Anterior cervical interbody fusion using autogeneic and allogeneic bone graft substrate: a prospective comparative analysis

RANDOLPH C. BISHOP, M.D., KAREN A. MOORE, R.N., M.S.N., AND MARK N. HADLEY, M.D.

Division of Neurosurgery, University of Alabama, Birmingham, Alabama

The authors conducted a prospective study of 132 patients requiring interbody fusion without instrumentation following anterior cervical discectomy to compare the efficacy of tricortical iliac crest allograft versus autograft fusion substrates. The objectives of the study were to assess the potential differences in interspace collapse, angulation, maintenance of cervical alignment and lordosis, and clinical and radiographic fusion success rates between the two fusion substrates. The impact of habitual cigarette smoking on fusion rates was also examined.

Autograft tricortical iliac crest bone was found to be superior to allograft bone as an interbody fusion substrate after both single- and multiple-level anterior cervical decompression procedures with respect to maintenance of cervical interspace height, interspace angulation, and radiographic and clinical fusion success rates. Cigarette consumption had a significant adverse effect on successful anterior cervical interbody fusion for both autograft and allograft substrate, an effect that was most pronounced among smokers treated with allograft bone (p = 0.004).

KEY WORDS • interbody fusion • allograft • autograft • smoking • cervical spine

INTERBODY fusion following an anterior cervical decompression procedure is an accepted surgical adjunct in the treatment of selected patients with symptomatic ventral cervical spinal root and/or cord compressive pathology. The ideal fusion substrate remains a controversial issue for patients requiring interbody fusion after undergoing single- or multiple-level anterior cervical interspace decompression. This study was undertaken to identify differences in efficacy of the two commonly used fusion materials: autograft and allograft tricortical iliac crest bone substrates. Also examined was habitual cigarette consumption, which may be an important variable with respect to successful cervical interbody fusion, but to date has yet to be definitively assessed in clinical studies.

Clinical Material and Methods

Patient Population

One hundred thirty-two patients were enrolled and followed in a prospective assessment of Smith–Robinson anterior cervical interbody fusion substrate use in the senior author’s (M.N.H.) practice between November 1991 and March 1995. The patients were assigned to either the allograft or autograft group in an alternating fashion before surgery. After discussing fusion substrate options with each patient, some patients opted for autograft bone rather than randomization. Efforts were made to assign the patients to groups as randomly as possible. All radiographic data, hospital records, and serial examination forms were assembled for each patient and reviewed.

Operation and Grafting Materials

All of the operations were performed in a similar manner via a right-sided transverse skin incision using an operating microscope. Following discectomy and osteophyte excision, the superior and inferior vertebral body end plates were decorticated. The choice of autograft or allograft substrate was made by each patient prior to surgery.

The allograft fusion substrate was freeze-dried, vacuum-sealed tricortical iliac crest from the University of Alabama Bone Bank. Autograft tricortical iliac bone was harvested from the patient’s anterior iliac crest using a method similar to that described by Kurz, et al.,18 but modified by the use of an oscillating saw. Using the Caspar distraction device, a near-normal disc space height and angle was recreated. The tricortical graft was cut and sculpted to fit snugly into the interspace and then impacted so that the cortical faces were positioned anteriorly and laterally and slightly countersunk with respect to the ventral aspects of the vertebral bodies. No patient was treated with internal fixation hardware.
Postoperative Review

Postoperatively, the patients were discharged from the hospital 1 day after being surveyed and were instructed to wear a Philadelphia collar for 8 weeks. Cervical spine x-ray films were obtained in the recovery room and again at 3-, 6-, and 12-month intervals. The average duration of follow-up review was 31 months (minimum 3 months, maximum 43 months).

All radiographs were assembled and reviewed by a junior author (R.C.B.) and a staff neuroradiologist blinded to the type of fusion substrate used. An assessment of radiographic union and a measurement of disc space height and angle were made on the basis of each follow-up x-ray film and recorded (Fig. 1). Exact measurements and percent changes were determined for each patient at each interspace treated. Union of the fusion construct was defined as occurring when bony trabeculae were seen crossing the involved interspace. Delayed union was defined as failure of the bone to bridge the interspace and the persistence of a linear lucency on the 3-month follow-up radiograph. Nonunion was defined by the same criteria exhibited on the 1-year follow-up x-ray film. The designation of clinical fusion failure was reserved for patients who had recurrent cervical pain, with or without radiculopathy, and radiographic evidence of disc space collapse, angulation, and failure of fusion.

Statistical Analysis

Data were analyzed using the Fisher’s exact test for statistical significance.

Results

One hundred seventy-eight interspaces were fused in 132 patients: 69 with tricortical iliac crest allograft bone and 109 with autograft bone. Autogeneic iliac grafts were harvested and used in 83 patients. This included one-level grafting in 60 patients, two-level grafting in 20, and three-level grafting in three patients. Eight patients (10%) had graft-site complications: two patients had minor harvest-site infections requiring local wound care and six patients experienced prolonged donor-site pain (range 2–6 months). Freeze-dried tricortical iliac allograft was inserted into 49 patients: this included one-level fusions in 32 patients, two-level fusions in 14, and three-level fusions in three patients. No patient was treated with internal fixation hardware.

Preoperative diagnoses included cervical spondylosis in 58% of patients, central disc herniation in 32%, and pseudarthrosis with instability in 10%. The study group included 72 females (average age 47 years; range 24–79) and 60 males (average age 43 years; range 16–79). Forty-five percent (59 of 132) of the patients were cigarette smokers with an average consumption of 1.5 packs per day over a period of 23 years.

Single-Level Anterior Cervical Decompression and Interbody Fusion

In the 92 patients treated with single-level anterior cervical discectomy followed by interbody fusion, the fusion rates were 97% for cases using autograft substrate and 87% for cases using allograft substrate. There were six single-level fusion failures (four involving allograft and two involving autograft). All four patients with allografts and one with an autograft required reoperation for graft dislodgment or collapse with recurrent neck pain (with or without radiculopathy) and instability. One patient with an autograft was relatively asymptomatic and did not require further intervention. The mean fused interspace height was less well maintained in cases using allograft fusion substrate than in those using autograft bone. The mean interspace collapse in cases using allograft was 2.4 mm (24% change) and the mean collapse in cases using autograft was 1.4 mm (14% change), a statistically significant difference (p = 0.004) (Fig. 2).

Mean interspace angulation decreased more with allograft bone than with autograft bone. The mean angle loss was 2.8° (32% change) with allograft compared to 1.4° (12% change) with autograft (p = 0.037).
Serial x-ray films revealed delayed union at 3 months in 15% of the patients with autograft and 43% of the patients with freeze-dried allograft \( (p = 0.02) \). Radiography performed at 1 year postsurgery revealed incomplete union in 6% of the patients with autograft and 27% of patients with allograft \( (p = 0.004) \). None of these patients had evidence of instability on flexion–extension x-ray films and none were symptomatic for pseudarthrosis.

**Multiple-Level Anterior Cervical Decompression and Interbody Fusion**

Forty patients underwent multiple level interbody fusion after anterior cervical decompression: 18 were treated with allograft substrate and 22 with autograft bone. Fusion rates were 89% in cases using allograft substrate and 100% in those autograft substrate. There were two fusion failures in the multiple-level group; both involved allograft bone and in both cases the patients required reoperation for collapse, recurrent neck pain, and radiculopathy that were due to failure of fusion with instability. The mean collapse for allograft bone was 3.0 mm (31% change) and the mean collapse for autograft bone was 1.8 mm (18% change) \( (p = 0.005) \). The mean interspace angle loss was 4.1° (42% change) with allograft bone compared to 1.9° (18% change) with autograft bone \( (p = 0.004) \). For multiple-level procedures the delayed, or incomplete, radiographic union rate at 3 months was 22% in cases using autograft and 59% in those using allograft bone \( (p = 0.03) \). The radiographic nonunion rate at 12 months was 13% in cases using autograft bone and 47% in cases using allograft bone \( (p = 0.005) \). None of these patients had symptoms of pseudarthrosis or radiographic evidence of instability.

**Smokers Versus Nonsmokers**

Forty-five percent of the patients in this study were cigarette smokers with an average consumption of 1.5 packs per day for an average duration of 23 years. All of the clinical fusion failures in this series (eight of 132 patients) occurred in cigarette smokers. The mean change in disc space height for a single-level autograft interbody fusion was 1.9 mm (19% change) for smokers and 1.0 mm (10% change) for nonsmokers \( (p = 0.02) \). The mean change in disc space height for a multiple-level autograft interbody fusion was 2.5 mm (25% change) for smokers and 1.2 mm (12% change) for nonsmokers \( (p = 0.03) \). Patients who had received allograft substrate demonstrated a mean change in disc space height for single-level procedure of 2.9 mm (29% change) in smokers and 1.9 mm (19% change) in nonsmokers \( (p = 0.005) \). Patients undergoing a multiple-level allograft procedure had a mean change in disc space height of 3.5 mm (36% change) if they were smokers and a mean change of 2.4 mm (25% change) if nonsmokers \( (p = 0.005) \). Autograft substrate was associated with a mean change in disc space angle for a single-level interbody fusion of 1.9° (19% change) in smokers and 1.0° (10% change) in nonsmokers \( (p = 0.004) \). Multiple-level autograft procedures had a disc space angle change of 2.8° (27% change) for smokers and 1.1 mm (10% change) for nonsmokers \( (p = 0.005) \). Allograft substrate demonstrated a mean change in disc space angle in single level interbody fusion of 3.6° (40% change) in smokers and 2.2° (26% change) in nonsmokers \( (p = 0.005) \). Multiple-level allograft procedures had a mean change in disc space angle of 5.2° (53% change) in smokers and an angle change of 3.3° (34% change) in nonsmokers \( (p = 0.004) \).

All eight clinical fusion failures occurred among smokers (eight of 59; 14%); seven having severe collapse, malalignment, or graft extrusion requiring reoperation. Of the remaining 51 patients who smoked, the delayed radiographic union rate at 12 months was 60%, compared to 21% for nonsmokers.

**Discussion**

A variety of surgical approaches have been used in the treatment of symptomatic patients with cervical spondylotic and/or discogenic disease refractory to medical management.\(^1\)\(^-\)\(^6\),\(^8\)-\(^11\),\(^17\),\(^23\) Anterior cervical discectomy/decompression is an accepted surgical procedure in appropriately selected patients. Interbody fusion is an adjunct frequently used after the procedure to help minimize postoperative morbidity, maintain cervical spinal alignment, eliminate potential instability, and preserve interspace height and angulation, thereby reducing postoperative neural foraminal compromise following interspace decompression.\(^3\),\(^5\)-\(^8\) Debate exists as to which bone graft fusion substrate is most efficacious. The present study was undertaken to compare the effectiveness of two different tricortical iliac crest interbody fusion substrates for single- and multiple-level anterior cervical interbody fusion procedures without instrumentation. The effect of smoking on bone healing was assessed for each substrate type used. Tricortical iliac crest grafts, both autograft and freeze-dried allograft, are commonly used in clinical practice after anterior cervical decompression. Single-level autograft fusion rates range between 83% and 97%.\(^2\),\(^4\),\(^6\),\(^23\),\(^31\),\(^34\) Allograft fusion rates following cervical interbody fusion have been reported to be between 82% and 94%\(^,\)\(^11\),\(^19\),\(^25\) and several studies have documented similar clinical outcomes for the two fusion substrates.\(^3\),\(^9\),\(^10\),\(^24\),\(^25\),\(^33\),\(^34\) Clinical success rates for multilevel-cervical interbody fusion procedures are lower than those for single-level fusion rates but they remain good.\(^3\),\(^33\),\(^34\) Cigarette use by patients has not been cited in the literature as an important variable in the clinical and radiographic success of anterior cervical interbody fusion procedures.

Bone healing and fusion at an interbody fusion site are largely dependent on three main factors: 1) the condition of the recipient site, 2) the fusion substrate, and 3) regional and systemic host features. A successful fusion requires proper preparation of the recipient site including decortication of adjacent vertebral endplates.\(^3\)

The fusion substrate must have mechanical strength, must provide a scaffolding (osteocoonduction) for the ingrowth of host vascular buds, and must be immunologically and chemically inert. Most fusion substrate materials provide mechanical strength and osteoconductive potential, albeit to variable degrees. Bone (and other interspace fusion devices such as hydroxyapatite) provides a porous, three-dimensional scaffold or matrix in which host vascularization can occur in the early stages of graft incorpora-
tion. The preparation and treatment of allograft bone, which requires removing cells and proteinaceous materials to reduce its immunogenic potential, weakens it.\textsuperscript{18–21,23} Pelker, \textit{et al.},\textsuperscript{20} found that freeze-dried tricortical iliac crest graft material had a 10\% loss of compression strength and a 70\% reduction in torsion strength compared to autogeneic tricortical iliac crest bone.

Osteoinduction, the ability of the graft to stimulate adjacent bone at the recipient site to initiate vascular ingrowth and the transformation and recruitment of osteogenic cells is a property unique to organic bone substrates.\textsuperscript{12,16,22,30} A variety of trophic factors and proteins within autograft bone are potent osteoinductive agents.

Autograft bone has substantially greater osteoinductive potential than allograft bone. There are a whole host of osteoinductive proteins and trophic factors within the autograft substrate, factors that are largely removed during allograft preparation and sterilization. In addition, surviving cells within a fresh autograft, including osteoblasts, osteocytes, and mesenchymal cells, have the potential to form new bone (osteogenesis), increasing the likelihood of successful fusion.\textsuperscript{21,29,30}

The third main factor of successful interbody fusion relates to regional and systemic host features. An immunological mismatch and an inflammatory reaction to a solvent used to prepare the allograft substrate are examples of regional or systemic responses to graft material that inhibit bone healing. These adverse features do not exist in cases in which autograft bone is used. For all of the reasons specified above, autograft tricortical iliac crest bone is a better interbody fusion substrate than allograft tricortical iliac crest bone.\textsuperscript{12,16,17,34}

We found that autograft tricortical iliac crest fusion substrate had a higher fusion rate and less interspace collapse and angulation for single- and multiple-level anterior cervical interbody fusions following discectomy than freeze-dried tricortical iliac crest allograft bone. Operative time was not significantly increased by the harvest procedure, which was usually completed while waiting for x-ray film confirmation of the proper cervical interspace level. Morbidity from autograft harvest from the anterior iliac crest was limited to eight patients (10\%), two of whom suffered superficial wound infections and six of whom experienced prolonged donor-site pain (range 2–6 months). This is substantially lower than the incidence of donor-site complications reported by Whitecloud\textsuperscript{22} and by DePalma, \textit{et al.}\textsuperscript{6}

Cigarette smoking appears to be detrimental to successful bone fusion. Over 3000 by-products of cigarette smoke have been discovered, many of which have been identified as antioxidants, vasoconstrictive agents, inhibitors of vascularization and vascular budding, and osteoblast inhibitors, or have been implicated as cofactors that reduce bone mineral density.\textsuperscript{2,4,5,7,8,13–15,27,28} The precise mechanism(s) by which habitual smoking interferes with bone growth and metabolism is complex and has not been fully elucidated.

We found that our patients who smoked had substantially higher delayed fusion rate and failed fusion rates and greater interspace collapse and angulation following single- and multiple-level cervical interbody fusion than patients who did not smoke. The deleterious effects of smoking on fusion were observed in cases involving both autograft and allograft fusion substrates, but were most pronounced and consistently statistically significant (\(p = 0.004\)) among smoking patients receiving allograft fusion material.

In summary, our results suggest that tricortical iliac crest autograft substrate for interbody fusion following single- and multiple-level anterior cervical discectomy is superior to allograft tricortical iliac crest material. Although allograft fusion substrate has an acceptable fusion success rate for single- and multiple-level procedures, it is associated with greater interspace collapse and angulation, increased failure rates, and more instances of radiographic nonunion than autograft bone. Smokers have a higher failure rate following cervical interbody fusion than nonsmokers. This is particularly apparent in smokers treated with allograft fusion substrate.

To maximize clinical and radiographic success following anterior cervical spine decompression procedures requiring interbody fusion, autograft tricortical iliac crest bone should be considered. This appears particularly important among patients who smoke.

\begin{flushright}
References
\end{flushright}

15. Hussain MK, Frantz AB, Ciarochi F, et al: Nicotine-stimulated...

Manuscript received August 29, 1995. Accepted in final form March 27, 1996.
Address reprint requests to: Mark N. Hadley, M.D., Division of Neurosurgery, 511 Medical Education Building, 1813 Sixth Avenue South, Birmingham, Alabama 35294–3295.