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Healos and Bone Marrow Aspirate Used for Lumbar Spine Fusion

A Case Controlled Study Comparing Healos With Autograft

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Study Design. A prospective case controlled study to compare the clinical and radiographic performance of Healos soaked in bone marrow aspirate (BMA) to iliac crest autograft when used in lumbar spinal fusion.

Objective. To evaluate the null hypothesis: Healos used with BMA is not an effective alternative to iliac crest autograft in lumbar spine fusions.

Summary of Background Data. Healos (a Type 1 collagen/hydroxyapatite matrix) is osteoconductive and when soaked for at least 20 minutes in BMA becomes osteoinductive. It is nontoxic and straightforward to use, avoiding the morbidity of autograft harvest. Animal studies and early clinical series in humans have suggested that Healos and BMA are an effective substitute for autograft in certain circumstances.

Methods. From July 2000, Healos and BMA were used as the graft material, instead of autograft harvested from the iliac crest, in all patients undergoing lumbar spinal fusion. Clinical outcome measures used were the Low Back Outcome Score (LBOS), a Patient Satisfaction Score, and the Prolo Economic Score (after Schnee). Standing anteroposterior and lateral radiographs were taken at 12- and 24-month follow-up visits. The first 50 cases in this consecutive series were age, sex, and operative intervention matched to historical controls who underwent surgery between 1997 and 2000 and in whom autograft from the iliac crest had been used as the graft material. Surgical outcome data in these patients had also been gathered prospectively. An independent radiologist, blinded to the graft material, using standard plain radiograph criteria for fusion, examined all the radiographs. An independent surgeon assessed clinical outcomes.

Results. For posterolateral lumbar fusions, there were equivalent radiologic fusion rates for the 2 groups with no significant difference in the subjective and objective clinical outcomes. The radiologic fusions rate was significantly lower when Healos had been used for lumbar interbody fusions. Clinical outcomes for both groups were similar. There were no lasting complications associated with Healos use compared with a 14% persisting donor site complication rate in the autograft patients.

Conclusion. The null hypothesis is only partially correct. Healos and BMA are not inferior to autologous iliac crest bone as a graft material in posterolateral lumbar spine fusions but are radiographically ineffective in lumbar interbody fusions.

Key words: Healos, bone marrow aspirate, iliac bone graft, fusion. **Spine 2006;31:E636–E640**

In suitably selected patients lumbar spinal fusion is an effective method of treatment for back and leg pain.[1] The aim of a fusion procedure is to produce an arthrodesis, relieve symptoms, and restore global spinal function. The gold standard fusion material is autograft from the iliac crest. However, the morbidity associated with this bone graft harvest is not inconsiderable and can be difficult for patients and surgeons to accept. Alternative fusion materials have been sought for many years and many different products are now available.[2–4]

Healos (DuPuy Spine, Inc.) is a Type I collagen/hydroxyapatite matrix that is prepared in 50 × 20 × 5 mm sheets. In isolation, it is only osteoconductive and it requires osteogenic factors to generate bone. Soaking Healos in bone marrow aspirate (BMA) for 20 minutes before application to the fusion site provides these. During this period, cells and growth factors from the marrow are adsorbed on to the Healos framework. This allows it to perform as a fully functional bone graft substitute and animal studies have demonstrated mature bone formation.[5] To date, there have been few reports of the efficacy of Healos in human spinal surgery. This study investigates the clinical and radiologic performance of Healos and BMA in lumbar spine fusions.

■ Materials and Methods

The study period was from July 2000 to March 2002. Fifty consecutive patients undergoing lumbar spine fusion were treated with Healos and BMA as the graft material. There were equal numbers of male and female patients with a median age of 49 years (Table 1). Smokers were excluded from this study. Fifteen patients underwent posterolateral fusion (PLF), 13 patients underwent posterior lumbar interbody fusion (PLIF), and 22 patients received 360° front and back fusion (Table 2). All procedures involved pedicle screw instrumentation and posterolateral fusion plus or minus the use of interbody cages.

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Table 1. Patient Demographics

	Male (n)	Female (n)	Median Age (yr)
Healos	25	25	49
Controls	25	25	48

Patients were closely matched by sex, operative intervention, and age, to controls in which the graft material was autologous iliac crest cancellous bone (Table 3). The autograft cases were all performed between 1997 and July 2000 (Table 1). The operative procedures were identical except for the use of the different graft materials. The senior author performed all procedures.

BMA was obtained from the iliac crest using a Jamshidi needle *via* the incision. The needle was initially directed at 30° to the horizontal, parallel to the plane of the crest. It was then inserted to a depth of 4 cm toward the anterior cortex and 3mL of BMA were extracted, before repositioning the needle to avoid dilution by venous bleeding. Repositioning involves 2 cm withdrawal of the needle and then redirecting it either toward the posterior cortex or 60° to the horizontal in a similar direction. This allows 4 distinct areas at 4 cm depth to be tapped. This can then be repeated at further 2 cm depth intervals at a total of 3 levels allowing a total of 36 mL BMA from each crest. 5 to 6 mL of BMA were applied to each strip of Healos and they were then left to soak for at least 20 minutes before application. The Healos strips were laid on the decorticated transverse processes and lateral aspects of the facets and pars interarticularis and packed into interbody cages where appropriate.

On average it takes 30 seconds to gain 3 mL of aspirate, 5 mL being needed per strip of Healos. Four strips of Healos were used for a 1 level fusion, 6 strips for 2 levels, 8 for 3 levels, and so forth. Bone graft harvest from the iliac crest took between 12 and 30 minutes depending on the volume required.[6,7,9]

All patients had standing anteroposterior and lateral radiographs taken at their 2-year follow-up, including flexion and extension views. Although radiographs were taken at each follow-up, they were not formally analyzed for the purposes of this study. For the assessment of interbody fusion, 7 radiologic criteria, based on the recommendations of Brantigan and Steffee,[10] were used. For the radiologic assessment of intertransverse fusions, three criteria were used: the presence of trabeculated bone between transverse processes, no implant loosening, and less than 2° of movement on lateral flexion and extension films. An independent consultant radiologist, blinded to the graft material used, performed the radiologic review.

Clinical outcome, measured 2 years after surgery, included assessment with the Low Back Outcome Score (LBOS),[11] a Patient Satisfaction Index,[12,13] and the Prolo Economic Score[14] (after Schnee).[8] Clinical review was performed by a research fellow not involved in the operative procedures and blinded to the graft material used.

Table 3. Matching

Sex	
Male	n = 25 pairs
Female	n = 25 pairs
Operation	n = 50 pairs
Age	
0–1 year difference	n = 23 pairs
2–4 years difference	n = 19 pairs
5–6 years difference	n = 8 pairs

■ Results

Radiologic

A total of 84% of the Healos group were fused at 2 years compared with 94% of the autograft group (Table 4). Subgroup analysis shows that most of the difference in the fusion rate is accounted for by poorer performance when Healos and BMA were used as the filler in interbody cages (Table 5). If the interbody cages are subtracted from the study, Healos and BMA were not inferior to autograft in posterolateral fusions.

Clinical

Using the LBOS (Table 6), there were 88% of the Healos group in the good and excellent categories, with 92% of autograft patients in these categories. Using the patient satisfaction index, there was a 92% success in the Healos group compared with a 94% success rate in the autograft group (Table 7). Analyzing patients using the Prolo economic score (Table 8), there was 88% success in the Healos group compared with 90% success in the autograft group. All results were analyzed with the χ^2 test, and no significant differences were found.

Complications

Seven patients (14%) in the control group had symptoms attributable to bone graft harvest at the 2-year follow up. All complained of persisting pain, and 2 had evidence of cluneal neuroma formation from clinical examination with a positive Tinel's sign over the iliac crest. Only 1 patient in the Healos group had symptoms related to bone marrow aspiration. This involved inflammation over the anterior iliac crest where BMA had been aspirated for the anterior component of a circumferential fusion. This resolved spontaneously within 2 weeks.

Table 2. Operative Procedures

	PLF	PLIF	360°
Healos	15	13	22
Controls	15	13	22

PLF = posterolateral fusion; PLIF = posterior lumbar interbody fusion.

Table 4. Fusion Analysis

	Autograft	Healos
Fused	47 (94%)	42 (84%)
Not fused	3 (6%)	8 (16%)

χ^2 = 1.1 (1 *df*); not significant.

Table 5. Subgroup Radiologic Fusion Analysis

	PLF	PLIF	360° Fusion
Autograft			
Fused	14 (93.3%)	12 (92.3%)	21 (95.5%)
Not fused	1 (6.7%)	1 (7.7%)	1 (4.5%)
χ^2	0.231722139 (1 *df*)	0.797234348 (1 *df*)	0.236012547 (1 *df*)
Healos			
Fused	14 (93.3%)	11 (84.6%)	17 (77.3%)
Not fused	1 (6.7%)	2 (15.4%)	5 (22.7%)
χ^2	0.913423511 (1 *df*)	0.154220104 (1 *df*)	0.000954274 (1 *df*)

There were a similar small number of other minor complications in both groups (Table 9).

■ Discussion

Fusion of the lumbar spine for back and/or leg pain has become increasingly common over the past few decades. However, there have been reports of nonunion rates of between 10% and 40%.[2] The reasons for fusion failure are numerous, but one important factor is the graft material used.

To produce an arthrodesis, osteogenic factors are required, together with an osteoconductive material. Traditionally, these are provided by autologous bone graft from the iliac crest.[9] The harvesting of this autologous bone graft does, however, produce persisting morbidity in up to 30% of patients.[3,5] The quest to find graft materials less damaging, but as effective as iliac crest autograft, has led to surgeons using a number of different bone graft substitutes.

There have been numerous developments promising much to aid bone formation in spinal arthrodesis. These include growth factors, other osteoinductive agents such as bone morphogenetic proteins, and many osteoconductive carrier systems. All of these new technologies may be used in isolation or in combinations producing a potentially huge array of different applications.

This study evaluated the performance of Healos and autogenous BMA, without the assistance of exogenous osteoinductive factors or growth factors. Healos is an osteoconductive matrix constructed of cross-linked collagen fibers coated with hydroxyapatite. Crosslinking of the bovine collagen produces a porosity of 99%, allowing cell penetration and attachment to the matrix. Once soaked in BMA and placed appropriately on decorticated bony surfaces, Healos becomes a fully functional bone graft substitute.

Our results suggest that Healos and BMA are not clinically or radiographically inferior to autograft in posterolateral fusions. That said, it is clear that Healos performed poorly in 360° and posterior lumbar interbody fusions, and we do not recommend its use in interbody cages. We postulate that there is an insufficient volume of osteoinductive and osteoconductive material in the cages. This in combination with inadequate load sharing within the construct is inefficient leading to a higher nonunion rate. It should be considered that an increased amount of graft material may be used in anterior interbody cages and still not perform as expected.

Using internationally recognized clinical outcome criteria and accepting the limitations of plain radiography in the assessment of fusion, there was no significant difference in the clinical outcome of the matched pairs in this series. Two possible explanations for this are that the sample size was too small to show significance or that the formation of a pseudarthrosis allowed relief of symptoms. It has been shown, however, that this is not as good in the long-term as a solid bony fusion.[15] A study examining long-term outcomes (5 years+) is in progress and further information will be available to establish whether this is the case or not in due course.

One weakness of our study was the imperfect age matching of subjects, although the largest age difference was only 6 years. However, all other variables have been matched, and the results suggest that Healos and BMA

Table 6. Low Back Outcome Scores

		%	
	No.	Success	Failure
Autograft			
Excellent	22		
Good	24	92	
Fair	3		
Poor	1		8
Healos			
Excellent	21		
Good	23	88	
Fair	4		
Poor	2		12

χ^2 = 0.45 (1 *df*); not significant.

Table 7. Patient Satisfaction Scores

	Autograft	Healos
Success	47 (94%)	46 (92%)
Failure	3 (6%)	4 (8%)

χ^2 = 0.16 (1 *df*); not significant.

Table 8. Prolo Economic Scores

	Autograft		Healos	
	Preoperative	Postoperative	Preoperative	Postoperative
E1	7	0	5	0
E2	17	1	14	1
E3	24	4	25	6
E4	2	14	6	11
E5	0	31	0	32
Success	90%		86%	
Failure	10%		14%	

χ^2 = 0.38 (1 *df*); not significant.

Table 9. Complications

	Autograft	Healos
Donor site pain/neuroma	7	0
Deep infection	1	1
Transient nerve root palsy	1	1
Temporary cauda equina syndrome	0	1
Deep venous thrombosis	1	1
Urinary tract infection	1	0
Fatal pulmonary embolus	0	1
Total	11	5

behave in a similar manner to autograft. We think that, in well-selected patients, it is effective in producing posterolateral fusion in the lumbar spine with a significant reduction in morbidity and may represent an advance in the quest for an ideal autograft substitute.

■ Key Points

- The authors of this study found Healos soaked in BMA easy to use. Preparation of the graft took significantly less time than taking autologous graft. Placement of the Healos/BMA complex was simple.
- The complications of autograft harvest were not present when Healos was used as the graft material.
- Using standard outcome measures, clinical results between the Healos and BMA, and autograft groups, were not significantly different.
- Radiographically, there were similar fusion rates, and subgroup analysis shows that most of the difference in the fusion rate is accounted for by poor performance when Healos and BMA were used as filler in interbody cages.

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■ Appendix

Criteria for Interbody Fusions

1. Trabeculae crossing the intervertebral space convincingly through the cages
2. Anterior/posterior sentinel sign (peri-implant bone-bridging)
3. Increased intracage density becoming isodense with time
4. Sclerotic zones at cage/endplate interface
5. No peri-implant lucencies (cages or screws)
6. Silhouetting of cages on anteroposterior angled view
7. Remodeling of bone at cage/endplate interface

4–7 signs = Fused
0–3 signs = Not fused

Criteria for Posterolateral Fusions

1. Bridging trabeculated bone from TP to TP at all levels
2. Less than 2° angulation on flexion-extension laterals at least 12 months postoperative
3. No peri-implant lucencies

3 signs = Fused
0–2 signs = Not fused

LBOS Scoring System

Excellent: 65–75; Excellent and Good = Success
Good: 50–64
Fair: 25–49; Fair and Poor = Failure
Poor: <25

Patient Satisfaction Scoring

Pain Relief Score
Complete: 3
Good deal of relief: 2
Little or no relief: 1
Worse: 0
Repeat Surgery
Would have operation again if needed: 1
Would not have operation again: 0
Recommendation
Would recommend operation to a friend/family member: 1

Would not recommend operation: 0
Satisfaction With the Process of Surgical Care
Satisfied with process of surgical care: 1
Dissatisfied with the process of surgical care: 0
Results 4–6 points = success if pain score 2 or 3
4 points when pain score only 1 = failure
0–3 points = failure

Prolo Economic Scoring

E1: Invalid
E2: No gainful occupation
E3: Working/active not at premorbid level
E4: Working/active at previous level with limitations
E5: Working/active at previous level without limitations
E1–E3: Failure; E4–E5: Success