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ORIGINAL ARTICLE

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A meta-analysis of autograft versus allograft in anterior cervical fusion

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Abstract We performed a meta-analysis of one- and two-level anterior cervical interbody fusion (ACDF) on data derived from published, peer-reviewed journal articles to determine whether there is a difference in fusion rate, graft complications, or clinical outcome in patients undergoing ACDF according to whether autograft or allograft was used. ACDF is a common procedure for cervical spondylotic radiculopathy. Most published studies comparing autograft and allograft have not demonstrated any difference between grafts. The medical literature dating from 1955 was reviewed. Of 395 titles, only four studies comparing autograft with allograft in ACDF were appropriate for this analysis. The data from these studies – 310 patients and 379 intervertebral levels – were pooled and statistical methods were applied. For both one- and two-level ACDF, autograft demonstrated a higher rate of radiographic union and a lower incidence of graft collapse. It was not possible to ascertain whether autograft is clinically superior to allograft. Although autograft has a higher fusion rate than allograft, clinical results do not depend solely on radiographic results. The risk of graft site morbidity and patient preference should be considered when choosing the type of graft for this operation.

Key words Anterior cervical fusion · Autograft · Allograft · Meta-analysis · Spine surgery

Introduction

Anterior cervical discectomy and fusion (ACDF) is a common surgical procedure used in the treatment of cervical spondylotic radiculopathy [1, 2, 3, 4, 7, 8, 9, 10, 11, 12, 14, 15, 18, 31, 32, 34, 35, 36, 38, 42, 43, 45, 46] Three commonly employed surgical techniques for anterior cervical fusion are the tricortical intervertebral graft methods of Robinson and Smith [31, 32, 38] and of Dereymaeker [15], the dowel method of Cloward [10, 11, 12] and the keystone method of Bailey and Badgley [5], although this latter technique was originally described for fracture and instability.

Although ACDF is a relatively safe and successful operation, the acquisition of autograft can increase the morbidity of operation for these patients. The complication rate of bone graft harvesting has been reported in the range of 9.4–49% [6], and includes pain; hematoma; infection; neuropraxia of lateral femoral cutaneous, iliohypogastric, and ilioinguinal nerves; fracture of ilium; gait disturbance; peritoneal perforation; hernia, and; cosmetic deformity [21, 22]. To avoid the morbidity of graft harvesting, investigators began using substitutes for autologous bone graft, such as ceramic implants [28, 37, 40], polymers [23, 41] and xenograft [24, 29, 39]. Cloward began using freeze-dried allograft in the 1950s, and the practice has been continued by other investigators with varying success [1, 2, 7, 10, 11, 12, 18, 20, 30, 35, 45, 46].

The primary advantage of allograft is that it avoids donor site morbidity. Other advantages include its ready availability, easy storage, and reductions in blood loss and

operating time. To prevent infection the grafts are sterilized, often with ethylene oxide, which does not appear to adversely affect the compressive strength [44]. However, transmission of disease can occur [13]. Other risks of allograft use include immunologic reaction, necrosis of the graft, fracture, delayed union and nonunion [27].

Several studies of the use of autograft versus allograft in ACDF have been reported [1, 7, 9, 45, 46]. These analyses have been either inconclusive or contradictory, with some authors finding equal fusion rates and clinical success [9, 45] and others finding superiority of autograft [1, 2, 7, 46]. Segal argues that, in the absence of a clear advantage of autograft, allograft should be used in order to avoid graft site complications [36].

We undertook the present meta-analysis of the literature on this subject in order to ascertain whether a difference in either clinical or radiographic outcome exists between patients receiving autograft versus those receiving allograft for one- and two-level ACDF for cervical spondylotic radiculopathy.

Materials and methods

A thorough search of the world literature on the use of autograft and allograft in anterior cervical fusion was conducted. The archives of the National Library of Medicine were searched via the Internet. All English language records (American and foreign) from 1966 through 1997 were searched with the key words "cervical" and "fusion" in the title. If the title indicated the article was related to anterior cervical fusion for non-traumatic and non-myelopathic conditions, the abstract was retrieved either through Grateful Med or through Lonesome Doc. Articles addressing trauma, tumors, infection, myelopathy, revision surgery, and cervicalgia without radicular signs and symptoms were excluded. If the abstract indicated the article specifically addressed the use of autograft and/or allograft in ACDF for cervical spondylotic radiculopathy, the original article was retrieved.

In addition, the bibliographies of recent textbooks, review articles, and research articles on this subject were scrutinized for similar references, which were retrieved. Classic monographs in languages other than English were also reviewed. Using this method, articles dating back to Robinson and Smith's original report were found.

A total of 395 articles were located, of which 61 were retrieved and read, because they specifically and directly addressed the topic of ACDF for radiculopathy. Of these, most related only to the use of autograft, or included other techniques, such as Cloward's. Unfortunately, we found no prospective randomized clinical trials in the literature. This analysis is based upon three prospective semi-randomized studies, and one retrospective review. We decided to pool and analyze the data only from articles that specifically compared autograft to allograft using the technique of Robinson and Smith, in either a retrospective review or prospective study, rather than to combine studies in which only one graft material was used. We also felt it important to look at the data for one-level, two-level, and multi-level fusions separately, since multi-level fusions tend to have a higher pseudarthrosis rate than one-level fusions anywhere in the spine. Finally, we felt that it was important to include papers with at least a 12-month follow-up of patients. Only complete articles from peer-reviewed journals were used in this analysis, which is based on four published articles representing 310 patients.

Patients from the four studies were divided into one- and two-level fusions. Using Chi-square analysis, the group of patients fused with allograft was compared to those fused with autograft in each author's series and in the series combined. Significance was defined as $P < 0.05$ and two-tailed values were used. In addition, the 95% confidence intervals for the fusion rates for autograft and allograft were determined [17].

Results

Clinical outcomes were not consistently reported. Two of the four papers did not mention clinical results at all [7, 9], and the other two did not use a grading system [1, 46]. Therefore, we were unable to analyze clinical outcomes of autograft versus allograft.

Radiographic union was reported in all four papers. Although the definition of union was different for each group of authors, the methods of Bishop et al. [7], Brown et al. [9], and Zdeblick and Ducker [46] were quite similar. We felt that each of these were commonly used and accepted definitions and could be used in this analysis.

Two hundred fifty-one patients had a one-level anterior cervical fusion, 149 with autograft and 102 with allograft. The pseudarthrosis rate with autograft, 6.0%, was lower than the rate with allograft, 14.7% ($P = 0.022$). The 95% confidence interval for autograft was 92.1–97.9%, and for allograft was 78.4–92.2%.

Fifty-nine patients had a two-level anterior cervical fusion – a total of 118 levels. Thirty-five patients (70 levels) were autograft and 24 patients (48 levels) were allograft. Twenty percent of patients with autograft and 45.8% of patients with allograft had a pseudarthrosis – a difference that was significant ($P = 0.034$). Although twice the number of allograft levels developed pseudarthrosis compared to autograft (25.0 vs 12.9%), this difference was not significant ($P = 0.90$).

Graft collapse was assessed in four papers, although the definition of collapse varied between authors (Table 1). Only Bishop et al. reported graft collapse for one- and

Table 1 Radiographic criteria for collapse

Author	Criteria
An et al. [1]	Greater than 2 mm loss of height compared to intraoperative radiographs
Bishop et al. [7]	Measured directly in millimeters and kyphotic angulation compared to postoperative films taken in recovery room
Brown et al. [9]	Greater than 30% decrease in graft height compared to immediate postoperative film
Zdeblick and Ducker [46]	Greater than 2 mm loss of height, or greater than 5° kyphotic angulation, compared to intraoperative radiographs

two-level fusions separately, but they did not report the data in a manner that could be included in this meta-analysis [7]. Rather than reporting collapse for each level, Zdeblick and Ducker reported incidence of graft collapse in all patients, including those with multi-level fusions [46]. Therefore, the rates of graft collapse from only two papers were pooled for this analysis, and these demonstrated that allografts had a higher incidence of collapse ($P = 0.009$).

Other graft complications, such as extrusion and fracture, were reported inconsistently and were infrequent. No analysis could be performed. The data for fusions of more than two levels were few and inconsistent, thus no meaningful analysis could be made.

Discussion

When the data from all four studies were pooled, we found a significantly higher rate of union, and a lower incidence of collapse, with autograft than with allograft for both one- and two-level fusions. Our analysis does not, however, address other graft complications, such as fracture and extrusion, nor does it address clinical results, since these parameters were reported inconsistently in the four papers.

An et al. reported the highest pseudarthrosis rates, but their criteria for fusion were the most restrictive [1]. Twenty-six percent of one-level autografts and 47% of allografts met the criteria for pseudarthrosis – a difference that was not statistically significant. Regarding two-level fusion, the number of patients with pseudarthrosis and the number of pseudarthroses were not significantly different between the two groups. These authors were unable to demonstrate a significant difference in collapse of either 2 or 3 mm between autograft and allograft. With respect to clinical results, the patients were not segregated into one- versus multi-level fusion. Good to excellent results were obtained in 84% of patients in both the autograft and the allograft categories. Because the percentage of patients with pseudarthrosis was higher in the allograft group, they concluded that "allograft gives a poorer healing rate and a higher collapse rate compared with autograft for one- and multi-level procedures."

In their one-level fusion patients, Bishop et al. found that 97% of the autograft group and 87% of the allograft group had a successful fusion, but this difference was not statistically significant [7]. They did, however, demonstrate a statistically significant difference between the two groups with respect to graft collapse (1.4 mm in the autograft group, 2.4 mm in the allograft group, $P = 0.004$) and with respect to kyphosis (1.4° in the autograft group, 2.8° in the allograft group, $P = 0.037$). They also found that the allograft group had a significantly delayed time to union ($P = 0.02$). These authors did not evaluate clinical results.

With regard to multi-level fusions, these authors found 100% union in the autograft group and 89% union in the allograft group, a difference that did not reach statistical significance. Incidence of graft collapse, angulation and delayed union were significantly higher in the allograft group, however.

Brown et al. looked only at radiographic results and found that the only difference between autograft and allograft was a higher rate of graft collapse in multi-level fusions using allograft ($P = 0.05$) [9].

In a study of 87 patients undergoing anterior cervical interbody fusion, Zdeblick and Ducker found that 95% of both autograft and allograft patients receiving one-level fusion achieved union [46]. Eighty-three percent of patients with two-level autografts and 38% of patients with two-level allografts fused – a difference that they calculated as significant at the $P = 0.03$ level. However, in their study, single-tailed values were used, while we employed a two-tailed analysis of their data. The *P*-value with two-tailed analysis was 0.060. When the two-level patients were analyzed with respect to fusion at each level, however, the autograft group had a lower pseudarthrosis rate than allograft patients (91.7 vs 68.8%, $P = 0.035$). Overall, pooling one- and multi-level fusions, the autograft union rate was 92% – significantly greater than the allograft union rate of 78% ($P = 0.04$).

The authors also pooled all levels to analyze graft collapse, which occurred more often in allografts, 30%, than in autografts, 5% ($P = 0.03$). One graft in each group extruded less than 3 mm. Clinical results between the two groups were similar, with 5% of the autograft group and 7% of the allograft group complaining of mild pain after 1 year.

Table 2 summarizes the significant findings in each of the papers reviewed and presents the significant findings

Table 2 Summary of significant findings in literature review and meta-analysis

Author	Finding
An et al. [1]	No difference between allograft and autograft, but a trend toward higher union rate and less collapse in autograft group. Similar clinical results between autograft and allograft.
Bishop et al. [7]	Trend toward higher union in autograft. Allografts had more collapse and greater kyphosis.
Brown et al. [9]	Similar union rates between autograft and allograft. Higher collapse rate in multi-level allografts.
Zdeblick and Ducker [46]	Similar union rates between autograft and allograft for one-level fusions. Higher union rates in two-level autografts. Higher collapse rate in allograft group.
Meta-analysis	Higher union rate in one-level autografts. Higher union rate in two-level autografts. Higher collapse rate in allograft group.

in the present analysis. In none of the papers, nor in this meta-analysis, did the use of allograft demonstrate any advantage over autograft with respect to radiographic criteria of union or collapse. Only when the data were pooled in the present analysis did the significantly higher union rate of autograft for one-level fusions become apparent. The pooled data and the study by Zdeblick and Ducker demonstrate a higher union rate using autograft in two-level fusions. The pooled data for graft collapse support the findings of three of the four studies in demonstrating that allograft had a higher collapse rate than autograft.

The present analysis is limited by the lack of prospective randomized clinical trials involving large numbers of patients in the literature. The Cervical Spine Research Society is currently studying this issue in a large, multi-center prospective project.

Given this limitation, the present study has shown that autograft is superior to allograft for one- and two-level anterior cervical fusions as far as radiographic criteria of success are concerned. However, as physicians we are concerned more with clinical outcomes than we are with radiographic results. Unfortunately, patient satisfaction and clinical outcomes were not adequately addressed in any of the studies upon which this meta-analysis was based. The question of whether pseudarthrosis is associated with clinical failure was not addressed in these papers.

Robinson et al. stated, "there was no clear correlation after operation between absence of fusion at the interspaces and the clinical result" [32]. Nevertheless, four of their nine patients were symptomatic from pseudarthrosis, and they felt that half of patients with pseudarthrosis would require reoperation. Newman maintains that good clinical results can be achieved only in the presence of solid arthrodesis [26].

From the published data, it is not possible to conclude whether graft collapse or kyphosis has any clinical significance. Some surgeons have reported good results with anterior cervical discectomy without interbody fusion, in which the disc space collapses greatly postoperatively. A graft collapse of more than 2 mm, in the absence of nonunion, may have little or no clinical relevance.

There are several flaws in the present study. Meta-analysis is a statistical analysis of data from several different studies of the same phenomenon, pooled to gain a broader perspective than can be achieved from each of the individual studies [16, 19, 25, 33]. Ideally, each of the studies upon which the meta-analysis is based would include large numbers of cases and have a similar design. We were able to find only 310 patients, representing 379 fused levels, in retrospective or prospective studies comparing the two graft types.

There were minor design differences in the four papers. All four studies used tricortical iliac crest graft obtained with an oscillating saw as the autograft and allograft; however, An et al. supplemented their allografts with demineralized bone matrix [1]. Three of the four papers were prospective and semi-randomized. Brown and co-workers' paper was a retrospective review [9]. A high-speed burr was used to perforate the endplates of the adjacent vertebrae in three of four studies. Postoperatively, patients were managed in a rigid collar for 6 weeks [1, 46] or 8 weeks [7], or a soft collar for 6 weeks [9]. Otherwise, the surgical approach and management was similar to that described by Robinson and Smith [31, 32, 38]. We did not feel that the differences in management, preparation of allograft or radiographic definition of union (Table 3) were sufficient to exclude any of these studies from the meta-analysis.

Table 3 Radiographic criteria for union

Author	Criteria
An et al. [1]	Grade 1: cleft between graft and bone with motion Grade 2: partial cleft but no motion Grade 3: solid arthrodesis (no cleft)
Bishop et al. [7]	Union: bony trabeculae crossing the interspace Nonunion – failure of bone to bridge the interspace
Brown et al. [9]	Union: complete bridging of trabeculae between adjacent vertebral bodies and the bone graft Partial union: less than 50% bridging trabeculae Nonunion: lack of trabecular bridging at both end plates with or without motion on flexion and extension films.
Zdeblick and Ducker [46]	Union: bony trabeculae crossing the disc space Nonunion: failure of bone to bridge across the disc space and persistence of a lucent line.

We did not include in our data pool studies of autograft only or of allograft only. We felt it important to analyze only those studies that compared autograft with allograft. While there is a large body of literature on anterior cervical fusion with autograft, the literature on allograft only is scarce, and we felt that the disparity would confound the analysis.

We also felt that to compare autograft-only papers to allograft-only papers would introduce errors associated with surgical technique and radiographic interpretation of pseudarthrosis. In the papers reviewed, the surgical technique and radiographic interpretations were similar enough to combine the data.

Meticulous surgical technique may have as much influence on union as the choice of graft, and the contributions of factors such as nutrition, sex, age, bone metabolic factors, and smoking on the success of autograft versus allograft have not been addressed in any published study.

Conclusions

The decision on whether to use autograft or allograft in anterior cervical fusion should not rest solely on published radiographic outcomes. While the present analysis demonstrates radiographic superiority of autograft, there are circumstances in which allograft is clearly a better choice of graft, such as in osteoporosis or in patients with prior autograft harvests. Allograft in these conditions would make a good second choice. Other factors the surgeon must consider are donor site morbidity with autograft, risk of transmission of infectious agents with allograft, and patient preference.

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