Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) in Posterolateral Lumbar Spine Fusion: Complications in the Elderly
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INTRODUCTION:
In 2010, 12.97% of the U.S. population was ≥65 years with an estimated increase to 20% in the following 30 years. The number of elderly patients requiring surgery is expected to increase. Posterolateral fusion is the most common type of fusion performed in the lumbar spine. Iliac crest bone graft (ICBG) for spinal fusion is currently considered the “gold standard”. Patient age, comorbidities, and declining bone quality must be considered when selecting graft material for fusion.

Potential alternatives and enhancements to ICBG have gained attention. The discovery of osteoinduction through demineralized bone protein extracts and identification of bone morphogenetic proteins (BMPs) offers the potential to obtain fusion without ICBG harvesting or enhances autologous bone grafts. The use of rhBMP-2 in lumbar fusions is intended to enhance fusion mass and reduce bone graft donor side morbidity. Enhanced fusion rates for ICBG with rhBMP-2 compared to ICBG alone have been stated. rhBMP-2 utilization worldwide has increased to 28.1% of all fusion procedures.

Age has been found as a risk factor for complications in posterior lumbar procedures. BMP supplementation might be the solution to this problem. We assume that there is a higher complication rate in older patients and in patients with comorbidities.

The purpose of this study was to determine whether there was a difference in the number of complications requiring reoperation in elderly versus younger patients.

METHODS:
This study was an IRB approved retrospective cohort review of patients undergoing instrumented lumbar posterolateral fusion utilizing rhBMP-2 (INFUSE) at a single spine center. Consecutive patients were identified that had initial treatment from 2002 through 2009, 7 years. Inclusion criteria were: posterolateral fusion with rhBMP-2 implant and age ≥18 years. Exclusion criteria: thoracic fusions, anterior lumbar interbody fusion, BMP products other than rhBMP-2, follow up <6 months, and insufficient medical/radiographic data.

Of 2406 lumbar fusions, 1438 (59.8%) patients underwent lumbar posterolateral fusion with the addition of rhBMP-2. 280 patients were excluded because of age under 18, additional anterior lumbar interbody fusion, utilization of rhBMP-7, and inadequate follow up. 1158 patients (468 (40.4%) males, 690 (59.6%) females) were identified. Average body mass index (BMI) was 30.7 kg/m².

278 levels were fused. All patients underwent local autografting utilizing posterior elements and were consented to decompression, arthrodesis and off label use of rhBMP-2. The surgeon determined the rhBMP-2 dose. The mean total rhBMP-2 dose was 12.5 mg per patient (range 4.2-36.0). The mean dosage per level was 7.7 mg (range 1.5 – 24.0). Mean follow up was 15.3 months. Complications related to the performed procedure were recorded.

This compared patients ≥60 years to patients ≥60 years and further defined subgroups for comparison. (Group 1: 18-49 years, n=292; Group 2: 50-59 years, n=261; Group 3: 60-69 years, n=278; Group 4: ≥70 years, n=327). Comorbidities and potential contributing factors were recorded.

RESULTS:
Overall length of hospital stay (LOS) was 4.6 days and increased with age from 4.2 to 5.2 days. ICBG did not influence LOS (p=0.878).

Repeat surgery was required in 117/1158 patients (10.1%) due to surgical complications. Most common reasons for reoperation were: 3.5% nonunion, 2.8% perioperative seoma formation, 2.2% infections, and 1.2% bone overgrowth.

Mean age was 59.2 years (18-89) with an almost even distribution between ≤60 years (47.8%) and ≥60 years (52.2%). No differences in BMI, non-steroidal anti-inflammatory drug administration, or allergies were noted. Smoking occurred less in older patients (χ²=0.001).

Diabetes, cardiovascular diseases, and steroid medication were more common in elderly (χ²=0.001). No difference in previous BMP exposure (4.0% vs. 5.1%, χ²=0.591) was found. Patients <60 years underwent more instrumented fusions (92.4% vs. 84.6% respectively, χ²=0.001) and additional interbody fusion (58.8% & 28.6% respectively, χ²=0.001). Number of levels fused was 2.4 vs. 1.7 (p=0.001) in the ≥60 years compared to the <60 years. Older patients had significantly more multilevel fusions (χ²<0.001). Older patients received a higher total rhBMP-2 dose (12.7 mg vs. 12.3 mg respectively; p=0.007), but due to more multilevel fusions had less rhBMP-2 dose per level (6.7 mg vs. 8.7 mg respectively; p<0.001). Revision surgery was performed12.0% (21/175) of the time in diabetic patients compared to 9.8% (96/983) of the non-diabetic patients (χ²=0.366). In diabetic patients, the most common indications for redo-surgery were nonunion 63.5% (11/175) and painful seroma formation 4.0% (7/175).

Intraoperative diagnosed and repaired dural tears were more common in elderly patients (χ²=0.010). Revision surgery for clinically relevant nonunion was necessary in 3.8% of <60 years compared to 3.3% in ≥60 year old patients (χ²=0.651). A greater infection rate was found in elderly patients (3.1% versus 1.3% respectively, χ²=0.031). No significant difference in seroma formation was diagnosed between the two age groups (χ²=0.537). Subsequently, patients were sub grouped in four groups attributing factors to age.

Complications | Group 1 | Group 2 | Group 3 | Group 4
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Dural tear | 5 (1.7%) | 5 (1.9%) | 9 (3.2%) | 18 (5.5%)
Seroma | 7 (2.4%) | 10 (3.8%) | 12 (4.3%) | 3 (0.9%)
Infection | 4 (1.4%) | 3 (1.1%) | 10 (3.6%) | 9 (2.8%)
Nonunion | 13 (4.5%) | 8 (3.1%) | 10 (3.6%) | 10 (3.1%)
Bone overgrowth | 4 (1.4%) | 3 (1.1%) | 3 (1.1%) | 4 (1.2%)

( ) indicate statistically significant differences between groups. Identical labels indicate statistically significant differences between any of the groups.

DISCUSSION:
To reduce the necessary amount of ICBG and enhance fusion, bone void fillers combined with rhBMP-2 became a common supplement in spinal fusion. Possible cost reduction was attributed to decreased LOS and fewer complications. Average LOS for all patients was 4.6 days. This is consistent with previous studies. Additionally, we demonstrated an increasing LOS with age.

Reduced rhBMP-2 efficacy in patients ≥65 years has been previously reported when compared to younger patients. We found no significant difference in nonunion rates comparing patients <60 years to patients ≥60 years. Subdividing these patients in 4 age groups did not reveal a greater nonunion rate in any of the groups. This is even more important because elderly patients had a lesser percentage of additional interbody or instrumented fusions. Equal fusion rates could be attributed to a greater total rhBMP-2 dose in older patients. Elderly patients in this study had more levels fused and underwent more multilevel fusions. Despite these factors resulting in a reduced rhBMP-2 amount per level, no declination of BMP effectiveness or nonunion rates was noted.

Complication rates for lumbar spine surgeries in elderly patients differ from 7.1% to 14.4%. Our revision rate of 10.1% is within acceptable limits. Risks of surgery on the lumbar spine were reported to increase with age but other studies did not show increased complications in elderly patients. This inconsistency may be caused by different age limits. In our study, all relations were calculated for different age groups. We showed that complication rates were different in these age groups. We tried to elucidate the efficacy and risk profile for different age groups, but did not find significant differences between the age groups.

SIGNIFICANCE:
Orthopaedic spine surgeons should be aware that there is no evident difference in nonunion rates or increased re-operation rates in different age groups which suggests rhBMP-2 to be a potent enhancement irrespective of age.