INFORMATICS IN BIOLOGY, HEALTH, AND FOOD

Interdisciplinary Explorations in Life Science

Volume 1. Number 1, Dec. 2024

DOI: 10.22034/ibhf.2024.208760

Original Article

Radiographic and Clinical Outcomes of OsvehOss Synthetic Bone Grafts in Spinal Degenetive Diseases, 12-Months Follow-up

Heidar khadivi Ayask[1], Nasrin Sasani [1*], Ahmad Safaie Yazdi[2], Farhad Motlagh Pirooz[2], Masoud Golestanipour[3], Ahmad Moloodi[3], Ali Hooshiar Ahmadi[4], Vahideh Sadat Ebrahimi[1]

[1] Osveh Asia Medical Instrument Co., Mashhad, Iran.
[2] Department of Neurosurgery, Farabi Hospital, Mashhad, Iran.
[3] Materials Research Group, Academic Center for Education, Culture & Research (ACECR), Mashhad branch, Mashhad, Iran.
[4] Faculty Member of Mashhad Branch of Islamic Azad University.

Received: 2024/08/28, **Accepted:** 2024/10/29; **Online Published:** 2024/10/31

Abstract

The emergence of synthetic bone graft substitutes as a viable option for treatment of a range of bony defects has revolutionized the field of tissue engineering. The iliac crest bone grafting (ICBG) technique for lumbar posterolateral fusion surgery is widely used; however, donor site problems such as pain and sensory disturbance have been reported. Local bone is available for fusion surgery, but its reliability as a graft has not been fully reported and documented. In addition, there has been a focus on finding suitable substitutes for autogenous iliac crest bone graft to promote spine fusion. Selecting a specific bone graft substitute can be daunting for the surgeon. In a current single-blind random assigned clinical trial study, we examined instrumented posterolateral fusion with OsvehOss bone grafts (OBG, Osveh Asia, Iran) versus MBCP bone grafts (Biomatlante, France) bone grafts (MBG) in a prospective randomized study. In this research, 19 patients diagnosed with L4-L5 degenerated spondylolisthesis underwent instrumented posterolateral fusion with an OBG (left) and MBG (right). Radiologic fusion and clinical outcomes were investigated. Based on Brantigan-Steffee bone fusion classification system scores, the results show no significant differences between OBG and MBG groups. Pearson correlation coefficient shows a positive correlation between OBG and MBG groups in fusion scores. No complications were observed in the OBG and MBG group postoperatively. The present study showed promising results regarding the efficacy of OsvehOss synthetic bone grafts with successful fusion and clinical scores to those of similar structure synthetic bone grafts.

Keywords: OsvehOss, Synthetic bone grafts, Spine fusion, Radiologic fusion.

Cite this article: Khadivi Ayask H, Sasani N, Safaie A, Motlagh Pirooz F, Golestanipour M, Moloodi A, Hooshiar Ahmadi A, Ebrahimi V. S. Radiographic and Clinical Outcomes of OsvehOss Synthetic Bone Grafts in Spinal Degenetive Diseases, 12-Months Follow-up. *Informatics in Biology, Health, and Food*. 2024;1(1):81-90.

Corresponding author: Nasrin Sasani **Email**: ns.sasani@gmail.com

Introduction

Bone graft substitutes are classified into two main categories: bone substitutes derived from biological resources and synthetic ones. Biologic products include demineralized bone matrix (DBM), platelet-rich plasma (PRP), hydroxyapatite (HA), coralline HA, and allografts (1,2). Synthetic bone graft substitutes include calcium sulfate, calcium phosphate (CaP) cement, β-tri-calcium phosphate ceramics (β-TCP), biphasic calcium phosphate (BCP), bioactive glasses, and polymer-based bone substitutes (3).

In recent years, research on biphasic calcium phosphates has led to increased utilization in spine surgery, owing to BCPs ability to support bone formation and reduce the need to harvest large amounts of autologous bone. This class of bone graft material is cost-effective, has been proven to have an appropriate safety profile, and has a low incidence of reaction or material-related complications. Additionally, BCP bone graft can resorb equally to anatomic bone, due to the ratio of HA and β -TCP (4). Posterolateral fusion with a bone graft has been widely one of the most common indications for spine surgery (5). Lumbar spinal fusion requires large quantities of bone grafts, and autologous bone grafts from the spinal process and iliac crest often provide insufficient quantities (6).

Autogenous bone offers an optimal balance of osteogenic, osteoinductive, and osteoconductive capacities, structural stability, and biocompatibility. However, donor-site morbidities, such as the risk of infection, hematoma, fracture, wound healing problems, and donor-site pain, limited the use of autografts (5,7,8). Hydroxyapatite (HA), Tricalcium phosphate (TCP), and biphasic (BCP) bone grafts, with a composition similar to mineral bone, are known to be safe and non-allergenic, with good bone bonding capacity and used as substitutes for bone grafts in orthopedic, maxillofacial and dental operations over the last 30 years (9). Advantages of ceramic bone grafts include low immunogenicity and toxicity, stability at physiologic pH levels, and the ability to withstand sterilization procedures without losing structural integrity (8).

Although recent studies reported the utility of synthetic bone grafts in spinal arthrodesis in adolescent idiopathic scoliosis, its efficacy in this situation is still a subject of controversy. In a prospective trial comparing synthetic bone grafts (porous biphasic calcium phosphate) with autograft alone, fusion rates were similar at 1 year, and donor site morbidity and blood loss were lower in the ceramic group (10). In one study using arthrodesis in dogs, with a biphasic material composed of 60% hydroxyapatite and 40% TCP, the biomechanical properties of the posterolateral fusion were equal to those with autograft and ceramic grafts, and the amount of new bone formation was related to contact area with bone and decortication of the host graft site (8,10). According to research of Spivak et al., the HA/TCP ceramic composite, either with or without added collagen, can serve as a scaffold onto which mesenchymal cells grow and differentiate into bone-producing osteoblasts, form creeping cones of bone in the scaffold, replace and finally degrade the scaffold, forming a solid fusion mass (11). Kim et al. (2012) found that a porous hydroxyapatite bone chip is a useful bone graft extender in PLIF when used in conjunction with local decompressed bone (12). In 2001, Muschik et al. in a prospective clinical study considered β-tricalcium phosphate to be a good bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis. They indicated according to clinical and radiological parameters, together with the bone mineral density results, β-tricalcium phosphate in granular form has similar fusion rates to autologous bone (13).

The spinal fusion mass is dependent upon the biodegradability of the bone graft, which, depending on the crystalline structure and size, porosity (volume fraction and size) and composition, may take from several months to several years (8). Also, clinical data on the use of ceramics as graft extenders for

autologous bone fusion of deformities have been presented by Delecrin et al., Heise et al., Le Huec et al., Passuti et al. and Ransford et al. (10,14,15,16,17).

Osveh Asia Medical Instrument Co. has produced new synthetic bone grafts based on the latest harmonized standards. OsvehOss, a macro and micro porous synthetic bone graft (> 70% Porosity, 200-500 microns), used in maxillofacial, periodontology and open fracture surgeries is available as granules, powder, block, wedge and paste as a bone regeneration device. This study was undertaken to evaluate the performance and clinical outcome of OsvehOss synthetic bone grafts in granular form and biphasic composition as a graft extender in spinal fusion.

Materials and Methods

The ethics committee of paramedical college of Azad University of Mashhad (Iran) approved the protocol for the human procedures used in this study. 19 patients (18 Female and 1 male, 25-78 years old) with a single or double level posterior lumbar interbody fusion with diagnosis of degenerative spinal disease underwent decompression and posterolateral fusion surgery at a single level between L4 and L5 using pedicle screws and bone grafts. Clinical investigation procedure performed in the Department of Neurology of Farabi and Arya hospitals (Iran) during the 1 year after approval of the Medical Equipment Department of Iran. All patients were followed up with posteroanterior and lateral radiographs 1, 3, 6, 9 and 12 months postoperatively. Exclusion criteria for patients were uncontrolled diabetes, alcohol consumption, pregnancy, smoking, blood coagulation, osteocyst and osteitis disease and any infection. Radiography images were used.

Postoperative bone fusion on plain radiographic films was evaluated using the classification system described by Brantigan and Steffee (18). Based on brantigan-steffe criteria, fusion means that at least half of the fusion area achieves to at least the density originally achieved at the surgery. Three expert radiologists investigated the radiography images and initialized them to radio-license, radio-opacity, and fusion in the right and left of the spinal cord.

Table 1: Bone fusion classification system by Brantigan-Steffee.

Grades	Description	Radiographic details
1	Unfused	Construct collapse, loss of height, cage displacement, broken screws
2	Probably unfused	Major gap or lucency in the graft site
3	Uncertain	≥50% of the graft shows no lucency between the grafted bone and vertebral bone
4	Probably fused	No lucency — bone bridges the entire fusion area with radiographic density at least similar to that obtained immediately post operation
5	Fused	No lucency — bone bridges the entire fusion area with radiographic density higher than that obtained immediately pos toperation

Bone densitometry (D) in graft area was evaluated quantitively using transmittance data according to the following formula:

T= transmitted light/incident light

O = 1/transmitted light

D=Log (O)

In the above relations, T is Transmittance, O is Opacity and D is equivalent to Optical Density. According to these relations, table 2 is used for bone densitometry of the fusion area.

Table 2: Bone densitometry using transmitted light in radiography images in this study

Transmittance	**Opacity**	**Density**
0.1 (10%)	10.00	1.0000
0.2 (20%)	5.00	0.6990
0.3 (30%)	3.33	0.5229
0.4 (40%)	2.50	0.3979
0.5 (50%)	2.0	0.3010
0.6 (60%)	1.67	0.2218
0.7 (70%)	1.43	0.1549
0.8 (80%)	1.25	0.0969
0.9 (90%)	1.11	0.0458
1.0 (100%)	1.0	0.0000

The visual analogue scale (Fig. 1) was used to evaluate pain. Also, the patients were followed for severe adverse events (SAE), 1, 3, 6, 9 and 12 months postoperatively. The obtained data was tested using a t-test to determine its degree of significance.

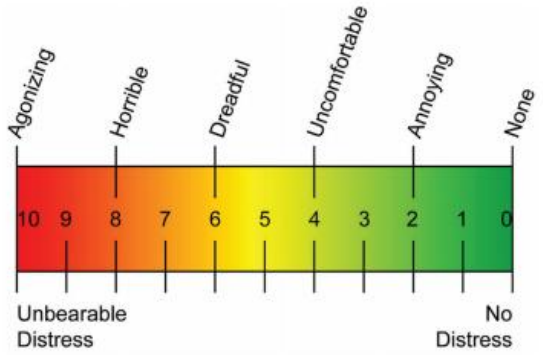

Figure 1: Visual analogue scale for pain (11)

Surgical technique

Patients with backache and leg pain continuing for at least 12 months were evaluated in this study. Patients were diagnosed with lumbar degenerated spondylolisthesis and spinal stenosis between L4 and L5 levels. X-ray examination, myelography, computed tomography (CT) after myelography, and magnetic resonance imaging (MRI) were performed on all patients for diagnosis. Patients who had previously undergone

spinal surgery, spinal tumor, infection and trauma were excluded. All patients underwent decompression (L4–L5 laminotomy) and posterolateral fusion surgery at a single level between L4 and L5 using pedicle screws and bone grafts. Figure 2 shows the surgical process of OsvehOss synthetic bone grafts in this clinical trial.

Figure 2: Mixture of OsvehOss synthetic bone grafts and blood of patient and application of grafts in spine surgery.

To reduce the impact of human factors in various patients and also assured fusion at one side (control group), the fusion surgery was undergone using OsvehOss synthetic one graft in the left (OBG group) and MBCP synthetic bone grafts in the right of spinal cord (MBG group) in each patient. Details of the patients' backgrounds are shown in Table 3.

Table 3: Demographic data of patients.

Feature	Minimum	Maximum	Mean	Std. Deviation
Age	25.00	78.00	53.0000	13.81815
Weight	56.00	84.00	74.5263	7.09748
Length	150.00	170.00	160.7895	5.42196
BMI	20.24	36.00	27.8557	3.77070
Systolic	100.00	160.00	122.7778	15.73888
Diastolic	60.00	90.00	72.7778	9.58280
Pressure	40.00	80.00	50.0000	11.75735

Statistical analysis

The statistical analysis was evaluated by using SPSS software (PASW® Statistic 18). Pearson's chi-square test, t-test, paired t-test and ANOVA (analysis of variance) test for each appropriate variable of interest. In addition, p value less than 0.05 was judged as significant.

Results

According to the protocol selected for the application of both OBG and MBG bone grafts

in each patient, the demographic data including age, gender, BMI, systolic, diastolic and pressure was not different in two bone graft groups and therefore the effects of human factors on results had minimized. The postoperative follow-up period and a number of fused segments were also similar for both groups. Figure 3 shows posteroanterior radiography of 38-year-old female patients immediately, 3 and 9 months postoperative.

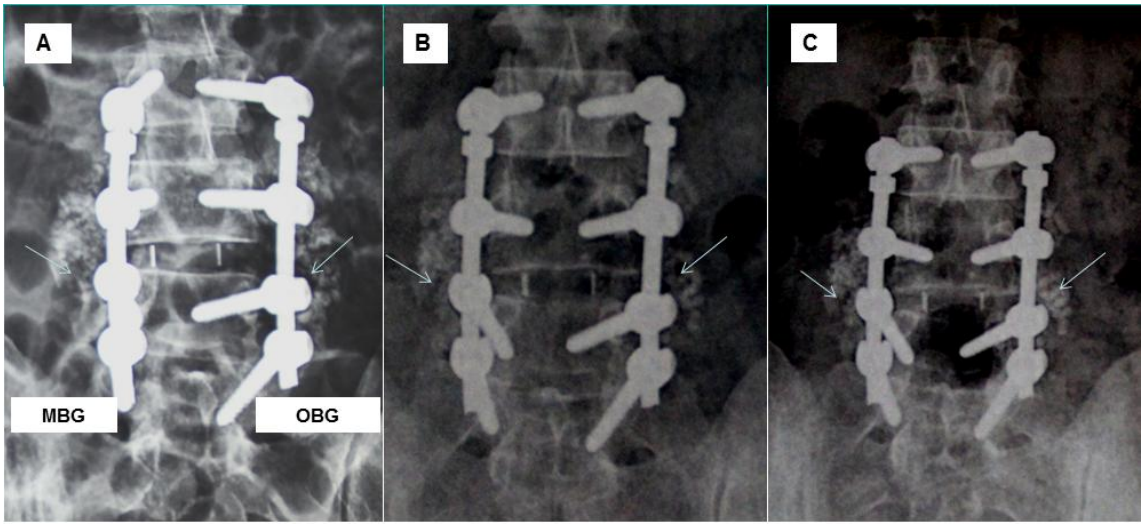

Figure 3: Posteroanterior radiography of the 38 years of female patient. (A): Immediate postoperative, (B): 3 months, (C): 9 months after operation.

A comparison of immediate postoperative with 6 and 12 months after operation in 44-years -old patients is shown in Figure 4. As can be seen in Figure 4-A, immediately after surgery, granules of bone grafts are separate with recognizable interfaces, especially in the OBG group. Six months postoperative, the integrity of granules is visible in both MBG and OBG groups.

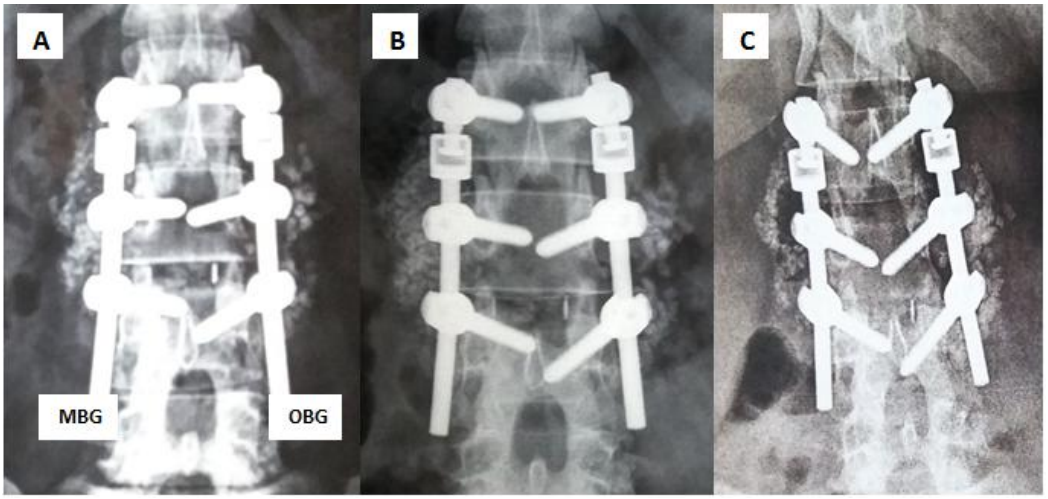

Figure 4: Posteroanterior radiography of the 45 years of female patient. (A): Immediate postoperative, (B): 6 months, (C): 9 months after operation.

Also, the posteroanterior radiography image of the 50-year-old female patient, 12 months after the operation shows integrity of pebble-like granules in the OBG group and a decrease in lucency area percentage. Also, 12 months follow up of 59 year old patient confirmed the increase in opacity and fusion in the OBG and MBG group relative to immediate postoperative condition.

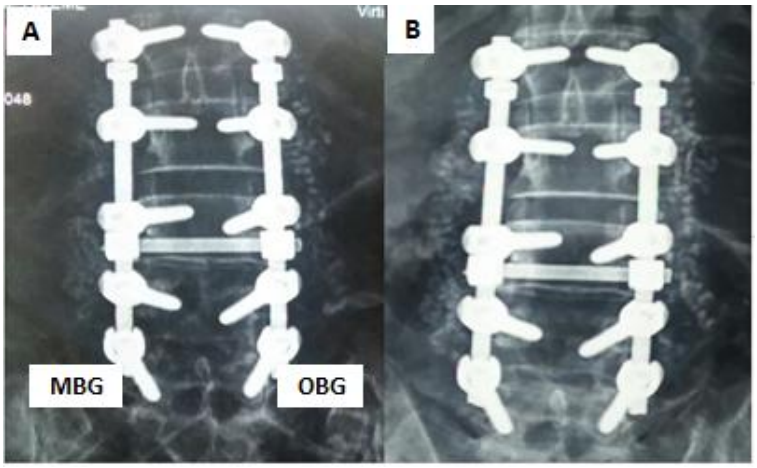

Figure 5: Posteroanterior radiography of the 50 years of female patient. (A): Immediate postoperative, (B): 12 months after operation

Evaluation of radiographic images of 19 patients up to 12 months of operation show primary resorption of OsvehOss bone grafts in about 3 months after surgery and then filling of lucencies, beginning of fusion and increase of opacity in graft area after 6 months postoperatively. Figure 6 indicates the mean of opacity scores obtained using Table 2 for both OBG and MBG groups up to 3 months postoperatively.

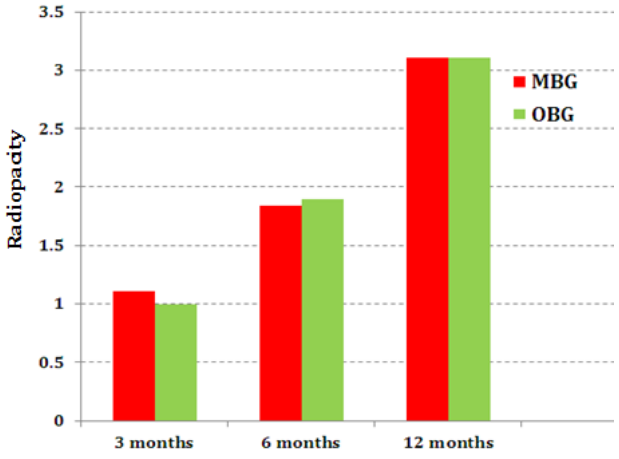

Figure 6: Mean of radioopacity scores for both OBG and MBG groups 3, 6 and 12 months postoperatively.

Statistical analysis for the mean of fusion scores according to Brantigan-Steffee was recorded in Table 4. R1, R2 and R3 are the mean fusion scores for MBG and L1, L2 and L3 for OBG at 3, 6 and 9 months after surgery, respectively.

Table 4: Mean fusion scores for MBG (R) and OBG (L), 3, 6 and 9 months after surgery.

Pair		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	R1	1.1053	19	.31530	.07234
	R2	1.8421	19	.37463	.08595
Pair 2	R1	1.1053	19	.31530	.07234
	R3	3.1053	19	1.37011	.31432
Pair 3	R2	1.8421	19	.37463	.08595
	R3	3.1053	19	1.37011	.31432
Pair 4	L1	1.0000	19	.00000	.00000
	L2	1.8947	19	.31530	.07234
Pair 5	L1	1.0000	19	.00000	.00000
	L3	3.0526	19	1.02598	.23538
Pair 6	L2	1.8947	19	.31530	.07234
	L3	3.0526	19	1.02598	.23538
Pair 7	R1	1.1053	19	.31530	.07234
	L1	1.0000	19	.00000	.00000
Pair 8	R2	1.8421	19	.37463	.08595
	L2	1.8947	19	.31530	.07234
Pair 9	R3	3.1053	19	1.37011	.31432
	L3	3.0526	19	1.02598	.23538

According to Brantigan-Steffee's recommended criteria of interbody fusion for OBG and MBG groups, there were no significant statistical differences among groups regarding the fusion rate with P-value<0.05. The fusion scores of 4.3158 and 4.2105 with Pearson Correlation of 0.453 were obtained for OBG and MBG group respectively. Figure 7 shows the linear correlation between fusion scores of MBG and OBG groups that indicate the suitable performance of OsvehOss synthetic bone grafts. There was no complication in the local bone graft groups. The mean of the visual analogue scale (VAS) for pain after surgery was 2.42 which was negligible in terms of clinical evaluation after spine surgery. No severe adverse event (SAE) was seen in patients up to 12 months postoperatively. The reliability of Brantigan-Steffee for measurement of fusion obtained 0.604 according to Cronbach's Alpha method. However, these studies did not clarify the amount of graft material acquired by decompression, although it is one of the major factors of successful fusion.

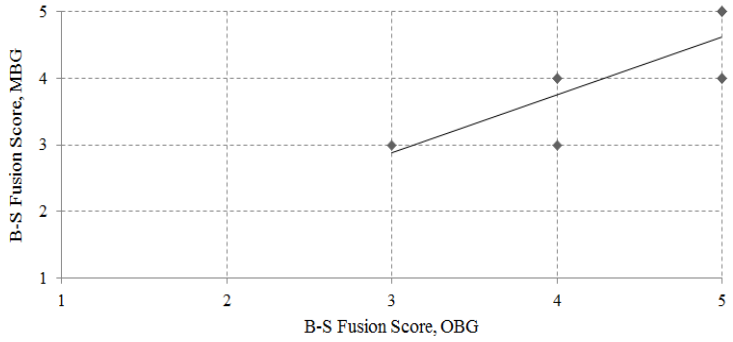

Figure 7: Linear relation between fusion scores for MBG and OBG bone grafts.

Discussion

Based on simple radiography (Figure 3), 3 months after surgery, radio-lucencies became more apparent showing resorption of grafts. As we can see in 9 months of

postoperative radiographs, radio-opacity increased and integration of grafts was observed. A decrease in lucencies, integration of granules and increase of opacity can be signs of fusion in both OBG and MBG groups. Although, the opacity has increased in bone grafts area containing lucencies compared with Figure 4-A, but total density is still smaller than bone density. 12 months after surgery, bone densitometry shows increase in opacity score in OBG group. According to Brantigan-Steffee score, fusion has been occurred at 6 months and completed after 12 months postoperatively. The results of opacity scores measurment showed that mean of opacity scores have no significant differences in OBG and MBG groups, 12 months after surgery (P-value<0.05). Based on the results of statistical analysis for the mean of fusion scores, there is an increasing trend in the fusion scores for 6 months follow up related to 3 months and 9 months related to 6 months part in MBG and OBG groups.

A synthetic bone made of hydroxyapatite/tricalcium phosphate (OsvehOss) was used as supplementary graft material in this study. OsvehOss is a non-toxic, non-immunogenic material of uniform quality and unlimited quantity with the convenience of sterilization and storage. In addition ,it demonstrated its efficacy and safety as a scaffold for osteoconduction in various settings of studies. Characterization of OsvehOss bone grafts demonstrated adequate porosity more than 70% appropriate pore size of 200-500µm and good three-dimensionally interconnected pore structure suitable for osteoconduction. In addition, satisfactory results as a graft extender were reported in animal studies. The results of current study concluded that successful clinical performance and fusions can be obtained using OsvehOss synthetic bone grafts. Therefore, OsvehOss synthetic bone grafts would be enough to utilize as a scaffold in interbody space as an extender of local bone graft.

Conclusion

The current research established for evaluation of clinical outcomes of OsvehOss synthetic bone grafts. The result shows no significant differences in opacity scores between OsvehOss and control group, 6 months postoperatively. Also, this study showed promising results regarding the efficacy of OsvehOss synthetic bone grafts with the successful fusion and clinical scores to those of similar structure synthetic bone graft. The complications were too rare in occurrence to find statistically significant. The mean of data for postoperative pain through visual analog scale (VAS) was negligible. No complication and severe adverse event seen for patient up to one year follow up. These results imply that OsvehOss synthetic bone grafts can be enough in quality to achieve lumbar fusion and pose a question on the usage of cost effectiveness of additional graft extenders.

Acknowledgment: The completion of this research paper would not have been possible without the support and guidance of Dr. Ahmad Safaei Yazdi and Dr. Farhad Motlagh Pirooz, neurosurgeon and spine surgeons. Also, we would like to express our sincere gratitude to Dr. Ali Houshyar Ahmadi for their invaluable guidance and support throughout the completion of this assignment. Special thanks to Osveh Asia Medical Instrument Company for providing synthetic bone grafts and financial support. Their extraordinary contributions have greatly improved the quality of this paper. It should be noted that this clinical evaluation project was conducted with the permission of the General Department of Medical Equipment of Iran.

References

1. Pierce N, Milo S, Henry G, David C, Katherine S, James R, Marcus BS. Biphasic calcium phosphate bone graft with a unique surface topography: a single-center ambispective study for degenerative disease of the lumbar spine. *Cureus*. 2024;16(4):e58218.

doi:10.7759/cureus.58218.
2. Campana V, Milano G, Pagano E, et al. Bone substitutes in orthopaedic surgery: from basic science to clinical practice. *J Mater Sci Mater Med*. 2014;25:2445–2461. doi:10.1007/s10856-014-5240-2.
3. Fernandez de Grado G, Keller L, Idoux-Gillet Y, et al. Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. *J Tissue Eng*. 2018. doi: 10.1177/2041731418776819.
4. Kornelis P. Retrospective evaluation of spinal fusion using a biphasic calcium phosphate bone graft with a novel submicron surface topography. *J Am Osteopath Acad Orthop*. 2022; VI(1). https://journal.aoao.org/?p=284.
5. Ohtori S, Suzuki M, Koshi T, Takaso M, Yamashita M, Yamauchi K, et al. Single-level instrumented posterolateral fusion of the lumbar spine with a local bone graft versus an iliac crest bone graft: a prospective, randomized study with a 2-year follow-up. *Eur Spine J*. 2011; 20:635–639. doi: 10.1007/s00586-010-1656-7.
6. Muschik M, Ludwig R, Halbhübner S, Bursche K, Stoll T. β-tricalcium phosphate as a bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis: preliminary results of a prospective clinical study. *Eur Spine J*.2001;10:S178–S184.
doi:10.1007/s005860100271.
7. Fernyhough JC, Schimandle JJ, Weigel MC, Edwards CC, Levine AM. Chronic donor site pain complicating bone graft harvesting from the posterior iliac crest for spinal fusion. *Spine*. 1992; 17:1474–1480. doi:10.1097/00007632-199212000-00006.
8. Berven S, Tay KB, Kleinstueck FS, Bradford DS. Clinical applications of bone graft substitutes in spine surgery: consideration of mineralized and demineralized preparations and growth factor supplementation. *Eur Spine J*. 2001;10:S169–S177.
doi:10.1007/s005860100270.
9. Daculsi G, LeGeros R, Nery E, Lynch K, Kerebel B. Transformation of biphasic calcium phosphate ceramics in vivo: ultrastructural and physicochemical characterisation. *J Biomed Mater Res*. 1989; 23:883–894. doi:10.1002/jbm.820230806.
10. Delecrin J, Takahashi S, Gouin F, Passuti N. A synthetic porous ceramic as a bone graft substitute in the surgical management of scoliosis: a prospective, randomized study. *Spine*.2000;25:563–569.
doi:10.1097/00007632-200003010-00006.
11. Spivak JM, Hasharoni A. Use of hydroxyapatite in spine surgery. *Eur Spine J*. 2001;10:S197–S204.
doi: 10.1007/s005860100286.
12. Kim H, Lee CK, Yeom JS, Lee JH, Lee KH, Chang BS. The efficacy of porous hydroxyapatite bone chip as an extender of local bone graft in posterior lumbar interbody fusion. *Eur Spine J*. 2012; 21:1324–1330. doi: 10.1007/s00586-011-2092-z.
13. Muschik M, Ludwig R, Halbhübner S, Bursche K, Stoll T. β-tricalcium phosphate as a bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis: preliminary results of a prospective clinical study. *Eur Spine J*. 2001;10: S178–S184.
doi: 10.1007/s005860100271.
14. Heise U, Osborn J, Duwe F. Hydroxyapatite ceramic as a bone substitute. *Int Orthop*. 1990; 14:329–338. doi: 10.1007/BF00178768.