC measurements was quite high at 39.5%; however, the CV for the graft BMD measurement was 8.8%. The average amount of bone graft used in the three treatment groups are seen in Table 3. The total amount of bone used ranged between 30 and 186 g. Out of this, the local bone constituted between 0 and 40 g. The average amount of graft applied at each level ranged between 15 and 114 g.

There was no difference between the three treatment groups with respect to fusion mass BMD or BMC (Table 3). The 100 μ A group received more graft due to more multilevel fusions; the amount of graft per level did not differ from the two other groups (Table 3). Compared to non-smokers, smokers had lower fusion mass BMD [Mean (SD): 0.447 g/cm^2 (0.155) vs. 0.517 g/cm^2 (0.168), $P = 0.0864$] and BMC [Mean (SD): 4.06 g (3.32) vs. 7.08 g (5.60), $P = 0.0163$]. Also, women had lower fusion mass BMD compared to men [Mean (SD): 0.460 g/cm^2 (0.128) vs. 0.552 g/cm^2 (0.207), $P = 0.0566$]. There was a linear relation between fusion mass BMD, BMD of the intact lumbar spine and the amount of bone graft applied. The latter relation was significantly stronger in men than in women (Fig. 2). Multivariate regression analysis showed fusion mass BMD to be dependent on the amount of bone

graft applied (but with a significant gender difference), BMD of the lumbar spine, age and smoking (Table 4). Fusion mass BMD did not correlate significantly with functional outcome, except for pain, as measured with the LBPRS, which was higher in patients with the lowest fusion mass BMD (Fig. 3).

CT-based fusion rate in this cohort was 34% (11/32) in the control group, 34% in the 40 μ A group (12/36) and 43% (3/7) in the 100 μ A group (not significant). The amount of graft amount applied at each level was significantly larger in patients classified as fused, based on CT scanning (Mean 54 g; range 24–114 g) compared to patients classified as non- or doubtful fusions (mean 40 g; range 15–72 g) ($P = 0.0078$). Patients classified as fused after 2 years had significantly higher fusion mass BMD at their 1 year DEXA scanning compared to their non-union counterparts [Mean (SD): 0.592 g/cm^2 (0.190) vs. 0.446 g/cm^2 (0.130), $P = 0.0001$]. The mean spinal BMD at the 1 year DEXA scanning was also higher in fused patients (0.974 g/cm^2) compared to non-union patients (0.905 g/cm^2 ; not significant).

Discussion

We assessed fusion mass quality 1 year after uninstrumented spinal fusion using DEXA scanning. DEXA was chosen as it is the most widely used non-invasive bone quality test used today and has excellent precision with a small radiation dose [35]. In experimental studies, DEXA

Fig. 2 a Correlation between amount of bone graft applied at operation and fusion mass BMD at 1 year follow-up. Correlation coefficient (r) is 0.6386 for men ($P = 0.0006$) and 0.2254 for women ($P = 0.1277$). There is significant difference in the slope between the two regression lines ($P = 0.0112$). **b** Correlation between lumbar

spine and fusion mass BMD at 1 year follow-up. Correlation coefficient (r) is 0.4386 for men ($P = 0.0173$) and 0.4623 for women ($P = 0.0006$). There is no difference in the slope between the two regression lines

Table 4 Linear regression with fusion mass BMD as dependent variable

Factor	Coefficient	SE	95% CI	<i>P</i> value
Bone graft amount	0.00243	0.00080	0.00084 to 0.00403	0.003
Lumbar spine BMD	0.28368	0.08498	0.11363 to 0.45374	0.001
Age	−0.00677	0.00322	−0.01320 to −0.00033	0.040
DC stimulation	−0.03565	0.03424	−0.10415 to 0.03286	0.302
Two-level fusion	0.06727	0.04328	−0.01933 to 0.15387	0.125
Three-level fusion	0.10313	0.05662	−0.01016 to 0.21643	0.074
Smoking	−0.07441	0.03962	−0.15369 to 0.00487	0.065
Central decompression	0.04482	0.04086	−0.03695 to 0.12659	0.277
Female gender	0.09481	0.08539	−0.07606 to 0.26568	0.271
Interaction female gender × bone graft amount	−0.00225	0.00097	−0.00418 to −0.00031	0.024
Constant	0.52597	0.25595	0.01382 to 1.03812	0.044

$R^2 = 0.514$, *SE* standard error, *CI* confidence interval

has been used to evaluate the bone quality of healing fractures [9, 31, 32]. These studies have shown acceptable correlation of the DEXA results with mechanical properties of the healing fracture [9, 31, 32]. One study has also shown that DEXA scanning was able to predict the development of atrophic pseudoarthroses in a canine osteotomy model [30]. Thus, we felt DEXA could provide some indication of the mechanical status of the fusion mass together with information on the bone status of the fusion mass.

We could not demonstrate any effect of DC stimulation on fusion mass behaviour assessed by DEXA. In the study by Jenis et al. [18], which demonstrated a positive effect of DC stimulation on bone density, the assessment was

performed using image analysis of the X-rays and not by DEXA or any other validated method. Thus, DC stimulation either has no effect or the effect is too small to overcome the influencing factors observed in this study.

We found that the fusion mass quality, measured as BMD, depended significantly on several factors. One of them was age, probably reflecting factors involved with the age-related decline in bone mass seen at all skeletal sites. Also, a linear correlation was found between fusion mass BMD and BMD of the lumbar spine not involved in the fusion. It could indicate that the fusion mass was remodelled to obtain characteristics similar to the spinal bone mass in that particular patient. Thus, each patient might have a “set point” of bone quality at which the fusion mass

Fig. 3 Functional outcome at the time of DEXA scanning depending on bone mineral density of the fusion mass. Bars represent mean, error bars represent standard error of mean

will end. Experimental studies on fracture healing in rats have investigated the effect of osteoporosis and reported different findings [13]. Studies looking into long-term changes have shown few differences at early time points, but development of differences in the late periods of fracture healing when remodelling begins to occur [24, 33, 43]. These and other studies have demonstrated remodelling of the fracture callus towards characteristics equal to those observed in osteoporotic bone. They have coupled the decreased strength of fracture healing in osteoporotic bone to a finding of irregular formation of the trabeculae and less mineral acquisition [13, 24, 33, 43]. Another factor found to influence the fusion mass negatively was smoking. Smoking has been shown to result in lower BMD, especially in the spine, probably by depressing the vitamin D/PTH system [10, 12, 19, 38], and it is a well-documented risk factor for lower fusion rates after spinal surgery [5, 16].

The amount of graft applied at the operation was linearly related to the fusion mass BMD after 1 year, however with a strong interacting effect of sex, as the relation was far more pronounced in men than in women. Only one study so far has looked into volume changes of the spinal fusion mass. Kim and Ha et al. performed a CT study in which they demonstrated a loss of initial bone graft volume of more than 30% from 2 weeks to 1 year postoperatively in instrumented posterolateral fusions using autograft. From 1 to 5 year postoperatively, the fusion mass volume remained stable. Any effect of gender was, however, not investigated in their study [17, 22]. The differences between genders observed in our study could be explained by an up-regulation in osteoclast activity in women, due to postmenopausal changes leading to greater bone resorption [21]. Furthermore, it has been shown that oestrogen can

modulate mechano-sensitivity of bone cells [6]. Thus, oestrogen might play a role via mechanical stimuli or by an effect on resorption in explaining the difference in dependency of graft amount on final fusion mass BMD observed in this study. Another factor could be that men are better adapted to incorporate the fusion mass, as shown by an increased ability of periosteal apposition by men compared to women of the same age [40]. Thus, there simply might be more viable bone cells at the posterolateral fusion bed in men compared to women leading to incorporation of a larger amount of the graft material present. Preparation of the fusion bed was one of the factors we did not control for in this study and it could be thought to vary between surgeons. It has been proven in experimental studies to influence the fusion result.

Another limitation to this study is its cross-sectional design, which prevents conclusions on longitudinal changes and whether the fusion mass has matured. In the only study so far that has applied DEXA for the assessment of fusion mass status after spinal fusion, Libscomb et al. [28] found that the majority of patients had reached a “steady state” after 1 year, suggesting that the results obtained in this study should be representative of the end status of bony fusion.

We found both the amount of bone graft used as well as spinal BMD to influence fusion rate. In her thesis, Laursen demonstrated that 25 g of autograft per segment included in the fusion seemed to be a critical size to achieve a solid posterolateral fusion as determined from X-rays [26]. Compared to this, our data suggest that a larger amount of allograft is needed to secure a solid fusion, but also that no “security limit” can be given due to the spread of the data. Regarding spinal BMD, Okuyama et al. [37] showed patients with a clearly defined fusion after a PLIF to have significantly higher BMD than patients with undetermined union or non-union. They suggested a spinal BMD of 0.674 (± 0.104) g/cm² to be a critical threshold below which non-union starts occurring [37]. As seen from our result, non-unions can occur well above this threshold in older patients undergoing uninstrumented fusion.

One difference between the assessment of the fusion mass BMD and the CT-based fusion evaluation is that DEXA measures the amount of bone mineral at the fusion site at all levels together and does not reveal anything about the presence of pseudoarthrosis of any kind. Thus, fusions with a significant amount of bone present might be classified as non-unions because of a single transverse line through the fusion mass at one level. Nevertheless significant less bone mineral was present at the fusion site in the non-unions as compared to those solidly fused. This might also explain why the association between fusion mass BMD and functional outcome was weaker than that observed in the primary report between CT-based fusion rate and functional outcome [3].

This study demonstrates that the quality of the posterolateral fusion mass is dependant on several factors. Special attention should be given to women and patients with manifest or borderline osteoporosis. Besides optimal preparation of the fusion bed, graft amount should be sufficient when using fresh frozen allograft. But, fusion rates are low and not changeable by DC stimulation using the current magnitudes tested in this study. Other graft materials and stimulatory devices should be tested in a proper fashion in this patient category to prove their efficiency, and the use of autograft might be considered in these patients until more effective fusion methods have been found.

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