RESEARCH ARTICLE

Comparison of outcomes and safety of using hydroxyapatite granules as a substitute for autograft in cervical cages for anterior cervical discectomy and interbody fusion

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Abstract

Background: After cervical discectomy, autogenic bone is packed into the cage to increase the rate of union between adjacent vertebral bodies, but donor site–related complications can still occur. In this study we evaluate the use of hydroxyapatite granules as a substitute for autograft for interbody fusion.

Methods: From November 2008 to November 2011, 236 patients participated in this study. Peek cages were packed with autologous bone grafts taken from the iliac crest in 112 patients and hydroxyapatite (HA) granules in 124 patients. Patients were followed for 12 months. The patients' neurological signs, results, and complications were fully recorded throughout the procedure. Radiological imaging was done to assess the fusion rate and settling ratio.

Results: Formation of bony bridges at the third month was higher in the autograft group versus the granule group. However, there was no difference between both groups at the 12-month follow-up assessment. No difference ($P > 0.05$) was found regarding improvement in neurological deficit as well as radicular pain and recovery rate between the two groups.

Conclusions: Interbody fusion cage containing HA granules proved to be an effective treatment for cervical spondylotic radiculopathy and/or myelopathy. Clinical and neurological outcome, radiographic measurement and fusion rate in cage containing HA are similar and competitive with autograft packed cages.

Key words: Autograft, Cage, Hydroxyapatite granules, Interbody fusion, Settling ratio

Introduction

Various methods have been examined to promote anterior cervical interbody fusion since anterior cervical approaches were introduced by Cloward and Smith and Robinson (1). These techniques enable stabilization of the cervical spine and preservation of the natural alignment. In most of these procedures autograft bone has been used as the fusion material. However, the choice of materials in interbody fusion and reconstruction of osseous defects after anterior discectomy or corpectomy is still controversial (2). Many materials have been used for interbody fusion and reconstruction in recent decades. Initially, autografts and allografts including tricortical iliac bony grafts, fibular struts, surgibone, or HA grafts were used, but a high morbidity rate was noted (3). Moreover, donor site complications were reported in approximately 25% of patients including hematoma, wound infection, lateral cutaneous femoral nerve injury and chronic pain (4, 5). In addition, graft collapse and graft expulsion have been noted. For the last few years, the cervical interbody fusion cage has been applied in the clinical setting (6,7,8). The cage is associated with the mechanical properties of an interbody graft, preventing collapse of the bone graft during the phase of resorption that leads to osseous nonunion. Autogenetic bone is packed in the inner space of the cage to increase the fusion rate between adjacent vertebral bodies; thus, donor site–related complications still occur. Several ma-

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Table 1. Baseline characteristics of our patients

Baseline characteristics	Autograft group	HA granule group
Age (years)	30-63	28-65
<45	25	33
45-60	66	67
>60	21	24
Gender (f/m)	46/66 (20%/28.5%)	55/69 (22.5%/28.5%)
Symptom		
Neck, radicular pain	59	60
Myelopathy Radiculopathy	19	22
+myelopathy	25	31
Nurick grading system	Autograft	HA granule
0	60	65
1	31	39
2	15	13
3	6	7
Surgical levels		
C3-C4	9	10
C4-C5	17	16
C5-C6	45	37
C6-C7	41	38
C4-C5-C6	-	15
C5-C6-C7	-	8
Total	112	124

terials have been examined as substitutes for autogenetic bone, including allografts, ceramics, and various osteoinductive agents (9). A bone substitute eliminates the need for autogenic and allogenic bone grafting and the associated complications especially related to the supply of donor bone for harvesting and the transmission of diseases. HA has been used extensively in experimental studies and in restoring or augmenting defects in orthopedic surgery as it is biocompatible and osteoconductive (7, 8, 10). Although HA has been used as a bone substitution, there are few studies that have examined HA as a material used in the packing of interbody cages.

The purpose of this study was to investigate the time of fusion, and biomechanically, radiographically, and clinically the potential of HA as a substitute for autografts, used for packing interbody fusion cages. This research has been approved by ethics committee of Mashhad medical university.

Materials and Methods

Patient population

This study was performed in the neurosurgery departments of Mashhad Medical University from November 2008 to November 2011. A consecutive series of 263 patients with 291 cages participated in this study. These patients with progressive upper extremity radicular symptoms and/or myelopathy resulting from cervical degenerative disc disease underwent discectomy from C3–C4 to C6–C7 for soft disc herniation or spondylosis. The inclusion criteria were at least having two months of radiculopathy and neck pain of degenerative origin with compatible MRI and clinical findings. The exclusion criteria were that the patient had more than two levels of cervical spine degenerative disease, continuous or combined ossification of the posterior longitudinal ligament, posterior cervical spine surgery, psychiatric disorder, drug abuse and significant comorbidities such as severe osteoporosis or diabetes mellitus. There were 151 men and 112 women with an average age of 47.2 years (range: 29-65 years), who participated in our study. In all patients, the diagnostic work-up included clinical examination, conventional and lateral flexion/extension plain radiography of the cervical spine. After informed consent was obtained, the patients were randomized to receive an interbody fusion cage packed with autograft or hydroxyapatite granules, except for the 28 patients with a two-level disc who received HA. Moreover, 263 patients were operated on and 27 were lost in follow up

Table 2. Recovery (Odom's criteria) in our patients

Recovery	Autograft group	Granule group
Excellent	62%(69/112)	52%(64/124)
Good/satisfactory	29%(33/112)	40%(50/124)
Poor	8%(10/112)	8%(10/124)

(eight autograft and 19 patients with granules). Of the remaining 236 patients 112 had cages filled with autografts and 124 with packed HA granules. Table 1 shows the patients' basic characteristics. We used the Nurick Classification to describe the baseline characteristics of our patients. Calculations were performed using the SPSS software package for statistical analysis, version 11. The independent samples t-test was used to compare the mean scores of the two groups on a given variable. The P value of less than 0.05 was considered significant in all our data analysis. We also used Kendall's tau-b to measure the association between complication and type of procedure.

Nurick Classification

Grade 0: No evidence of spinal cord disease.
Grade I: Symptoms of spinal cord disease, but no difficulty in walking.
Grade II: Slight difficulty in walking.
Grade III: Difficulty in walking, but not so severe as to require assistance.
Grade IV: Able to walk only with another person's assistance or with the aid of a frame.
Grade V: Chair- or bed-bound.

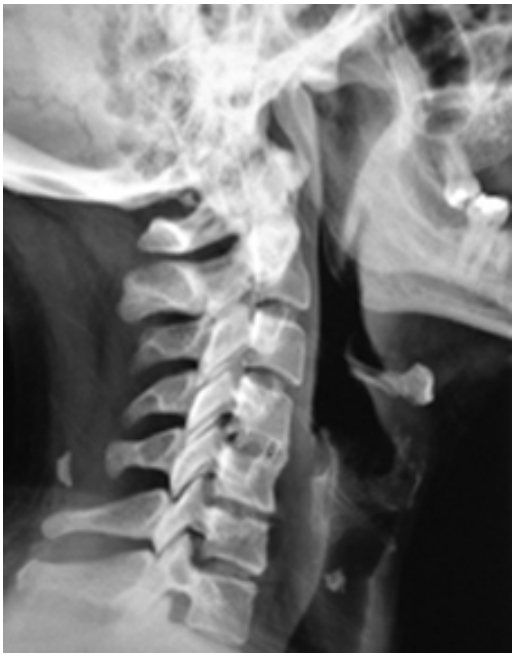

Figure1. A 43 year old man in autograft group (after 12 months follow up).

Table 3. Radiographic measurement in our patients

Radiology		After 3 mo	After 12 mo
Bony bridges	Autograft group	16.6%(19/112)	54%(60/112)
	Granule group	8%(10/124)	47%(29/124)
Disk/ cage height ratio	Autograft group	0.9 – 1.2	0.7 -1.3
	Granule group	0.8 – 1.3	0.7 -1.3

Surgical technique

Under general anesthesia and in the supine position, surgical procedures were performed using a standard right anterior approach under lateral fluoroscopic control. After insertion of a vertebral body distractor a total discectomy was performed under an operating microscope. Posterior osteophytectomy was performed if necessary using Kerrison micropunches and a high-speed drill. The posterior longitudinal ligament was opened and the neural structure decompressed, and so the origin of the nerve roots was visable in all cases. The size of the cage was selected based on preoperative radiographic studies and intraoperative measurements. Using cage trials under fluoroscopy, the appropriate size of the cage was assessed.

The cage was then filled with cancellous bone from the anterior iliac crest that was harvested through a mini-incision or with HA granules depending on preoperative selection. A standard cervical cage was then inserted

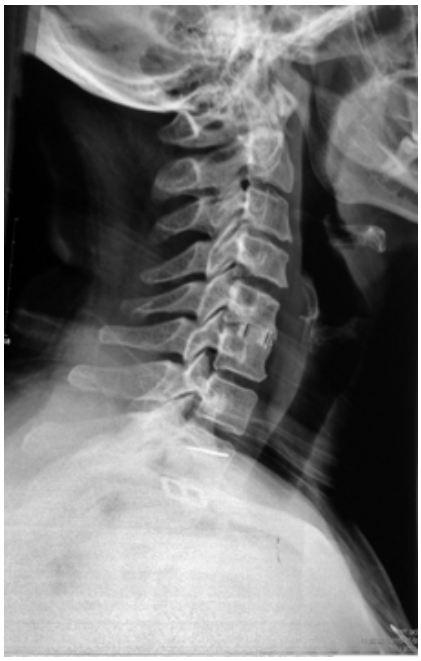

Figure 2. A 48 year old man in HA granule group (after 12 months follow up).

under fluoroscopy for exact placement. The cervical distractor was then removed and the cage was tested for stability. All of the patients were kept in a soft collar for four weeks.

Results

Clinical outcome

The neurological outcomes, both preoperatively and at discharge, three and 12 months after surgery in both groups were measured. Postoperative, 97% patients in the autograft and 95% in the granule group described an improvement in radicular pain. Radiculopathy remained unchanged in 3% of the autograft and 5% of the granule group. Exacerbation of radicular pain was not reported in this period. At the three month follow up improvement of radicular pain increased to 100% in both of the groups. Neurological deficits improvement in 93% of the patients in the autograft and 90% the granule group and were unchanged in 7% versus 10% three months after surgery.

Odom's criteria (Table 2) helped us to evaluate the recovery rate of patients' occupational capacity and ability. In the autograft group 62% of patients had rating of excellent, 29% good or at least satisfactory and 8% had a rating of poor at the end of the follow up period.

In granule group 52% of patients had a rating of excellent, 40% good or at least satisfactory and 8% poor at the end of the follow up period (Table 2).

Complications

A 35-year-old patient from the granule group developed delayed cervical hematoma with anterior swelling of the neck. He did not have any sign of compression due to hematoma and was treated conservatively. A 43-year-old female patient from the granule group experienced dysphonia; however, her symptoms resolved after four months.

Complications related to the autograft wound site were not observed, but some of our patients in both groups experienced transitory dysphagia probably because of intubation and retraction of the esophagus during surgery. No severe pain, infection or hematoma was seen in the donor site, although many patients had complained of autograft donor site pain and discomfort. Moreover, no additional surgeries were required for any cause in both groups.

Radiologic assessment

Plain radiographs in anterior-posterior and lateral views were performed postoperatively before discharge and at the third and twelfth month after surgery (Figure 1, 2). Two different measurements on the lateral radiographs were taken for each case, postoperatively and at follow-up periods, including disk height/cage height ratio and segmental kyphosis. Segmental kyphosis or lordosis was measured by the angle between the upper and lower adjacent end plate line. For assessment of fusion, two factors were considered: bony bridges surrounding the cage at the surgical level and segmental motion less than 3° in dynamic studies. Dynamic cervical radiographs in flexion and extension were used to assess segmental cervical motion.

When settling was present, it was then characterized as a superior, inferior migration or a bi-directional migration. The relationship between the vertebral endplate and the cage is important because it may indirectly decrease the height of the disc space and cause narrowing of the neural foramina.

The disc height/cage ratio was 0.9–1.2 in the autograft group and 0.8–.3 in the granule group at three months, and 0.7–1.3 in the autograft group and 0.7 – 1.3 in granule group at 12 months.

Bony bridges were present in 16.6% in the autograft group and 8% in the granule group at three months and in 54% in the autograft group and in 47% in the granule graft at 12 months after surgery (Table 3). Segmental motion > 3° was found only in one patient at the follow up period (three months after surgery in the granule group).

No patient experienced more than 10% of the so-called significant change of settling ratio in this study.

Segmental kyphosis was not seen in patients at the follow up period.

Discussion

The aim of interbody fusion after discectomy is to provide spinal stability or arthrodesis and to reduce morbidity of surgery. Also, early radiographic stability could possibly lead to successful fusion (9,11,12). Usually postoperative spinal stability is closely related to clinical outcomes. Although anterior cervical discectomy and fusion is an established procedure to treat CDD, there are controversies regarding different technique for fusion (13). The use of autologous grafts from the iliac crest has been considered the gold standard for interbody fusion; nevertheless, graft-related complications including graft collapse with disc space height loss leading to kyphosis and particularly donor site morbidity has favored the use of newer, artificial interbody spacers such as cages (14-15). Cervical cages may prevent foraminal height loss and development of postoperative kyphosis, a problem commonly observed if cervical discectomy is performed without interbody fusion (16, 17). The current cage design is an open box cage with a large cranial contact surface complementary with the vertebral end plate geometry and with a large bony contact area to promote fusion between the vertebral bodies. Bhadra *et al* concluded that the SynCage-C technique allows bony fusion to occur (18). Bone substitutes such as calcium phosphate ceramics have been used as alternatives to autogenous bone graft for cervical cage packing (17,19). In the present study, we compared the clinical and radiological outcomes of anterior cervical fusion with an interbody cage containing autograft versus HA granules following one or two level cervical discectomy in the treatment of patients with radiculopathy, myelopathy, or a combination of both due to soft disc herniation or spondylosis. All patients included in this study were randomly assigned to either receive autograft or HA granules. The results showed a similar rate of fusion in the two groups. Formation of bony bridges at the third month was higher in autograft versus the granule group (16.6% vs. 8%).

But there was no difference between both groups at the twelfth month follow-up assessment. None of the patients in these two groups showed instability 3, 6 and 12 months after surgery. Malplacement of cages were not seen in both groups. Although two cases of dysphagia and hematoma were seen in the granule group, these two related techniques do not play an importance when comparing the two studied groups. In addition, clinical outcomes and symptom relief were statistically similar in both groups.

The possibility of using these biomaterials in cervical interbody fusion has been investigated in animal models and in clinical practice, but there is a lack of literature regarding the use of HA for cervical interbody fusion (20). Autograft has features including osteogenesis, osteoinduction and osteoprogenitor, but HA granule's feature only includes osteoconductive materials, thus theoretically fusion should be faster and more complete with autograft when compared with HA granule. Granules are weak in mechanical strength when load-bearing capacity is regarded, but can be used for cage packing because load-bearing is not important. In summary, anterior cervical discectomy with the interbody fusion cage containing HA granules proved to be an effective treatment for cervical spondylotic radiculopathy and/or myelopathy. Clinical and neurological outcomes, radiographic measurement and fusion rate in the cage containing HA are similar and competitive with autograft packed cages. Moreover, the use of HA does not have potential complications related to autograft donor site.

The limitations of this study were the challenges of assessing interbody fusion, because the criteria in determining radiological fusion is not well defined and universally accepted, so it is often difficult to arrive at a true assessment of fusion based on plain radiography particularly when interbody fusion cages are used. Fine-cut CT scans with reconstruction have been shown to be more reliable and sensitive for the detection of pseudoarthrosis than plain radiography (17,18). Another limitation was that we could not directly determine if trabeculation in some patients had occurred (21). Also, another limiting characteristic of this study was the exclusion of patient with bone healing diseases such as osteoporosis and diabetes mellitus, because bone metabolism defects in these patient may cause autografts to be superior to granules for fusion development.

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