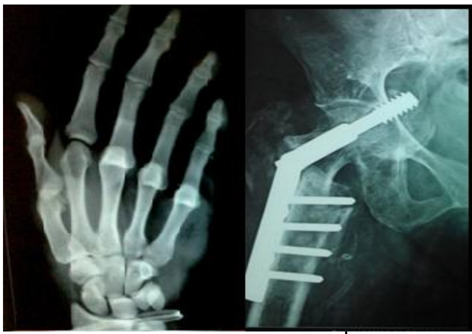

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Role of DBM in lumbar spinal fusion surgery

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Abstract
Introduction: Spinal arthrodesis is the primary goal of all fusion procedures for lumbar spinal disease. Due to the limited availability of Autologous bone, some alternative bone graft substrate which is safe, produce similar results, and can be harvested in considerable volume was needed. Hence we explored the potentials of demineralized bone matrix (DBM) for this procedure.
Purpose: We aimed to decrease the donor site morbidity to get sufficient graft and to access the efficacy of DMB in terms of anatomical and functional outcome.
Methods: 30 patients were included in the study. Patients were followed up postoperatively at one year follow up. Patients were evaluated before and after the procedure using Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI). The radiological outcome in the study group was assessed by using Lenke Classification of Posterolateral Fusion.
Results: All patients had significant improvement in the VAS and ODI scores post operatively at one year follow up. Radiological evaluation of Lumbar fusion rates assessed with Lenke fusion Classification for PLF at the end of one year was 83.33% Grade A fusion rates which is excellent. Younger patients of either sex had better outcomes compared to the older age group patients.
Conclusions: Mean improvement across all fields was 81.40% which is excellent. The available literature shows similar outcomes compared to iliac crest bone graft which is considered as the gold standard for spinal fusion. DBM can be considered as a reliable alternative to autograft when it is used as a graft extender in combination with autograft.

Keywords: Lumbar, PLF, VAS, ODI, DBM

1. Introduction

Spinal fusion procedure has become one of the most common means of treating spinal morbidities such as trauma, deformity, and degenerative disc diseases. In recent times the spinal fusion technique has been augmented with the use of autogenous bone grafting, but with the added complication of donor site morbidity and graft volume limitations, the pseudoarthrosis rates still range between 5 and 43% [1]. It is estimated that the number of spinal fusions performed in the United States, could be greater than 200000 per annum, with the majority of these being lumbar fusions [2]. Ideally in order to promote fusion the graft or bone substitute should have osteoinductive and osteoconductive properties.

Demineralized bone matrix (DBM) is processed allogenic bone that has been demineralized by extensive decalcification procedures. These procedures include chemical and radiation steps to minimize immunogenic response and the risk of infection. The bone inductive activity of demineralized bone matrix (DBM) has been well established [3]. The decalcification of cortical bone exposes these osteoinductive growth factors buried within the mineralized matrix, thereby enhancing the bone formation process. DBM also appears to support new bone formation through osteoconductive mechanisms. Case reports and analyses of several nonrandomized, retrospective clinical series suggest that DBM in combination with autologous marrow or bone demonstrates similar performance characteristics to autograft in posterolateral lumbar spine fusion [4]. Recent studies also suggest that the clinical level of evidence that supports the use of DBM in trauma and Orthopaedic surgery is limited and consists mainly of poor quality and retrospective case-series [5].

The purpose of this study is to decrease the donor site morbidity, to get sufficient graft and to access the efficacy of DMB in terms of Anatomical and functional outcome. Use of demineralized bone matrix along with local graft which is more biologically active would probably fasten the process and quality of fusion.

2. Materials &Methods

We conducted a prospective hospital-based study at Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore. A purposive sampling technique was employed. The study population consisted of 30 patients of both genders, between 18-65 years of age that have been admitted for low back ache. All patients of either sex undergoing primary posterior stabilization with posterolateral fusion in lumbar spine for degenerative spondylolisthesis and canal stenosis were included in the study. Patients that have a systemic infection, osteoporosis or osteomalacia to a degree to which spinal instrumentation would be contraindicated were not included in the study. Further, if the patient was undergoing cancer treatment, if patient had lytic spondylolisthesis below 18 years of age, or if the patient had high grade spondylolisthesis, the patient was excluded from the study. The participants were evaluated clinically and radiologically before surgery and post operatively at 3 months, 6 months, 9 months and 12 months. Only those patients who were available for 1year follow up were included in the study. A detailed case history, subjective and physical findings of the patient was recorded as per the questionnaire. Routine plain roentgenograms of the lumbar spine with erect flexion and extension views were obtained and the results recorded. An MRI scan of Lumbosacral spine was done in presence of radicular pain or neurological deficits. Based on all available information, a therapeutic and surgical plan was then laid out with a predetermined goal in mind for the surgery. Intra-operative findings confirm or alter the pre-operative plan and modifications are made accordingly. Consent was taken for surgery from the patient and his/her guardian. The surgical procedure was planned individually based on patient's age, symptoms and radiological features.

In the operating room, the back was prepped and draped in the usual fashion. A midline incision was made over operative level (example: L5/S1). Once the lumbar fascia was identified, dissection was carried down onto the appropriate level spinous process. A hemostat was placed between the spinous processes and its position was confirmed on a lateral radiograph which included the sacrum. Dissection was then carried down the lamina bilaterally to the level of the facet joints and transverse processes. Transverse processes were decorticated in PLF, which will act as bed for bone graft. Segmental, bilateral polyaxial pedicle screw fixation will be placed at all levels treated, by free hand technique. Reduction screws are used selectively as per preoperative planning. The starting point was identified at the juncture of two lines drawn down the transverse process and up the pars. This was at the most inferior portion of the superior facet. The starting point was made with an awl and the pedicle entered with a blunt gear shift up to midpoint of the vertebral body. The hole was tapped to the same level. A feeler was used to confirm solid superior, inferior, medial, and lateral walls and to confirm the presence of bone at the end of the tunnel. Next the screw was inserted. All the screws were inserted in the same manner. Final screw position is confirmed using image intensifier.

Decompression was performed for PLF. Connecting rod fixation was performed. Bone grafts were harvested from local bone (Laminectomy Bone Chips) and was morselized and mixed with morselized DBM placed posterolaterally between the facets and transverse processes of the vertebrae. We procured our demineralized bone matrix from bone bank at Ramaiah Advanced Learning Center, Bangalore. DBM was prepared and procured fresh and was customized based on the individual patient need from the bone bank and patient was explained about the benefits associated with it and detailed personal information was taken of the patient and were explained about the complications of the surgeries and to contact immediately if any antigenic response were encountered.

Functional outcome was assessed by Oswestry disability index (ODI) and the Visual Analogue Scale–Numeric Distress scale (VAS). Fusion was measured by analysing radiographs. Fusion in PLF is graded by Lenke classification which is shown in Table 1.

Surgical outcome was assessed in terms of the surgical time, estimated blood loss, length of hospital stays and post-operative complications such as Infection, Sciatica, Deep vein thrombosis and Pulmonary embolism, Pleural effusion, Epidural seroma, Muscle weakness.

Figure 1 and 2 shows the DMB Reconstitution with Local Bone Graft. Figure 1 shows the local bone graft and Figure 2 shows the DMB.

Figures 3, 4, and 5 show the mixing process, the final mixture, and the placement of the graft respectively.

Data was entered in Microsoft Excel (version 2007) and was analysed using R Studio (Version 1.1.463) and R Commander statistical packages. Shapiro-wilk test was used to test the normality of data and tests were applied to the variables accordingly. Frequencies and percentages were generated. Wilcoxon's signed rank test was used to compare the median Scores between pre and 12 month follow up. ODI and VAS scores were compared across different groups of variables using Mann Whitney U Test and Kruskal Wallis Rank Sum Test. The correlation between variables was assessed using Spearman's rank correlation test. P value less than 0.05 is considered statistically significant.

Table 1: Lenke classification of posterolateral fusion success

Lenke classification of posterolateral fusion success		
Grade A	Definitely solid	Bilateral trabeculated stout fusion masses present
Grade B	Possibly solid	Unilateral large fusion mass and a contralateral small fusion mass
Grade C	Probably not solid	Small fusion mass bilaterally
Grade D	Definitely not solid	Bone graft resorption or obvious pseudarthrosis bilaterally

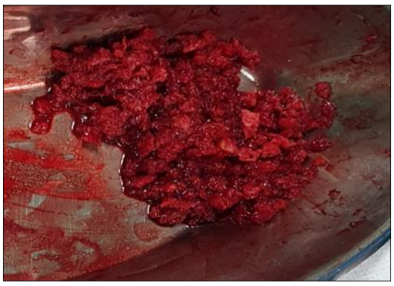

Fig 1: Local Bone Graft

Fig 2: DMB

Fig 3: Mixing Process

Fig 4: Final Mixture

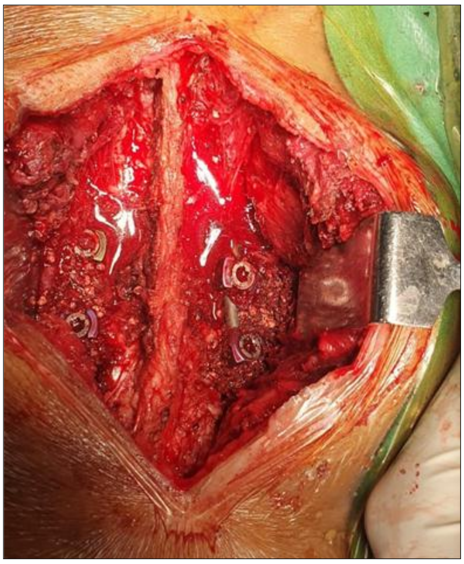

Fig 5: Placement of graft

3. Results

The study was conducted in 30 patients with degenerative spondylolisthesis and canal stenosis who underwent posterior stabilisation with decompression with PLF using demineralised bone graft. The patients were followed up for a period of one year and the results were analysed. Table 2 shows the age distribution of the patients. Out of the total patients, 16 were males and 14 were females.

The distribution of subjects by level affected and disease condition is shown in Table 3.

The mean pre-operative ODI scores in the study group was 62.76±3.54. The mean ODI scores at one year follow up was 18.8±2.61 which indicates that the percentage of improvement in the study group was 70.04±2.62. The mean pre-operative VAS scores were 7.37±0.71 which improved to a score of 0.67±0.74, leading to a percentage improvement of 90.90±4.05 in the study group.

The radiological outcome analysis at the one year follow up was assessed by using the LENKE fusion grade (Table 4).

One patient was encountered with excessive discharge from the sutured site which was taken for repeat surgery after a week after culture reports were found to be negative after 48hrs of incubation and the patient underwent debridement. Intraoperatively a deep haematoma was found under the thoracolumbar fascia with no visible local inflammatory reaction. DBM was in place. Thorough debridement was performed and the haematoma was removed. All the layers were sutured back and prophylactic antibiotic cover was started. Wound healing was delayed and sutured were removed on post op day 16 of revision surgery. There was no wound related complication on further follow up. The patient was a known case of T2DM and was also a chronic smoker which might have contributed towards the complication. Clinical Outcome using VAS score was 90.90± 4.05, mean % improvement in the Functional Outcome using ODI score was 70.04± 2.62, mean % improvement in the Radiological Outcome using LENKE Grading was 83.33% The mean overall improvement in clinical, functional and radiological outcome was 81.40%.

Wilcoxon's signed rank test was used to compare the median VAS Score between pre and 12 month follow up which is shown in Table 5. It also compares the median ODI Score between pre and 12 month follow up.

There was a statistically significant difference in the 12 month follow up median ODI scores among the subjects across age groups by Kruskal- Wallis Rank Sum Test (chi squared=7.65, p=0.02). Further pair-wise comparison of p-values between age groups by Bonferroni test showed significant difference in the ODI score only between age group <40 years and >50 years (p=0.02). There was also statistically significant difference in the 12 month follow up median VAS scores among the subjects across age groups by Kruskal- Wallis Rank Sum Test (chi squared=7.52, p=0.02). Further pair-wise comparison of p-values betweenage groups by Bonferroni test showed significant difference in the ODI score only between age group <40 years and >50 years (p=0.02). There was a positive correlation between 12 month follow up ODI scores and age [rho = 0.6, $p<0.001$] using Spearman's Rank correlation test. There was a positive correlation between 12 month follow up VAS scores and age [rho = 0.6, $p<0.05$] using Spearman's Rank correlation test. MannWhitney U test was used to compare the 12 month follow up median ODI scores between the two disease conditions. There was minimal difference in the 12 month follow up median ODI score between spondylolisthesis and canal stenosis which was not statistically significant(p=0.16). MannWhitney U test was used to compare the 12 month follow up median VAS scores between the two disease conditions. There was no difference in the 12 month follow up median VAS score between spondylolisthesis and canal stenosis (p=0.75).

Table 2: Age distribution of patients

Age in years	Number of patients	Percentage
20-30	3	10.0
31-40	7	23.3
41-50	9	30.0
51-60	9	30.0
>60	2	6.7
Total	30	100.0

Table 3: Patient distribution by disease condition and level affected

Level	Disease condition	
	Spondylolisthesis	Canal Stenosis
L3-L4	2 (12.5)	3 (21.4)
L4-L5	9 (56.3)	9 (64.3)
L5-S1	5 (31.2)	2 (14.3)
Total	16 (100.0)	14 (100.0)

Table 4: Radiological outcome by LENKE fusion grading system

LENKE fusion classification	No. of patients	Percentage
Grade A	25	83.3
Grade B	5	16.7

Table 5: Comparison of median ODI Score VAS Score between pre and 12 month follow up using Wilcoxon's signed rank test

Variable	(n=30)		V-value	p-value
	Baseline	12 month follow up		
VAS Score	Median (Q1, Q3)			
	7 (7,8)	1 (0,1)	465	<0.001
ODI Score	Median (Q1, Q3)		V-value	p-value
	62 (60,64)	18 (16.5, 20)	465	<0.001

4. Discussion

The DBM procured in our study was sterilized using alcohol and acid without exposing them to radiation to remove the antigenic capacity of the allograft. These morselized DBM had bmp proteins which helped in the new bone formation. Bae *et al*. have pointed out that the variability of BMP concentrations among different lots of the same DBM formulation was higher than the inter-product variability or concentrations of BMP among different DBM formulations.[6]

In the present study of 30 patients undergoing lumbar spinal fusion surgeries, posterior stabilisation with decompression with PLF using demineralised bone graft were trailed with conservative management for a period of two months and those who failed with it were evaluated clinically and radiologically and the need for the surgery was assessed. Subjects who met the inclusion and exclusion criteria and consented for the use of Demineralized Bone Matrix were included. In our study we saw L4-L5 were the most common level involved in condition like canal stenosis and degenerative spondylolisthesis. Our study showed younger patients of either sex had better improvement in the clinical, functional and radiological outcome compared to the older age group patients. In our study we observed a better improvement in the VAS of 6.6 which is approximately 90% improvement. Table 6 shows other studies that have used VAS for comparison.

In our study we observed a mean ODI score of 18.8 at the end of one year of follow up which is 70% improvement in the values and falls in the excellent category according to ODI Score interpretation. The ODI comparison with different studies is shown in Table 7.

The present study reported Lenke Grade A fusion rates of 83.33%. Our results showed excellent fusion rates which were at par with fusion rates of iliac crest bone graft crest bone graft in most of the studies. Table 8 shows the FUSION comparisons with different studies.

The pre op and post op comparison of VAS and ODI score showed p value <0.001 which is of statistical significance. Limitations of our study were a few as well. One of the limitations of the study was the sample size. Follow up duration of one year was also less compared to other studies.

Table 6: Other studies that have used VAS for comparison

Study	Number of patient	Improvement in VAS
Ohtori *et al*. [7]	42 cases of PLF with local bone graft	6.5
	40 patients with iliac bone graft	5.7
Cobo Soriano *et al*. [8]	184 patients undergoing decompressive lumbar surgery and instrumented posterolateral fusion	6.1
Niek Koenders *et al*. [9]	25 studies with 1777 participants	4.4
Challier *et al*., 2017 [10]	30 cases of TLIF	3.8
	30 cases of PLF	3.3
Present study	30 cases of PLF with DBM	6.6

Table 7: Other studies that have used ODI for comparison

Study	Number of patient	ODI values
Ohtori *et al*. [7]	42 cases of PLF with local bone graft	22
	40 patients with iliac bone graft	11
Cobo Soriano *et al*. [8]	184 patients undergoing decompressive lumbar surgery and instrumented posterolateral fusion	17.1
Niek Koenders *et al*. [9]	25 studies with 1777 participants	17.3
Etemadifar *et al*. [11]	25 cases of TLIF	53.2 % improvement
	25 cases of PLF	56.7 % improvement
Present study	30 cases of PLF with DBM	18.3

Table 8: FUSION comparisons with other studies

Study	Number of patients	Percentage Fusion
Levin *et al*., 2018 meta-analysis of 2 RCT and 5 cohort [12]	Pooled fusion in 118 cases of PLF	84.7%
	Pooled fusion in 123 cases of TLIF	94.3%
Alexander Tuchman *et al*. there systemic review of iliac crest bone graft versus local Autograft or Allograft of 3 RCT and 3 cohort study [13]	Pooled fusion in 241 cases local autograft or allograft	80%
	Pooled fusion in 241 cases treated with iliac crest bone graft	85%
Sengupta *et al*. [14]	40 patients treated with morselized autograft	65%
Putzier *et al*. (2009) [15]	20 cases with freeze dried allograft	80%
	30 cases with ICBG	85%
Kang *et al*. [16]	30 patients treated with DBM	86%

	16 patients treated with ICBG	92%
Schizas *et al.* [17]	26 patients treated with DBM augmented with local bone	69.7%
	4 patients with ICBG	76.9%
Present study	30 cases of PLF with DBM	83.33%

5. Conclusion

This study has highlighted the advantages of using DBM as an alternative to autograft when it used as a graft extender in combination with autograft. All patients had significant improvement in the VAS and ODI scores post operatively at one year follow up. Radiological evaluation at the end of one year, using Lenke fusion classification, fell into Grade A which is excellent. Overall the complication rates were low. Mean improvement in clinical, functional, and radiological outcome was excellent (81.40%).

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