Is allograft a more reliable treatment option than autograft in 2-level anterior cervical discectomy and fusion with plate fixation?

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Abstract

This study aimed to assess the efficacy of allograft in 2-level anterior cervical discectomy and fusion (ACDF) with plate fixation by comparing its clinical and radiological outcomes to those of autograft.

Thirty-five patients with femur cortical allografts and 32 patients with tricortical iliac autografts were evaluated. All surgeries were performed by a single senior surgeon. During routine follow-up (at 3 months, 6 months, and annually after the surgery), the fusion rate, subsidence rate, and fused segmental lordosis angle were assessed by radiologic evaluation. Clinical outcomes were assessed using the visual analog scale (VAS), neck disability index (NDI) scores, and Odom criteria. This study was conducted using the results of the 2-year postoperative follow-up.

Among 67 patients, 62 (92.5%) showed successful bone fusion at 2 years postoperatively: 91.4% (32/35) in the allograft group and 93.8% (30/32) in the autograft group. The fusion rate was 37.1% (13/35) in the allograft group and 68.8% (23/32) in the autograft group at 6 months and 68.5% (24/35) in the allograft group and 93.8% (30/32) in autograft group at 1 year. Eight (72.7%) of the remaining 11 patients with allograft achieved bone fusion without any intervention at the 2-year follow-up. The fusion was achieved faster in the autograft group than in the allograft group \((P = .003)\). There was no significant difference in the subsidence rate or change in the fused segmental lordosis angle between the 2 groups; there was also no significant difference in clinical outcomes (NDI scores, VAS scores, Odom criteria) between the 2 groups. However, the intraoperative blood loss was significantly greater in the autograft group, and the operative time was also significantly longer in the autograft group \((P < .001)\). In the autograft group, 6 patients (18.8%) had minor complications at the donor site.

In 2-level ACDF with plate fixation, the radiologic and clinical outcomes of autograft and allograft were similar at 2-year follow-up, although fusion was observed earlier in the autograft group.

Abbreviations: ACDF = anterior cervical discectomy and fusion, ASH = anterior segmental height, NDI = neck disability index, PEEK = polyetheretherketone, PSH = posterior segmental height, VAS = visual analog scale.

Keywords: allograft, anterior cervical discectomy and fusion, autograft, clinical outcome, fusion rate, subsidence

1. Introduction

Anterior cervical discectomy and fusion (ACDF) has become a common surgical procedure for the treatment of degenerative cervical disc disease since it was first reported in 1955 by Robinson and Smith.\textsuperscript{[1–3]} Although ACDF is a relatively safe and successful procedure, selecting the ideal interbody graft material is essential to achieve successful fusion and optimal clinical outcomes. A tricortical iliac crest autograft is still considered the gold standard.\textsuperscript{[4]} However, the incidence of complications associated with harvesting from a donor site has been reported to range from 9.4% to 49%, including pain, hematoma, infection, neuropathy of the lateral femoral cutaneous nerves, iliac fracture, and gait disturbance.\textsuperscript{[5]} The primary advantage of using allograft bone instead of autologous bone is the avoidance of donor site morbidity. Other advantages of allograft use include easy preparation, reduced blood loss, and a shorter operating time.

Single-level ACDF has shown high fusion rates with both autograft (83%–97%)\textsuperscript{[1,2,6]} and allograft (87%–92%).\textsuperscript{[2,7]} However, in multilevel ACDF, contract stress and unacceptable increases in micromotion can reduce the fusion rate.\textsuperscript{[8]} Several
studies have reported that multilevel ACDF autograft is superior to allograft in terms of fusion rates.\textsuperscript{9,10} Since the introduction of an anterior cervical plating device, plate fixation has been used in multilevel ACDF to support alignment, increase internal stability, and improve fusion rates.\textsuperscript{11,12} However, the effectiveness of allograft vs autograft in 2-level ACDF with plate fixation remains debatable owing to small sample sizes and the designs of previous studies.\textsuperscript{13–15} In particular, no study has yet reported on subsidence occurring in the endplate related to allograft vs autograft in 2-level ACDF with plate fixation.

Therefore, the purpose of this study was to determine the radiologically evaluated fusion rates and incidence of subsidence as well as the clinical outcomes of patients who underwent 2-level ACDF using plate fixation with either allograft or autograft.

2. Materials and methods

A retrospective cohort study was conducted using the prospectively collected data of patients who underwent 2-level ACDF with plate fixation. All 2-level ACDFs with plate fixation had been performed using femur cortical allograft since April 2011. Prior to that, tricortical iliac autograft was used. Between November 2007 and May 2016, 80 patients underwent 2-level ACDF with plate fixation (39 using allograft and 41 using autograft). Autografts were harvested at the anterior iliac crest, while allografts were obtained from fresh-frozen and non-irradiated cortical bone from the femur (Allo-Spine Cervical Spacer, CG Bio, Seoul, Korea).

These patients were followed-up at postoperative 1, 3, 6, and 12 months and every year thereafter. This study was conducted using the results of the 2-year follow-up. Exclusion criteria for this study were as follows:

- non-completion of routine follow-up for a minimum of 24 months;
- insufficient data for exact radiological evaluation including C7-T1 fusion;
- occurrence of an additional decompression procedure; and
- occurrence of revision surgery due to previous nonunion or infection.

Routine follow-up for a minimum of 24 months did not occur in 7 patients (2 with allograft and 5 with autograft). Four patients had insufficient data for exact radiological evaluation (2 with allograft and 2 with autograft). One patient in the autograft group had an additional posterior decompression, while 1 patient in the autograft group was a nonunion revision case. Finally, among the 80 patients, 67 patients were included in this study, including 35 patients who received a femur cortical allograft and 32 who received a tricortical iliac autograft. This study was approved by the Ethics Committee of Samsung Medical Center, Sungkyunkwan University and informed consent was waived due to the retrospective nature of this study.

2.1. Radiological evaluation

Anteroposterior and lateral plain radiographs were obtained preoperatively, immediately postoperatively, and at 3 months, 6 months, and every year after the surgery. Flexion and extension lateral views were added at 3 months after the surgery.

Anterior segmental height (ASH) and posterior segmental height (PSH) were measured as the distances between the anterior or posterior margin of the upper endplate of the upper vertebra and the lower endplate of the lower vertebra (Fig. 1A). Segmental lordosis was measured using Cobb method to evaluate local sagittal alignment (Fig. 1A). Patients with \(<2\) mm of widening of the interspinous distance between the upper and lower vertebrae on the lateral flexion-extension plain radiograph during routine follow-up were considered to have successful bone fusions (Fig. 1B and C).\textsuperscript{16}

Subsidence was defined as minor when the reduction was \(\geq 2\) mm and \(<3\) mm or major when the reduction was \(\geq 3\) mm in the ASH or PSH immediately after surgery and on any follow-up radiograph. Increases in lordosis were assessed from before surgery to immediately after surgery. Decreases in lordosis were evaluated from immediately after surgery to the final follow-up. Radiologic measurements were performed using an embedded picture archiving and communication system (PACS, GE, Centricity, GE Healthcare IT, Barrington, IL, USA). To reduce measurement error, the pictures were enlarged (double magnification).
2.2. Clinical evaluation

Pain intensity was evaluated using the visual analog scale (VAS) (range, 0–10) for the neck and arm. Functional ability was evaluated using the neck disability index (NDI) score (range, 0–100). VAS and NDI scores were assessed routinely before surgery and at 3 months, 6 months, and every year after the surgery. Pre- and postoperative differences were analyzed at follow-ups. At 2 years after the surgery, clinical outcomes were assessed using Odom criteria. All score assessments were performed by an independent outpatient observer.

2.3. Statistical analyses

Parameters were compared between the 2 groups using the independent t test for continuous variables and the Chi-Squared test for categorical variables. Kaplan–Meier survivorship analysis with the log-rank test was used to analyze fusion points and compare differences in fusion duration between the allograft and autograft groups. Statistical analysis was performed using IBM SPSS version 21.0 (IBM Corporation, Armonk, NY, USA). P values < .05 were considered statistically significant.

3. Results

3.1. Study population

All patients underwent continuous 2-level ACDF with plate fixation. Fusion levels in the allograft group included C3-5 (n = 2), C4-6 (n = 10), and C5-7 (n = 23). In the autograft group, fusion levels were C3-5 (n = 1), C4-6 (n = 12), and C5-7 (n = 19). In the allograft group, there were 19 men and 16 women with a mean age of 55.2 ± 9.3 years. In the autograft group, there were 17 men and 15 women with mean age of 56.7 ± 6.6 years. The mean follow-up period for all patients was 36.1 months (range, 24–96 months). Demographic and clinical data between the autograft group and the allograft group were compared (Table 1).

3.2. Radiological outcomes

3.2.1. Intervertebral union rate and duration. Among 67 patients who were subjected to complete radiographic measurement during the 2 years of follow-up, 62 (92.5%) obtained successful bone fusion (91.4% in the allograft group and 93.8% in the autograft group). The fusion rate was 2.9% (1/35) in patients with allograft and 28.1% in patients (9/32) with autograft at 3 months, 37.1% in patients (13/35) with allograft and 68.8% in patients (23/32) with autograft at 6 months, and 68.5% in patients (24/35) with allograft and 93.8% in patients (30/32) with autograft at 12 months. Eight (72.7%) of the remaining 11 patients with allograft achieved bone fusion without any intervention at 2-year follow-up.

Based on the log-rank test, the mean duration of the confirmed fusion at 2-year follow-up was 13.6 months in the allograft group and 7.7 months in the autograft group. Patients in the allograft group needed significantly more time to achieve bone fusion than those in the autograft group (Fig. 2) (P = .003).

3.2.2. Subsidence incidence and segmental lordosis. In the allograft group, the mean decreases in ASH and PSH from immediately after surgery to the final follow-up were both 1.3 mm in the upper segment and 1.9 mm and 1.5 mm, respectively, in the lower segment. These values in the autograft group were both 1.4 mm in the upper segment and 1.9 mm and 1.4 mm, respectively, in the lower segment (Table 2). The greatest decreases in ASH and PSH occurred between the immediate postoperative period and the 3-month follow-up. The decrease in ASH was greater than the decrease in PSH in the lower segments regardless of the graft type.

A minor subsidence of ≥2 mm and <3 mm was noted in 10 upper segments (28.6%) and 16 lower segments (45.7%) in the allograft group and 11 upper segments (31.4%) and 15 lower segments (46.9%) in the autograft group. Major subsidence of ≥3 mm was noted in 3 upper segments (8.6%) and 6 lower segments (17.1%) in the allograft group and 1 upper segment (3.1%) and 5 lower segments (15.6%) in the autograft group (Table 3). Subsidence occurrence did not significantly differ between the 2 groups. However, subsidence occurred in the lower segments more frequently than in the upper segments regardless of the graft type (Table 3).

![Figure 2. Kaplan–Meier survival curve showing differences in the fusion point during follow-up between the allograft and autograft groups.](image-url)
Improvement in the segmental lordosis angle was observed in both groups upon comparison of the preoperative and immediately postoperative measurements. At the final follow-up, there was no significant difference in the segmental lordosis angle changes between the 2 groups (Table 2) (P = .231).

### 3.3. Clinical outcome

Clinical outcomes using the visual analog scale (VAS) and neck disability index (NDI) scores during follow-up are summarized in Figure 3A, B, and C. There were no significant differences between the 2 groups (P > .05). Using Odom criteria at the final follow-up, there was no significant difference in clinical outcomes between the 2 groups (Table 3) (P = .821).

### 3.4. Estimated blood loss and operative time

The mean intraoperative estimated blood loss was 88.6 ± 64.2 ml in the allograft group and 206.7 ± 84.8 ml in the autograft group. The mean operative time was 110.2 ± 17.5 minutes in the allograft group and 142.1 ± 21.5 minutes in the autograft group. The intraoperative blood loss was significantly greater and the operative time was significantly longer in the autograft group (P < .001).

### 3.5. Adverse events

Two patients with allograft and one patient with autograft reported hoarseness of voice, which recovered spontaneously within the 6-month follow-up period. In the autograft group, 6 patients (18.8%) had minor complications at the donor site after

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**Table 2**

| Segmental height (mm) | Preop. | Postop. (immediate) | 3 months | 6 months | 1 year | Last follow-up (2 years) |
|-----------------------|--------|---------------------|----------|----------|--------|--------------------------|
| Allograft Upper (N = 35) | ASH † 34.4 ± 3.4 | 36.2 ± 3.1 | 35.4 ± 3.2 | 35.0 ± 3.1 | 34.9 ± 3.2 | 34.9 ± 3.2 |
| PSH † 35.1 ± 3.4 | 36.1 ± 3.1 | 35.4 ± 3.1 | 34.9 ± 3.0 | 34.7 ± 2.9 | 34.8 ± 2.9 |
| Lower | ASH † 35.5 ± 3.6 | 37.8 ± 3.3 | 36.8 ± 3.4 | 36.2 ± 3.3 | 35.9 ± 3.3 | 35.9 ± 3.4 |
| PSH 35.6 ± 3.0 | 36.6 ± 3.0 | 35.8 ± 3.0 | 35.3 ± 2.9 | 35.0 ± 2.9 | 35.1 ± 2.9 |
| Autograft Upper (N = 32) | ASH † 33.8 ± 2.4 | 36.5 ± 2.4 | 35.5 ± 2.6 | 35.1 ± 2.6 | 35.0 ± 2.6 | 35.1 ± 2.6 |
| PSH † 35.0 ± 2.2 | 36.3 ± 2.1 | 35.1 ± 2.5 | 34.9 ± 2.6 | 34.8 ± 2.6 | 34.8 ± 2.6 |
| Lower | ASH † 34.5 ± 3.1 | 36.9 ± 2.9 | 35.5 ± 3.1 | 35.1 ± 3.2 | 35.0 ± 3.2 | 35.0 ± 3.3 |
| PSH 34.7 ± 2.8 | 35.8 ± 2.7 | 34.7 ± 3.0 | 34.4 ± 3.1 | 34.3 ± 3.1 | 34.4 ± 3.2 |

ASH = anterior segmental height; PSH = posterior segmental height.

**Table 3**

| Subsidence occurrence and clinical outcomes in the allograft and autograft groups at final follow-up. | Allograft (N = 35) | Autograft (N = 32) | P value |
|---------------------------------------------------------------|-----------------|-----------------|--------|
| Subsidence (mm) ≥ 2 mm | Upper 10 (28.6%) | 11 (31.4%) | .609 |
|                      | Lower 16 (45.7%) | 15 (46.9%) | .924 |
| ≥ 3 mm               | Upper 3 (8.6%) | 1 (3.1%) | .547 |
|                      | Lower 6 (17.1%) | 5 (15.6%) | .887 |
| Clinical outcomes   | Excellent 10 (28.6%) | 9 (28.1%) | .821 |
|                     | Good 9 (25.7%) | 9 (28.1%) | .887 |
|                      | Fair 13 (37.1%) | 13 (40.6%) | .921 |
|                     | Poor 3 (8.6%) | 1 (3.1%) | .547 |

Figure 3. Graphs showing clinical outcomes using the (A) VAS score for neck pain, (B) VAS score for arm pain, and (C) NDI score for the allograft and autograft groups during follow-up.
iliac crest bone grafting. One patient developed hematoma, 3 patients experienced chronic pain, and 2 patients reported paraesthesias at the donor site. No signs of instrumentation failure such as plate migration, screw loosening, or breakage were observed in either group.

4. Discussion

The material used for interbody fusion in ACDF has undergone significant transformation since its introduction through a surgical technique by Robinson and Smith in 1955. Autograft is considered the gold standard due to its unique combination of osteogenicity, osteoconductivity, and osteoinductivity.\(^\text{[4]}\) However, due to associated donor site morbidity, autograft alternatives, such as various types of cages and allobones have been introduced. Polyetheretherketone (PEEK) cages are widely used because their physical stiffness more closely resembles normal bone than that of titanium or carbon cages. In addition, it is easy to radiologically analyze the fusion state with PEEK cages.\(^\text{[18]}\) However, Kast et al.\(^\text{[18]}\) reported a 29% rate of subsidence over 2 mm with a union rate of 76%, while Lee et al.\(^\text{[19]}\) have reported a subsidence rate of 44.7% with a union rate of 95%. Clearly, there are relatively large differences between these results.

Several previous studies have reported allograft fusion rates of around 90%, without significant difference compared to those of autograft in 1-level ACDF.\(^\text{[1,2,7]}\) However, as the number of fusion levels increases, fusion rates decrease in ACDF without anterior plate fixation and the fusion rates of autograft become higher than those of allograft.\(^\text{[9,10]}\) In that sense, anterior plate fixation in multilevel ACDF is expected to show lower nonunion rates, as it can improve the stability of motion segments, thereby reducing the chance of graft migration or collapse. However, few reports have explored the fusion rates of allograft or autograft including clinical outcomes in multilevel ACDF with plate fixation. In the present study, the fusion rate in patients who underwent 2-level ACDF with plate fixation was found to be 91.4% in the allograft group at the 2-year follow-up, while it was 93.8% in the autograft group. The difference between the 2 groups was not significant. However, the time required for fusion was significantly longer in patients who received allograft than in those who received autograft. Autograft is known to be more effective than allograft in terms of osteoinduction, as it can facilitate vascular ingrowth and the transformation of osteogenic cells by simulating bones close to the recipient site.\(^\text{[20]}\) As allograft is less effective in terms of osteoinductivity, it takes longer than autograft to induce bone fusion. In the case of multilevel ACDF, allograft is likely to result in a higher incidence of pseudarthrosis due to a greater level of contact stress and micromotion. In theory, the addition of anterior plate fixation should narrow this fusion rate gap because it increases the chance of fusion by maintaining stability until the allograft fusion is complete. In addition, previous studies have shown that the cage and anterior plate construction method, as compared to the cage-alone method, can reduce the rate of pseudarthrosis and complications including cage migration and subsidence. Especially in multilevel surgery, the importance of the usage of anterior plate fixation becomes more significant due to increased rates of pseudarthrosis.\(^\text{[21]}\)

The fusion rates during the 1-year follow-up differed between the allograft and autograft groups, at 93.8% and 68.5%, respectively, though no significant symptomatic difference was detected between the groups. Therefore, pseudarthrosis may not necessarily be a symptomatic indication for reoperation. In particular, 8 of 11 patients with pseudarthrosis in the allograft group at the 1-year follow up achieved bone fusion by the 2-year follow-up without any intervention. Therefore, unless the patient’s clinical symptoms have worsened, reoperation may not be necessary for at least 2 years following the allograft, even in the presence of pseudarthrosis. Some studies reported delayed union when using allograft; without any intervention, 72.4% of 29 patients showing pseudarthrosis at the 1-year follow-up achieved bone fusion after 2 years.\(^\text{[22]}\) However, other studies have suggested that pseudarthrosis may result in neck pain and poor functional outcomes, and additional surgery may be necessary to stabilize the nonunion segment.\(^\text{[23,24]}\) Hence, determining the timing of reoperation is complicated in the context of pseudarthrosis. A previous study reported that patients who needed reoperation due to pseudarthrosis, even after 2 years, had persistent, severe neck pain. In other words, spontaneous union can be expected if the neck symptoms start to decrease within 1 or 2 years. However, if the symptoms persist or worsen, bone fusion is not likely to occur and reoperation may be considered at an earlier time point.\(^\text{[22]}\)

There was no significant difference in the subsidence rate between the allograft and autograft groups in the present study. However, regardless of the type of graft, higher occurrence rates were observed in the lower segments as compared to the upper segments. This can be explained by gravity and the concentration of the load of cervical motion in the lower segments as the 2 motion segments are fixated by an anterior plate in a 2-level ACDF. Therefore, in cases where severe radiculopathy symptoms are observed in the root of the lower segments, foramen decompression should be performed with extra caution during surgery. Moreover, in the autograft group, most cases of subsidence occurred within 6 months postoperatively. After the point at which autograft fusion was almost complete, significant subsidence was not observed, which suggests that subsidence rarely occurs after fusion. In contrast, in allograft patients, subsidence was observed beyond the 6-month follow-up. Mechanical micromotion might have persisted until fusion was complete, thereby affecting the progression of subsidence. However, there was only a difference in the timing of subsidence occurrence between the two groups and not in the frequency of its final occurrence. The allograft used in this study was a fresh-frozen and non-irradiated bone cage composed of the cortical lateral wall of the femur. Therefore, the disc space was strongly supported by the cortical portion, showing no difference in the frequency of the final subsidence even if the union was delayed. Our results illustrate that allograft is a feasible alternative to traditional autograft in 2-level ACDF. While the use of allograft may result in a longer time to achieve bone fusion, many potential problems may be precluded by the use of anterior plate fixation. The use of allograft not only showed advantages in terms of operation time and bleeding control but also the rate of complications that typically arise in the donor site when using autograft. Even though the additional costs of allograft may be an economic burden for some patients, further investigation of the actual economic impact with respect to the length of hospital stay and rate of complications is warranted.

This study has several limitations. First, the inherent weakness of this study was its retrospective study design. However, all clinical and radiographic data in this study were recorded prospectively and independently using the routine follow-up
In conclusion, in 2-level ACDF with plate fixation, no significant differences in the radiological or clinical outcomes were found between the allograft and autograft groups, though differences in fusion time were observed. Given the increased potential for morbidity with autograft use, including increased operative time and bleeding, allograft can be considered a reliable treatment option if anterior plate fixation is applied.

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