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Clinical Study

Mesenchymal stem cell allograft as a fusion adjunct in one- and two-level anterior cervical discectomy and fusion: a matched cohort analysis

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Abstract

BACKGROUND CONTEXT: Live mesenchymal stem cell (MSC) allograft-containing allogeneic bone grafts have recently gained popularity and currently account for greater than 17% of all bone grafts and bone graft substitutes used in spinal surgery. Although the claim of cellular bone matrices containing osteogenic cells with osteoinductive properties is attractive, little is known about their clinical success when used in anterior cervical discectomy and fusion (ACDF).

PURPOSE: The objective of this study was to report on the radiographic fusion rates in one- and two-level instrumented ACDF using an MSC.

STUDY DESIGN/SETTING: This was a retrospective review of prospectively matched cohort of patients with radiologic assessment of fusion as the primary end point.

PATIENT SAMPLE: Two matched cohorts of adult patients who underwent ACDF with MSC or standard allograft were included.

OUTCOMES MEASURES: The outcome measures included radiographic and clinical evidence of healing at 1 year.

METHODS: A consecutive series of 57 patients who underwent a one- or two-level instrumented ACDF procedure between 2010 and 2012 were retrospectively analyzed. All fusion constructs comprised an interbody allograft, an anterior plate, and Osteocel (NuVasive, San Diego, CA, USA). These patients were matched to a control group of 57 patients.

RESULTS: Of the 57 cases in both cohorts, 29 (50.9%) were single-level, and 28 (49.1%) were two-level instrumented ACDFs. There were no significant differences in patient age ($p=.71$), gender, comorbidity burden (Charlson Comorbidity Index [CCI]: 1.95; 2.42, $p=.71$) or body mass index ($p=.79$). At the 1-year follow-up, 50 of 57 (87.7%) patients in the Osteocel cohort demonstrated a solid fusion compared with 54 of 57 (94.7%) in the control group ($p=.19$). Seven (12.3%) patients in the Osteocel cohort were reported as having a failed fusion at 1 year.

CONCLUSIONS: This is the first non-industry sponsored study to analyze a matched cohort assessing the 1-year arthrodesis rates associated with a nonstructural MSC allograft in one- and two-level ACDF procedures. Although not statistically significant, patients treated with MSC allografts demonstrated lower fusion rates compared with a matched non-MSC cohort.

Keywords: Anterior cervical discectomy and fusion; Mesenchymal stem cell allograft; Radiological assessment of fusion; Pseudarthrosis; Structural allograft; Cellular bone matrices

FDA device/drug status: Investigational (Osteocel® [Nuvasive, San Diego, CA, USA]).

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EVIDENCE & METHODS

Context
The use of allografts within the cervical spine, including mesenchymal cell allografts, have increased substantially in recent years. The efficacy of these grafts have not been extensively evaluated in non-industry sponsored research. The authors present results of a matched cohort analysis where 57 patients treated with Osteocel mesenchymal cell allografts were compared with a matched group treated with bone allograft. One year fusion rate was the main outcome measure.

Contribution
The authors report that no significant differences in demographic or medical factors were detected between the cohorts post-matching. No statistically significant differences in fusion rates were encountered between the two groups.

Implications
Although a matching procedure was utilized in this study, the effort is limited by a small sample of patients treated at a single center. There is also the potential for selection and indication bias in this setting, despite the fact that the cohort was consecutive. If patients selected for mesenchymal allograft were considered to be at greater risk of non-union for extrinsic factors, particularly variables that were not considered in the match process, the two groups could still be dissimilar in certain important respects. Retrospective matching can only account for factors included in the matching algorithm and the potential for residual confounding must still be acknowledged. Given the limitations in sample size and the potential for selection and indication bias that cannot be addressed with more robust statistical methods (given limitations in the sample size) the results of this work likely represent Level IV evidence.
—The Editors

Introduction

Cervical spinal arthrodesis is routinely performed for degenerative and traumatic cervical pathology. Currently, autologous iliac crest bone graft (ICBG) is considered the ''gold standard'' graft material to aid in achieving an interbody fusion [1,2]. Despite the high fusion rates reported with autologous ICBG (>90%), its utilization has been associated with significant harvest site morbidity (eg, pain, infection), prolonged surgical times, and greater blood loss. In addition, its finite availability limits its utilization in multilevel constructs and revision procedures. To mitigate these limitations, cadaveric allografts, bone graft extenders, and osteobiologic materials have evolved as alternatives to ICBG to aid in achieving cervical spinal fusion [8,9].

Initially, bone morphogenetic protein (BMP) represented a potentially advantageous bone graft substitute with high fusion rates, no harvest site morbidity, and a relatively infinite supply. However, mounting evidence has demonstrated that BMP is associated with significant postoperative morbidity in the setting of anterior cervical discectomy and fusion (ACDF) [4–6]. In fact, on July 1, 2008, the Food and Drug Administration issued a warning regarding off label use of recombinant human bone morphogenetic protein-2 in the cervical spine.

Live mesenchymal stem cell (MSC)-containing allogeneic bone grafts, also known as cellular bone matrices (CBMs), have recently gained popularity and currently account for greater than 17% of all bone grafts and bone graft substitutes used in spinal surgery [7]. Potential advantages include long-term cell proliferation, self-renewal capabilities, and multipotent differentiation [3]. To our knowledge, this is the first non-industry sponsored study evaluating fusion rates associated with MSC allografts in the setting of one- and two-level ACDF procedures.

Methods

A consecutive series of 57 patients (85 cervical levels) who underwent an instrumented one- or two-level ACDF procedure between 2010 and 2012 at a single center institution were retrospectively analyzed. Only patients with clinical (radiculopathy or myelopathy) and radiographic evidence of degenerative cervical spine disease were included. All fusion constructs comprised an interbody allograft, an anterior plate, and Osteocel (NuVasive, San Diego, CA, USA). Osteocel is a first generation CBM that results from the combination of demineralized bone matrix, cancellous cadaveric bone, and MSCs. These patients were matched with regard to diagnosis, number of fusion levels, smoking status, and comorbidity burden to a control group of 57 patients (85 cervical levels) who underwent an ACDF. The fusion construct in the control group included a structural interbody bone allograft (VERTIGRAFT [DePuy, Raynham, MA, USA]) and anterior plating without Osteocel or other graft enhancers. Patients who required a concurrent corpectomy, multilevel fusions, posterior fusions, revision procedures, and emergency cases were excluded from this analysis.

Data collection

Patient age, gender, race, smoking status, and comorbidities were assessed in both cohorts. To assess patient comorbidities, a modified Charlson Comorbidity Index (CCI) was calculated [10]. These modifications were as follows: a history of myocardial infarction was omitted; and liver disease was given an adjusted weight of two points rather than one point for mild disease and three points for moderate to