Treatment of AVN-Induced Proximal Pole Scaphoid Nonunion Using a Fifth and Fourth Extensor Compartmental Artery as a Vascularized Pedicle Bone Graft: A Retrospective Case Series

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Background: Scaphoid nonunion (SN) is a challenging condition in wrist pathology, often resulting in severe consequences if left untreated. Surgical intervention, particularly using vascularized bone grafts (VBGs), is a promising but uncertain approach. The 4+5 extensor compartment artery (ECA) pedicled graft, less commonly used for SN, has potential benefits due to its vascular supply and accessibility to the scaphoid. This study aimed to evaluate the effectiveness of the 4+5 ECA pedicled graft combined with headless compression screw fixation in treating avascular necrosis (AVN)-induced proximal pole SN. Radiological results, functional outcomes, and complications related to this method were assessed.

Material/Methods: This was a retrospective analysis of 19 proximal pole SN cases with AVN treated using the 4+5 ECA-VBG technique from 2016 to 2022. Patients underwent preoperative evaluation and postoperative follow-up for at least 1 year. Data on surgery, demographics, radiological assessments, and functional outcomes were recorded and analyzed statistically.

Results: All patients achieved radiographic union within 8.5 weeks postoperatively, with revascularization of proximal pole necrosis. Significant improvements in functional outcomes were observed, including pain reduction, increased wrist range of motion, improved grip and pinch strength, and enhanced wrist scores. No major complications were reported.

Conclusions: The 4+5 ECA-VBG technique, with headless compression screw fixation, showed high success rates in treating AVN-induced proximal pole SN. This method offers comprehensive restoration of wrist function and minimal complications, making it a viable option for SN management, especially in AVN cases. Further research is needed to confirm these results and establish standardized protocols for SN treatment.

Keywords: Fracture Fixation • Osteonecrosis • Scaphoid Bone • Vascular Grafting

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Introduction

The scaphoid bone is crucial for wrist function and stability, as about 80% of its surface is covered by cartilage [1]. It is the carpal bone most frequently injured, representing 60% of all carpal fractures, and mainly affects young males [2,3]. These fractures frequently occur as a result of falling onto an outstretched hand, and approximately 25% involve the proximal pole. Diagnosis is typically made through specialized radiographs, although computed tomography (CT) or magnetic resonance imaging (MRI) may be necessary for confirmation. Restoration of scaphoid length is essential for wrist function recovery, highlighting the significance of timely diagnosis and appropriate treatment. Treatment may involve prolonged immobilization with a cast, percutaneous surgical fixation, or open reduction and internal fixation. Nonunion occurs in 25-45% of scaphoid fractures, particularly in males in their 30s, attributed to the bone’s unique instability and limited blood supply [4]. Factors such as fractures at the proximal pole, vertical oblique fractures, displacement greater than 1 mm, advanced age, delayed initial treatment, inadequate immobilization, and smoking increase the risk of nonunion [5]. The dorsal branch of the radial artery, supplying approximately 80% of the proximal scaphoid through retrograde blood flow, contributes to the high association of proximal pole fractures with avascular necrosis (AVN) [6]. The most important factors leading to scaphoid avascular necrosis are associated with the location of the fracture. Fractures in the proximal segment have a 100% rate of avascular necrosis, which decreases to 33% in the distal segment; therefore, the location of the fracture is a significant factor in determining the risk of developing avascular necrosis [7].

Longer delays in surgery and fractures in the proximal third of the bone are associated with a decreased likelihood of achieving bone union [8]. The dorsal branch of the radial artery, supplying approximately 80% of the proximal scaphoid through retrograde blood flow, contributes to the high association of proximal pole fractures with avascular necrosis (AVN) [6]. Complications in scaphoid nonunion include pain, restricted hand function, degenerative arthritis, radiocarpal arthrodesis, and carpal collapse [9]. Consequently, the optimal treatment of scaphoid nonunion remains controversial, with most hand surgeons agreeing on the need for surgical intervention but differing on the specific approach [10].

Various surgical options have been preferred, with internal fixation and vascularized bone grafts (VBGs) commonly used today [11,12]. However, there is no standard practice for graft selection. Non-vascularized bone grafts (NVBGs), free VBGs, or pedicled VBGs are options for graft selection. VBGs, particularly in instances of AVN and prior unsuccessful surgical procedures, facilitate the revascularization of the scaphoid bone, resembling the process of primary fracture healing, and enhance the rates of union [5,13]. Studies have reported successful and reproducible outcomes with VBG use, particularly in AVN cases [14,15]. Dorsal-distal radius VBG grafts have been reported as superior in AVN-associated nonunion and are often the preferred choice due to their proximity to the scaphoid bone [16-18]. The 4+5 ECA graft, initially applied to the scaphoid by Sotereanos and commonly used for lunate AVN, is one of these graft options [19].

Here, we present the clinical and radiological outcomes of applying the 4+5 ECA-VBG technique in conjunction with compression screw fixation for nonunion of the proximal pole of the scaphoid, along with surgical details. This retrospective study included 19 patients with scaphoid nonunion and avascular necrosis treated with fourth and fifth extensor compartmental vascularized bone graft at a single center between 2016 to 2022, with 1-year follow-up.

Material and Methods

Patients

Before conducting this study, institutional review board and ethics committee approvals were obtained (IRB approval no: 48670771-514.10 – 23/06/2020), and the participants were enrolled in the study only after signing a written informed consent form. The research was conducted in accordance with the principles set out in the Helsinki Declaration. A retrospective review of the digital patient database at the author’s institution was conducted to identify patients with proximal pole scaphoid pseudarthrosis on the background of AVN between March 2016 and September 2022. Diagnosis of all patients was established through physical examination and direct radiographs. CT scans were performed to evaluate fracture morphology and size of the fractured fragment. Preoperative MRI was conducted for all patients to support the diagnosis of AVN. The inclusion criteria were age 18 years or older, having a fracture that had not healed for at least 6 months, at least 1-year follow-up, and having pseudarthrosis with AVN in the proximal pole of the scaphoid. All proximal pole SN cases with AVN treated using the 4+5 ECA-VBG technique were included. Exclusion criteria were previous wrist surgery, congenital or acquired deformities, neurological or systemic inflammatory diseases, advanced arthritis, and significant collapse. Patients meeting the inclusion criteria were called for a final follow-up visit, and all patients attended the final follow-up.

Surgical Technique

Patients were admitted to the hospital 1 day before surgery, and routine antibiotic prophylaxis with 1 g of sodium cefazolin...
was administered half an hour before the operation. All patients received standard treatment and were operated on in supine position under general anesthesia by the same surgeon using a loop magnifier. A tourniquet was applied to the affected extremity, but an Esmarch bandage was not used. A longitudinal incision of around 10 cm was made on the dorsal aspect of the wrist to reveal the fourth and fifth dorsal extensor compartments (Figure 1). The fourth dorsal extensor compartment was then opened. The extensor digitorum communis (EDC) was retracted radially, and the 4th and 5th ECA were exposed proximal to the radiocarpal joint approximately 1-2 cm distal to the distal radius. Cortico-cancellous bone graft with its pedicle was marked at the distal radius. The scaphoid capsule was incised under the wrist extensors to access the pseudarthrosis site of the scaphoid. While preserving the integrity and natural structure of cortical bone, the fibrous tissue and avascular bone in the nonunion area were debrided and cleaned to enhance bone vascularity. The diagnosis of AVN was confirmed by the absence of pinpoint bleeding in the scaphoid bone. A groove was created in the nonunion area on the proximal pole for graft placement. Multiple holes were made in the radial bone donor area using K-wires. Cortico-cancellous graft was obtained from the distal radius with the 4th and 5th ECA pedicles using a No. 15 scalpel and hammer (Figure 2). The pedicle length of the grafts was approximately 4 cm, and it was noted that the graft could reach the proximal portion of the scaphoid. The tourniquet was briefly loosened to assess any bleeding on the surface of the graft. The tourniquet was then re-inflated, and the graft was transferred to the nonunion site. Dorsal interosseous neurectomy was performed to reduce postoperative pain. The pedicled bone graft was placed between the fractured fragments and temporarily fixed with 2 K-wires. Permanent fixation was achieved in all cases with a headless cannulated screw under fluoroscopic control. In some cases, a K-wire was placed in the scapho-capitate joint to increase stabilization. Care was taken to preserve scaphoid height and normal anatomy during graft placement. A short-arm cast including the thumb was applied. Suction drains were placed, and the skin and subcutaneous tissues were closed. The drain was taken out after 24 h. The patients were discharged on the first day after the surgery.

**Data Collection**

Patient age, gender, tobacco use, side of injury (dominant/non-dominant), mechanism of injury, presence of associated acute injuries, initial treatments after fracture, time from fracture to surgery, follow-up duration, radiographic fracture union time, immobilization duration, and any comorbidities affecting healing (eg, diabetes, vasculopathy) were meticulously recorded. The presence and intensity of pain were evaluated with the visual analog scale (VAS), range of motion (ROM) (flexion-extension and radioulnar deviation) was measured with a goniometer, hand grip strength (kg) was evaluated using a hand grip dynamometer, and hand pinch strength (kg) was measured.

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**Figure 1.** In a 34-year-old male patient, the 4th and 5th extensor compartment arteries (ECA) were identified approximately 1-2 cm distal to the wrist joint, as indicated by the red arrow.

**Figure 2.** Pedicle osteo-osseous graft harvested from the area marked with a circle at the distal radius.
using a hydraulic pinch meter (kg). Functionality was determined through the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire (0: no limitations, 100: maximum limitation) and the Mayo wrist score (91-100: excellent; 80-90: good; 60-79: satisfactory; and <60: poor) [20,21]. Radiologic evaluation included measurement of scaphoid height/length ratio, radio lunate angle, lateral intra-scaphoid angle, scapholunate angle, and Natrass carpal height ratio. Functional and radiologic evaluations were recorded preoperatively and postoperatively and compared with the contralateral side.

Follow-Up and Postoperative Care

All patients underwent approximately 6 weeks of immobilization followed by ROM exercises under brace control, along with a rehabilitation program focusing initially on fingers and subsequently on the wrist, which was applied as a standard protocol. Splints were removed at 2 weeks after surgery, and a circular plaster was applied around the thumb. All plaster casts were removed at 6th weeks postoperatively. A removable wrist brace was worn for 6-8 weeks following the removal of the cast. During this time, patients were instructed to remove the brace at least 4 times a day for range of motion (ROM) exercises. Rehabilitation started with finger exercises followed by wrist movements. Monthly radiographs were taken until the sixth month postoperatively to assess fracture healing. Consolidation of the fracture was assessed radiologically at each follow-up session. Posteroanterior, lateral, and scaphoid (posteroanterior or ulnar deviation) views of the wrist were obtained on plain radiographs. A CT scan was additionally conducted to verify the union and evaluate the healing of AVN in the scaphoid. The presence of at least 3 cortical radiological calluses at the fracture line was considered as consolidation of the fracture. Radiological and clinical evaluations were routinely performed at 3, 6, and 12 months after surgery and at the time of final follow-up. Complications encountered were obtained from hospital records. Specific complications such as nonunion, resorption, infections, and implant failures were noted as appropriate.

Statistical Analysis

The data obtained in the study were analyzed statistically using SPSS Windows Version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics including mean, median (min-max values), standard deviation, and interquartile range (IQR) were used for data presentation. The independent sample t test was employed to compare variables demonstrating a normal distribution between the groups. For variables not showing normal distribution, the Mann-Whitney U test and Kruskal-Wallis H test were employed to compare variables demonstrating a normal distribution between the groups. For variables not showing normal distribution, the Mann-Whitney U test and Kruskal-Wallis H test were applied. A P value ≤0.05 was considered statistically significant.

Results

Demographic Characteristics

Nineteen fractures (8 right, 11 left) in 18 patients with an average age of 26.2 years (range, 18-39 years) and a mean follow-up duration of 29.4 months (range, 14-50 months) underwent 4-5 ECA-VBG. Sixteen of the patients were male and 3 were female. In 9 patients, the dominant side was affected. The primary causes of fractures were sports injuries in 6 (32%) cases, simple falls in 5 (26%) cases, motorcycle accidents in 4 (21%) cases, falls from bicycles in 3 (16%) case, and occupational accidents in 1 (5%) case. All patients were followed up, and all met the inclusion criteria. The place where the patient first sought medical care after trauma was an external center in 10 cases and the author’s hospital in 9 cases. Twelve cases were followed with casts for durations ranging from 8 to 16 weeks. Seven patients were unaware of their fracture or it was not diagnosed. The demographic characteristics of cases, mechanism of injury, initial treatment, time to surgery, union time, follow-up periods, and complications are shown in Table 1. All fractures had displaced enough to be seen on radiographs. Four patients had a history of smoking. There was no history of open wounds or any neurovascular abnormalities. The average interval between the fracture and the surgery was 9.9 months (range, 6-22 months), with a mean surgical time of 97 min (range, 75-120 min) min. Casts on patients were removed on average 7.9 weeks (range, 6-10) weeks after surgery. All patients were followed up for at least 1 year.

Radiological Findings

All patients achieved good union radiographically (X-ray, CT) in a mean of 8.5 weeks (range, 6-12 weeks) with confirmed revascularization of the proximal pole necrosis.

Functional Outcomes

On average, all patients who had fully recovered returned to their pre-injury activity levels without any restrictions within 4.6 months (range, 3-7 months) after union. Patients who wanted to return to sports activities (except bilateral case) were able to return to their previous level of play. Anatomical union was observed at the final follow-up (Figures 3-7). Significant enhancements were observed in postoperative joint range of motion, grip and pinch strength, VAS score, DASH score, Mayo wrist score, radio lunate angle, and lateral intra-scaphoid angle (Table 2). Marked improvement was noted in patient satisfaction and pain levels following the surgery. The average VAS score decreased from 9.8 (range, 8-10) before surgery to 0.21 (range, 0-2) after the surgery (P<0.001). In 17 patients, the pain disappeared completely, and 2 had mild pain during strenuous activities. Postoperative ulnar deviation and

Figures 3-7
Table 1. The demographic characteristics of cases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at surgery (year)</th>
<th>Sex</th>
<th>Dominant hand</th>
<th>Injured side</th>
<th>Smoker</th>
<th>Mechanism of injury</th>
<th>Initial treatment</th>
<th>Time from injury to surgery (month)</th>
<th>Time to union by CT (week)</th>
<th>Follow-up time (month)</th>
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<td>Left</td>
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<td>8</td>
<td>18</td>
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<tr>
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<td>Right</td>
<td>Right</td>
<td>No</td>
<td>Simple fall</td>
<td>None</td>
<td>22</td>
<td>6</td>
<td>24</td>
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</tr>
<tr>
<td>3</td>
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<td>Left</td>
<td>Yes</td>
<td>Simple fall</td>
<td>Casting</td>
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<td>8</td>
<td>34</td>
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</tr>
<tr>
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<td>Left</td>
<td>No</td>
<td>Sports injury</td>
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<td>12</td>
<td>8</td>
<td>40</td>
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</tr>
<tr>
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<td>19</td>
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<td>10</td>
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<td>6</td>
<td>27</td>
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<td>Right</td>
<td>Left</td>
<td>No</td>
<td>Simple fall</td>
<td>None</td>
<td>8</td>
<td>8</td>
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<td>Right</td>
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<td>24</td>
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</tr>
<tr>
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<td>Right</td>
<td>Left</td>
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<td>Casting</td>
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<td>20</td>
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<td>8</td>
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<td>36</td>
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<td>Left</td>
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<td>Casting</td>
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<tr>
<td>11</td>
<td>24</td>
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<td>Right</td>
<td>Right</td>
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<td>Motorcycle accident</td>
<td>Casting</td>
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<td>8</td>
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<tr>
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<td>Right</td>
<td>Yes</td>
<td>Work accident</td>
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<td>Casting</td>
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<tr>
<td>14</td>
<td>28</td>
<td>Male</td>
<td>Right</td>
<td>Right</td>
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<td>Left</td>
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<td>Right</td>
<td>Right</td>
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<td>Casting</td>
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<td>8</td>
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<td>38</td>
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<td>Right</td>
<td>Left</td>
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<td>Casting</td>
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<td>10</td>
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<tr>
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<td>25</td>
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<td>Right</td>
<td>Left</td>
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<td>8</td>
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<td>26</td>
<td>Male</td>
<td>Right</td>
<td>Left</td>
<td>No</td>
<td>Bike accident</td>
<td>None</td>
<td>10</td>
<td>8</td>
<td>50</td>
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</tbody>
</table>

extension-flexion angles significantly improved compared to preoperative values, although normal-side angles were not reached. The mean preoperative wrist flexion was 55.9° (range, 40-70°), which increased to 75.8° (range, 65-85°) postoperatively (P<0.001). On the healthy side, the mean was 81.5° (range, 75-90°). Preoperative wrist extension was 47.8° (range, 30-60°), which increased to 65.1° (range, 50-65°) postoperatively (P<0.001). On the healthy side, the mean was 68.2° (range, 60-70°). Preoperative radial deviation was 13.3° (range, 8-15°), which increased to a mean of 16.2° (range, 10°-20°) postoperatively (P<0.01). On the healthy side, the mean was 17.3° (1525°). Preoperative ulnar deviation was 28.7° (range, 20-30°), which increased to a mean of 31.4° (range, 2535°) postoperatively (P<0.01). On the healthy side, the mean was 36.9° (range, 30-40°). Grip strength (kg) at last follow-up was 40.1 kg (range, 30-54 kg), and reaching 93.1% of the healthy extremity. Pinch strength (kg) last follow-up was 7.2 kg (range, 6-9 kg), and reaching 89.2% of the healthy extremity. The initial DASH score was 64.5 (range, 50-75) before the procedure, which decreased to 11.58 (range, 16-30) during the final evaluation (P<0.001). Prior to the surgery, the average modified Mayo wrist score was 48.9 points (range, 40-65), with 4 cases assessed as fair and 15 as poor. After surgery, the mean score increased to 80.6 points (range, 60-90), encompassing 17 cases graded as excellent and 2 as good. This improvement was statistically significant (P<0.001), with no instances deemed moderate or poor (Table 3). Upon analyzing the outcome metrics based on demographic and clinical parameters, there was no notable disparity in average DASH scores,
Mayo scores, grip strength, and pinch strength values between smokers and non-smokers.

During the treatment, no major complications such as infection, loosening/displacement of screws, displacement of fractures, and graft extrusion were observed. Complex regional pain syndrome developed in only 1 patient, who improved after appropriate physical therapy. There were no morbidities in the donor area or issues with the implants, and there were no requests from patients for implant removal. None of the patients required revision surgery. No development carpal malalignment or radiocarpal arthritis was observed at the final follow-up.

Figure 3. Preoperative AP graph of the same patient’s proximal pole scaphoid nonunion.

Figure 5. Preoperative magnetic resonance image of proximal pole scaphoid nonunion of the same patient.

Figure 6. Last follow-up X-ray of the patient.

Figure 4. Preoperative computed tomography image of proximal pole scaphoid nonunion treated with 4+5 ECA-VBG technique.
The most important finding of this study was that among 18 patients with 19 fractures, the implementation of 4+5 ECA-VBG procedures yielded good outcomes. Specifically, all patients achieved good union radiographically within a mean of 8.5 weeks, accompanied by confirmed revascularization of proximal pole necrosis. Furthermore, functional recovery was good, with patients returning to their pre-injury activity levels without restrictions within an average of 4.6 months after union. Significant improvements were observed in postoperative joint range of motion, grip and pinch strength, pain scores, functional scores, and patient satisfaction levels. Additionally, the absence of major complications such as infection or graft extrusion, coupled with the absence of morbidities in the donor area or issues with implants, underscores the efficacy and safety of the intervention.

This study offers valuable perspectives on the effectiveness of the 4+5 ECA pedicled graft technique for treating AVN-induced proximal pole SNs, with the patient group experiencing high success rates and no reports of important complications. SN can lead to degenerative changes and consequently decreased function and dissatisfaction in patients. The predominance of young males and working individuals contributes to the significant socioeconomic impact of this condition [22,23].

Consequently, the treatment of SN, particularly when AVN is present, remains a serious challenge for orthopedists. While numerous surgical techniques and graft options have been described, none have definitively shown superiority over others [24-28]. Furthermore, there is no consensus on the preferred graft choice, as it depends on factors such as the location and character of the nonunion, the presence of significant deformity, and the surgeon’s experience [10,29,30]. VBGs have become increasingly popular in recent years as an alternative method due to their superior success rates compared to traditional non-vascularized bone grafts (NVBGs), particularly in cases of AVN at the proximal pole [3,24,31]. Various vascularized grafting methods, including dorsal and volar pedicled vascularized bone grafts (PVBGs) and free vascularized bone grafts (FVBGs), have been utilized. Many researchers advocate for the use of VBGs, particularly in instances of AVN at the proximal pole, citing the inadequacy of traditional NVBG techniques and the technical difficulties associated with free bone grafts [15,16,32].

In numerous studies and meta-analyses, VBGs have demonstrated significantly higher success rates (ranging from 88% to 100%) compared to NVBGs, particularly in cases of AVN at the proximal pole. For instance, Merrell et al reported success rates of 47% for NVBGs and 88% for VBGs in cases of AVN at the proximal pole [14]. Additionally, Malizos et al concluded that PVBGs should be preferred, particularly in instances of AVN.

**Table 2. Preoperative and postoperative radiographic parameters.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scapholunate angle</td>
<td>58.3 (29-89)</td>
<td>56.9 (34-95)</td>
<td>=0.658</td>
</tr>
<tr>
<td>Radiolunate angle</td>
<td>20.4 (0-55)</td>
<td>14.8 (1-49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral intrascaphoid angle</td>
<td>52.8 (25-85)</td>
<td>29.6 (15-38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Natrass carpal height ratio</td>
<td>1.56 (1.34-1.73)</td>
<td>1.58 (1.42-1.74)</td>
<td>&lt;0.762</td>
</tr>
<tr>
<td>Scaphoid height to length ratio</td>
<td>0.72 (0.5-1.0)</td>
<td>0.61 (0.5-0.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
at the proximal pole or in previously failed surgeries, due to their mechanical and biological superiority [18].

Among the various vascularized graft options, the combination of 4+5 ECA graft has emerged as a promising choice. This combination, despite being less commonly used for SN, has high union rates, ranging from 88% to 100% in the literature [19,33,34]. Especially in Kienböck’s disease, the use of pedicled local vascularized grafts has overcome some of the disadvantages of free grafts. However, the use of grafts in patients with Kienböck’s disease has shown varied outcomes, with some patients experiencing improvement, while others have experienced disease progression. Studies similar to the present one have shown excellent results in cases of scaphoid nonunions, with high consolidation rates [35,36]. Notably, the present study also found successful union in all patients using the 4+5 ECA graft. The ease of access to this graft, its long pedicle, and ample vascular supply, allowing it to reach the proximal pole of the scaphoid easily, influenced the choice.

Regarding fixation methods, various materials have been used, each with its own advantages and limitations. However, achieving stable fixation is crucial for treatment success. Studies have reported variable outcomes depending on the fixation material used, with some favoring headless cannulated compression screws and others preferring AO mini screws or K-wires [37-40]. The assessment of treatment success extends beyond achieving union. This study evaluated functional outcomes using Mayo and Q-DASH scores, demonstrating significant improvements postoperatively. Notably, all patients returned to their pre-injury work and activities, highlighting the comprehensive success of the treatment approach. Additionally, the choice of graft and fixation methods significantly influenced postoperative pain, range of motion, and functional recovery.

**Conclusions**

In conclusion, the 4+5 ECA grafting technique offers sufficient and viable bone to correct scaphoid bone loss and restate carpal height without any adverse effects at the donor site, which is particularly crucial in cases of AVN at the proximal pole. Further studies are needed to validate these findings and establish standardized protocols for SN treatment.

The limitations of this study consist of its retrospective nature, limited sample size, and short duration of follow-up. Although all patients underwent physical and radiological examination at follow-up, MRI was not routinely used. While MRI is considered the criterion standard for assessing nonunion healing and AVN, it is not essential in diagnosing these conditions. Furthermore, the study excluded patients with proximal pole fractures and nonunion treated with other graft types, which may have influenced the results. In addition, although all surgeries were performed by a single experienced surgeon using the same technique, variations in surgical technique may exist among different surgeons. Due to the limited sample size, there is a possibility of selection bias influencing the outcomes of the study. Additionally, since this was a single-center study, the results may not be universally applicable to other populations or environments.

### Declaration of Figures’ Authenticity

All figures submitted have been created by the author, who confirms that the images are original with no duplication and have not been previously published in whole or in part.
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