Tricalcium-phosphate and hydroxyapatite bone-graft extender for use in impaction grafting revision surgery

AN IN VITRO STUDY ON HUMAN FEMORA

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Impacted morsellised allografts have been used successfully to address the problem of poor bone stock in revision surgery. However, there are concerns about the transmission of pathogens, the high cost and the shortage of supply of donor bone. Bone-graft extenders, such as tricalcium phosphate (TCP) and hydroxyapatite (HA), have been developed to minimise the use of donor bone. In a human cadaver model we have evaluated the surgical and mechanical feasibility of a TCP/HA bone-graft extender during impaction grafting revision surgery.

A TCP/HA allograft mix increased the risk of producing a fissure in the femur during the impaction procedure, but provided a higher initial mechanical stability when compared with bone graft alone. The implications of the use of this type of graft extender in impaction grafting revision surgery are discussed.

The increasing number of revision operations which are undertaken can be attributed to an increase in primary cases and the higher life expectancy of the patients.¹ A major challenge in revision surgery is poor bone stock which has been addressed successfully by the use of morsellised bone allografts.²⁻⁷

However, the risk of transmission of pathogens,⁸ the high costs, and the shortage of supply^{9,10} cause concern. Galea, Kopman and Graham¹¹ estimated that the demand for bone graft has already exceeded the supply in the United Kingdom. Bone-graft extenders have been developed to reduce the need for donor bone. Tricalcium phosphate (TCP) and hydroxyapatite (HA) have proven biocompatibility and the ability to act as an osteoconductive material.¹²⁻¹⁴ These materials are best combined with donor bone in a weight relation of 50:50 thus reducing the required amount of donor bone by half.^{15,16}

Border et al¹⁷ used an artificial acetabular model to evaluate the mechanical stability after reconstruction of the acetabular defect with bone graft and TCP/HA mixes. In this study a higher initial stability was obtained with a 50:50 mixture of bone graft and TCP/HA as compared with bone graft alone. The cups in the TCP/HA allograft mix group displaced 0.87 mm after 15 minutes of dynamic loading at 3000 N, whereas a displacement of 1.35 mm was seen in the allograft group.¹⁷ This mixture has not been tested in the femur.

Our aim therefore was to compare a 50:50 mixture of allograft and TCP/HA with 100% allograft in a simulated revision of a total hip arthroplasty (THA) using human femora. We evaluated the behaviour of the two materials during impaction grafting and also the immediate post-operative mechanical stability.

Materials and Methods

We used 14 femora from seven human cadavers. All the femora underwent the same preparation to simulate the state of segmental bone loss encountered during a revision THA. This involved performing an osteotomy through the neck as in a primary case, followed by removal of all cancellous bone. The right femora were designated to the experimental group and were grafted with equal amounts of TCP/HA bone-graft extender and donor bone. The left femora served as controls and were grafted with 100% human allograft bone. The TCP/HA bone-graft extender (BoneSave; Stryker Howmedica Osteonics Inc, Allendale, New Jersey) had a particle size of 2.0 to 4.0 mm, a pore size of 400 to 600 µm, and inter-connectivity pore size < 100 µm and a porosity of 50%.

Before usage, fresh-frozen donor bone, obtained from the bone bank of the Department of Orthopaedics of the Vrije Universiteit Medical Centre and stored at -80°C for at least six months, was morsellised into chips of approximately 4 mm with a bone mill (Stryker

Fig. 1

Apparatus for mechanical testing of the femora.

Howmedica Osteonics Inc). Standard materials were used to perform the operations *in vitro* consisting of a bone plug, a central guide wire, Simplex bone cement (Stryker Howmedica Osteonics Inc) and Exeter stems (Stryker Howmedica Osteonics Inc).

Operative procedure. A procedure was performed on all prepared femora according to the Exeter X-change technique (Stryker Howmedica Osteonics Inc). First, using the guide-wire, a femoral plug was inserted and placed at a standardised depth of 20 cm from the greater trochanter. The graft materials were impacted into the femora. Finally, femoral stems of appropriate size were cemented into the femora, with stems of equal size being inserted into each pair.

During the impaction procedure the impaction force and the number of strikes were measured with a specifically modified sliding hammer as developed by one of the authors (KP). Separate measurements were taken for both the distal and proximal impaction procedures which were distinguished by the changeover from distal to proximal impactors. The measurement frequency was 200 kHz.

Mechanical testing. After the operative procedure, the distal ends of all the femora were embedded in bismuth with the artificial head positioned precisely above the centre of

Table I. The amount of graft used in the control (100% graft) and TCP/HA mix groups

Cadaver number	100% graft	TCP/HA mix
1	88.3	78.6
2	62.9	52.1
3	67.3	62.6
4	65.1	64.8
5	74.5	76.4
6	77.3	76.2
7	90.6	84.5

the knee. In order to test mechanical stability, the femora were placed in a hydraulic materials testing device (Instron 8872; Instron Corporation, Canton, Massachusetts) and loaded under a compressive sinusoidal force of 400 to 2000 N. This load was applied via a flat plate, allowing a horizontal shift of the femoral head under bending of the specimen (Fig. 1). The loading frequency was 6 Hz and all specimens underwent a total of 50 000 cycles. There was a pause after 1000 and 10 000 cycles for a rest period of five minutes. These rest periods were used to quantify total deformation and the component elastic and plastic deformation. Elastic deformation was defined as the amount of recovery during the rest period. By subtracting the elastic deformation from the total deformation, the plastic deformation, also referred to as subsidence, was calculated.

Imaging. Radiographs were taken before and after preparation of the femur, after the surgical procedure and after cyclic loading. Plain photographs of the femora were taken to document the operative procedure and the failure mechanism.

Pre-operatively, dual-energy x-ray analysis (QDR-2000; Hologic Corporation, Waltham, Massachusetts) of the femora was carried out to quantify the bone mineral density (BMD).

Statistical analysis. The Wilcoxon paired test and Mann-Whitney U tests were used to analyse the impaction forces. All group data from the mechanical tests were analysed using a paired, two-tailed Student *t*-test. Significance was set at $p \leq 0.05$.

Results

Operative procedure. A size 0 femoral stem was inserted into two pairs and a size 1 stem into five pairs. In specimens 1, 2 and 4 of the experimental group, a fissure developed in the proximal femur. No fissures were observed in the control group. The fissures were treated with three cerclage wires around the proximal cortex of the femur, after which the femoral stems could be inserted as planned.

The mean amount of allograft used in the control group was 75.1 g (SD 11.0) (62.9 to 90.6) and in the experimental group 70.7 g (SD 11.3) (52.1 to 84.5) (Table I). The amount of graft in the control (100% graft) group was significantly higher than in the TCP/HA mix group ($p = 0.05$). The amount of donor bone was decreased on average by 52.9% (48.7 to 58.6).

Table II. Mean impaction forces (in kN) in the control (100% graft) and TCP/HA groups

	Specimen							TCP/HA groups			
	1	2	3	4	5	6	7	Mean	SD	95% CI	p value
Distal impaction											
100% graft	15.7	9.7	10.5	11.1	11.9	15.7	10.5	12.2	2.5	10.3 to 14.0	0.67
TCP/HA	21.9	11.2	7.1	12.3	11.2	11.7	14.1	12.8	4.5	8.1 to 14.9	
Proximal impaction											
100% graft	20.4	17.7	10.7	12.6	10.5	13.1	7.7	13.2	4.4	9.9 to 16.5	0.18
TCP/HA	24.5	11.1	6.7	9.8	10.2	7.9	7.7	11.1	6.1	6.6 to 15.6	
Mean impaction											
100% graft	17.8	14.7	10.6	12.0	11.4	15.4	9.4	13.0	3.0	10.8 to 15.2	0.46
TCP/HA	23.1	11.2	7.0	11.5	10.7	10.2	10.3	12.0	5.1	8.2 to 15.8	

Table III. Plastic deformation (mm) during the 1000 and 9000 cycles run in the control (100% graft) and TCP/HA groups

	Specimen number													
	1		2		3		4		5		6		7	
	Graft	TCP/HA	Graft	TCP/HA	Graft	TCP/HA	Graft	TCP/HA	Graft	TCP/HA	Graft	TCP/HA	Graft	TCP/HA
1000 cycles plastic deformation	0.11	0.11	1.93	1.10	2.52	0.80	0.49	0.25	3.93	0.75	0.43	0.27	1.48	0.53
9000 cycles plastic deformation	0.03	0.11	0.41	0.49	1.21	0.92	0.40	0.24	1.60	0.79	0.41	0.22	1.22	0.34
		*		*		†		*		‡				§

* fissure during surgery

† failure at 9120 cycles during 40 000 cycle run

‡ split down the shaft during 9000 cycle run

§ failure at 11 644 cycles during 40 000 cycle run

Impaction force. The mean distal impacting force was 12.2 kN (95% confidence interval (CI) 10.3 to 14.0) for the control group and 11.5 kN (95% CI 8.1 to 14.9) for the experimental group (Table II). The difference was not statistically significant ($p > 0.05$, Wilcoxon test). The mean number of distal impacts in the 100% graft group was 123 and in the TCP/HA mix group it was 127.

The mean impaction force at the proximal end of the control and the experimental groups was 13.2 kN (95% CI 9.9 to 16.5) and 11.1 kN (95% CI 6.6 to 15.6) respectively (Table II). There was no statistical difference between the two groups ($p > 0.05$, Wilcoxon test). The mean number of proximal impacts in the control group was 123 and in the experimental group 92. The mean overall impaction force in the control group was 13.0 kN (95% CI 10.8 to 15.2) and in the experimental group 12.0 kN (95% CI 8.2 to 15.8) (Table II). Again, there was no significant difference between the two groups ($p > 0.05$, Wilcoxon test). The mean overall number of impacts in the 100% graft group was 230 and in the TCP/HA mix group it was 263.

The impaction forces of specimen 1 in the experimental group were significantly higher compared with the rest of the group ($p < 0.0001$ Mann-Whitney tests). They were also higher in the control group compared with the rest of the group, but these differences were not statistically significant.

Mechanical testing. From each group one specimen failed during cyclic loading. The failure of the 100% allograft specimen occurred after 19 120 cycles and that of the TCP/HA mix specimen after 21 644 cycles. In both cases, the

Fig. 2

Graph showing subsidence, indicating that most subsidence occurred during the first part of the test run.

proximal part of the prosthesis shifted medially, resulting in a vertical fracture down the proximal part of the femur. In another specimen in the TCP/HA mix group a split of approximately 10 cm occurred in the lateral aspect of the proximal femur during the 9000 cycle run. Nevertheless, this femur remained intact during further mechanical testing.

Most of the subsidence occurred during the first part of the cyclic loading, after which the rate of subsidence decreased (Fig. 2). In 11 of the 14 specimens the plastic deformation after 1000 cycles was higher than after 9000 cycles (Table III).

The femora reconstructed with 100% allograft produced higher plastic deformation after 10 000 cycles (Fig. 3). The

Table IV. Plastic deformation (mm) and ratio of graft over TCP/HA mix after 10 000 cycles for both groups

Specimen number	Graft	TCP/HA mix	Ratio Gr/TCP
1	0.13	0.21	0.63
2	2.34	1.59	1.47
3	3.74	1.72	2.18
4	0.89	0.49	1.82
5	5.53	1.54	3.59
6	0.84	0.49	1.72
7	2.69	0.86	3.12
Mean	2.31 (SD 1.89)	0.99 (SD 0.62)	2.34

mean subsidence in the control group was 2.31 mm (SD 1.89) and in the experimental group it was 0.99 mm (SD 0.62) (Table IV). This difference was statistically significant ($p = 0.048$). Also, the femora of the control group showed greater variation in subsidence as shown by a higher SD (Table IV). The ratio of the mean subsidence of the control over the experimental group was 2.34. This indicated that subsidence in the control group was more than two times greater than in the experimental group.

The elastic deformation of the specimens was calculated at the end of each five-minute rest period. After the 1000, as well as after the 9000 cycle run (accumulative 10 000), the elastic deformation in the control group was higher than that in the experimental group (0.34 *vs* 0.28 and 0.49 *vs* 0.38, respectively). Furthermore, the values of elastic deformation of the control group after 10 000 cycles were associated with higher STANDARD DEVIATIONS (0.43 *vs* 0.30) indicating greater variability in the elastic deformation in this group.

Imaging. The mean total BMD in the control group was 0.762 g/cm² (SD 0.186) and 0.742 g/cm² (SD 0.177) in the experimental group. There was no statistically significant difference between the two groups ($p = 0.22$). There was no relationship between a low BMD and the occurrence of either fissures or failure during the mechanical tests. All post-operative radiographs showed well-positioned prostheses.

Discussion

Bone substitutes used for impaction grafting should promote bone healing at the site of the defect and should provide sufficient initial mechanical stability. In experimental studies such materials have given complete healing of bone defects.^{12,13,16,18-20} and a high mechanical stability was found after reconstruction of an acetabular defect in an artificial acetabular model.¹⁷ Using an ovine model, Pratt et al¹⁹ tested different ratios of TCP and HA and found that an increased ratio of TCP over HA (80:20) and a limited number of particle sizes improved the performance of impacted aggregates as graft expanders. Moore et al¹⁶ showed in a canine ulnar model that pure HA/TCP was not osteoinductive, and that a 50:50 mixture of HA/TCP and cancellous bone was as equally effective as pure cancellous bone.

Fig. 3

Plastic deformation after 10 000 cycles for the graft and the TCP/HA mix groups.

In spite of the fact that we have attempted to ensure that the created defects were uniform across all femora by following a standardised procedure, the mean amount of TCP/HA mix required for reconstruction was significantly less than that of allograft alone. This difference may be attributed to the lower compressibility and the near absence of visco-elastic behaviour of the TCP/HA mixed with bone (50:50 weight mixture).¹⁵

Also, this characteristic of the ceramic may result in a greater transmission of force to the cortex during the impaction procedure. Three of the seven femora with the TCP/HA/allograft mix developed fissures during proximal impaction, whereas no fissure occurred in any of the specimens in the 100% allograft group. Another possible explanation for the occurrence of the fissures is the lower BMD in the relevant femora. This was not supported by the data analyses.

During the impaction procedure a large number of TCP/HA particles were removed each time the impactors were withdrawn. A possible explanation may be that the TCP/HA particles were less 'sticky' than bone graft. This relative removal of TCP/HA particles alters the actual composition of the mixture. The addition of clotted blood to increase the cohesion between the TCP/HA particles has been used in general practice, but to date no research has been published on its efficiency.

The plastic deformation in the allograft group after 10 000 cycles was statistically significantly higher than in the TCP/HA mix group. A mean subsidence ratio of the control over the experimental group of 2.34 was calculated, indicating that subsidence in the allograft group was more than two times higher than that in the TCP/HA mix group. When the femora with the fissures were excluded from the analysis, the ratio increased to 2.78 but the decrease in the number of specimens resulted in the loss of statistical significance. The SD of the graft group was three times higher. Subsidence in the TCP/HA mix group was thus not only smaller, but also more reproducible. An explanation for this finding may lie in more cement penetration through the

interparticle space of TCP/HA particles as suggested by Bolder et al,¹⁷ resulting in more solid construction.

It has been shown *in vitro*, that there is less subsidence of the stem in an impacted bone bed when larger bone chips are used or when the bone is impacted with more force.²¹ A relationship between subsidence and impaction force was also observed in our study. The impaction forces in specimen 1 of the experimental group underwent impaction under forces 1.5 to 2.0 times greater than the rest of the group and the subsidence was the least. In all other femora the surgeon used less impaction force, consequently the subsidence in these femora was greater. Also the control group showed greater elastic deformation than the experimental group after 1000 and 10 000 cycles. These observations suggest less reversible deformation in the TCP/HA mix group as compared with the graft group. It has also been reported that TCP/HA particles have a much higher elastic modulus in comparison with human grafts (135 N/mm² for human bone grafts and 522 N/mm² for 80:20 TCP/HA).¹⁵

We have shown that the use of TCP/HA as a graft extender gives a high initial mechanical stability compared with bone graft alone. A similar finding was reported in an acetabular model.¹⁷ From a biomechanical point of view, we conclude that this type of TCP/HA is a viable graft extender for use in impaction grafting of the femur. In light of the current shortage of donor bone, graft extenders have an important role in impaction grafting. It is however very important that surgeons are aware that TCP/HA mixtures need to be handled differently than 100% allograft.

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