SURGICAL MEDICAL SCIENCES / CERRAHİ TIP BİLİMLERİ

# Early Clinical Results of Arthroscopic Bone Grafting and Percutaneous K-Wire Fixation for the Treatment of Scaphoid Non-Union

Skafoid Kaynamama Tedavisi için Artroskopik Kemik Greftleme ve Perkütan K-Teli Tespitinin Erken Klinik Sonuçları

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## Abstract

**Objectives:** The aim of this study was to examine the clinical results of patients treated with arthroscopic autologous bone grafting and K-wire fixation in surgery for scaphoid non-union, and the factors affecting the success of this method.

**Materials and Methods:** This single-centre retrospective study included 9 patients (7 males, 2 females) with a mean age of 31 years (range, 20-45 years). Radiological evaluations of the patients were made from direct radiographs and computed tomography images. The disability of the arm shoulder and hand (DASH), Mayo wrist score (MWS), and visual analog scale (VAS) scores were used in the evaluation of functional results. The range of flexion -extension of the wrist was evaluated pre and postoperatively. Grip strength of the operated hand was measured postoperatively and was compared with the non-operated contralateral hand.

**Results:** The mean time to union of the scaphoid bone was 8.5 weeks. Non-union was observed in 3 patients. The VAS score of the patients decreased from 6.5 preoperatively to 1.7 postoperatively, and the wrist range of movement increased from 81° to 101°. These values were determined to be 75% of those of the non-operated side. The DASH score and MWS improved postoperatively.

**Conclusion:** The main reasons for failure are not observing bleeding points in the fracture ends with debridement of the non-union area and early removal at the end of 8 weeks of the fixation made with K-wires in a second operation. The use of headless screws instead of K-wires in this technique can reduce the rates of surgical failure.

Key Words: Scaphoid Non-Union, Arthroscopic, Bone Grafting

Öz

Amaç: Bu çalışmada skafoid kaynamama cerrahisinde artroskopik otolog kemik grefti ve K-teli fiksasyonunu ameliyatı yapılan hastaların klinik sonuçlarını incelemek ve bu yöntemin başarısını etkileyen faktörlere dikkat çekmek amaçlanmaktadır.

Gereç ve Yöntem: Tek merkezli retrospektif yapılan çalışmaya, ortalama yaşı 31 olan (aralık, 20-45 yaş) 9 hasta (7 erkek, 2 kadın) dahil edildi. Hastaları radyolojik olarak değerlendirmek için direkt skafoid seri grafileri ve bilgisayarlı tomografi kullanıldı. Fonksiyonel sonuçları değerlendirmede el bileği fonksiyonunu değerlendirmek için kol omuz ve el yetersizliği (DASH), Mayo bilek skoru (MWS), görsel analog skala (VAS) skorları kullanıldı. Hastaların ameliyat öncesi ve sonrası el bilek fleksiyon-ekstansiyon aralığı değerlendirildi. Ameliyat sonrası ameliyat olan el ile karşı etkilenmemiş elin kavrama kuvveti ölçüldü.

**Bulgular:** Ortalama skafoid kemiğin kaynama süresi 8,5 haftadır. Dokuz hastanın 3'ünde kaynama izlenmemiştir. Hastaların VAS skoru 6,5'ten 1,7'ye düştü. El bilek hareket açıklığı 81 derecen 101 dereceye çıktı. Bu değer karşı tarafın %75'i kadardır. DASH skoru ve MWS ameliyat sonrası iyileşti. Son takiplerinde, elde kavrama kuvveti karşı tarafın %78'i kadardı.

**Sonuç:** Skafoid kaynamama alanının debridmanı ile kırık uçlarında noktasal kanama gözlenmemesi ve K-teliyle yapılan tespitin ikinci bir ameliyatla 8 hafta sonunda erken çıkarılması başarısızlığın en önemli sebepleridir. Bu teknikte K-telleri yerine başsız vidaların kullanımı cerrahi başarısızlığı azaltabilir.

Anahtar Kelimeler: Skafoif Kaynamama, Artroskopi, Kemik Greft

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## Introduction

The scaphoid is the carpal bone of the wrist which is the most frequently fractured (1). Healing of the scaphoid bone is not easy because of both the cartilage coverage adjacent to the carpal bones and the anatomy of the vascular structures providing nourishment (1,2). In literature, the treatment of scaphoid non-union has been attempted with several surgical techniques such as cancellous, corticocancellous, vascularised and non-vascularised bone grafting (3). Failure rates of up to 45% have been reported in these studies (4). More minimally invasive methods have been developed for fractures of this bone because of the risk of damage to the capsule and vascular structures in open surgery, and delayed union and joint stiffness associated with open surgery in the postoperative period (5).

The arthroscopic repair and percutaneous grafting method was first described in literature by Slade and Dodds (6) in 2008, and a success rate of 98% was reported in scaphoid nonunion. However, the arthroscopy technique characteristics were explained more than the clinical results in that study. Without performing open capsulotomy and without altering the vascularity of the scaphoid bone, better functional results and less joint stiffness are expected in this technique (6).

The aim of this study was to examine the postoperative clinical and radiological results of 9 patients applied with percutaneous K-wire fixation using arthroscopic cancellous bone grafting because of scaphoid non-union, and to evaluate the factors affecting the success of this method.

### Materials and Methods

The study was approved by Ankara University Faculty of Medicine, Human Research Ethics Committee (date: 19.12.2022, approval no:  $\dot{1}11-675-22$ ). The study initially enrolled 13 patients who presented at the hand surgery polyclinic of our hospital between January 2020 and November 2022 because of non-union of the proximal third or mid-third of the scaphoid. Four of these patients were excluded; 2 patients who had undergone an operation on the wrist for another reason, one patient with Scaphoid Non-union Advanced Collapse grade  $\geq 2$  arthrosis, and one patient with carpal deformity. The study continued with 9 patients. The patient information was retrieved retrospectively from the hospital electronic records system, patient files, and from the Ministry of Health Public Health Institute Death Registration System. The patient data were evaluated in a 24-month period postoperatively.

The demographic characteristics of the patients (age, gender, fractured side) were recorded (Table 1). The mechanism of injury, and the time from injury to surgery were also recorded.

In the physical examination of the patients for preoperative clinical evaluation, sensitivity in the snuffbox region was examined. In the radiological examination, anterior-posterior, lateral, 45° semipronation and semisupination oblique and ulnar deviation direct radiographs were examined. The cases were separated into two groups as stable and unstable non-union. Displacement of 1mm, poor alignment or humpback deformity (lateral intrascaphoid angle >45°) and dorsal intercalar segment instability (radiolunate angle >15°) were used as markers of unstable non-union (Table 2) (7).

As computed tomography (CT) scans showing increased proximal fragment radiodensity are strongly associated with a histological diagnosis of osteonecrosis, CT scans were taken to determine osteonecrosis in proximal non-union (8). As every patient did not undergo magnetic resonance imaging (MRI), the MRI scans were not included in the study. Fractures in which trabecular bone bridging did not form in the fracture line after surgical treatment, or sclerosis seen in the fracture ends together with cystic changes forming a permanent space, were accepted as non-union. For the classification of scaphoid non-union, the Alnot, Slade and Geissler classification systems were used (Table 3a, b). Intracarpal ligament injuries determined during arthroscopy were classified according to Geissler, and TFCC lesions according to Palmer. Poor prognostic factors which could affect postoperative union were scored (Table 4) (9).

All the operations were performed by the senior author. The percutaneous minimally invasive technique with arthroscopic bone grafting, as described by PC Wong and Ho (10) was used as the surgical technique. In the intracarpal ligament evaluation during arthroscopy, dorsal scapholunate (SL) ligament lesion was determined in all 9 (100%) patients. According to the Geissler classification, type 2 lesion was present in 6 patients and type 1 lesion in 3. Debridement and a thermal shrinkage process with radiofrequency were applied to patients observed with type 2 ligament lesion. Palmer type 1A TFCC lesion was observed in 2 patients and debridement was performed in these 2 cases. During arthroscopic surgery, fibrous tissue in the fracture ends was debrided extensively until points of bleeding were obtained from the bone.

The spongious graft harvested from the iliac bone was placed in the non-union line with the help of a cannula (3 mm) and a trocar (2.7 mm), and the K-wires were advanced (Figure 1). The patients were followed up for 8 weeks postoperatively with a thumb-supporting short-arm plaster cast. At the end of 8 weeks, the plaster cast was removed, the K-wires were removed, and the patients were admitted to the rehabilitation program. Bone healing was evaluated both clinically and radiologically in the postoperative period. Healing was evaluated clinically as the absence of sensitivity in the snuffbox region, and radiologically as the formation of bone trabeculae in the pseudo-arthrosis line on wrist posteroanterior, lateral, and scaphoid series (Figure 2).

Table 1: Demographic characteristics of patient												
Patient no	Gender	Age	Occupation	Trauma mechanism	Time since injury (Month)	Side	Dominant hand	Alnot's Fracture Classification	Slade and Geisler Classification	Ligament injury	Location	Point bleeding
1	М	45	Plumber	Fall	252	Left	Right	3a	Grade 3	SL Grade 2*	Proximal 1/3	D+/P-
2	М	33	Topographical engineer	Fall	36	Left	Right	2a	Grade 2	SL Grade 1*	Proximal 1/3	D+/P+
3	Μ	33	Officer	Fall	24	Right	Right	2b	Grade 3	SL Grade 2* TFCC 1A**	Proximal 1/3	D+/P-
4	Μ	28	Student	Fall	30	Left	Right	2b	Grade 3	SL Grade 2* TFCC 1A**	Proximal 1/3	D+/P-
5	Μ	31	Tailor	Fall	120	Right	Right	2a	Grade 2	SL Grade 2*	Middle 1/3	D+/P+
6	Μ	20	Student	Fall	10	Right	Right	2b	Grade 2	SL Grade 2*	Middle 1/3	D+/P+
7	F	31	Lawyer	Fall	18	Left	Right	2a	Grade 2	SL Grade 2*	Proximal 1/3	D+/P+
8	F	37	Worker	Fall	12	Left	Right	2a	Grade 2	SL Grade 1*	Middle 1/3	D+/P+
9	Μ	23	Salesman	Direct blow	6	Left	Right	3a	Grade 2	SL Grade 1*	Proximal 1/3	D+/P+

M: Male, F: Female, SL: Scapholunate ligament, TFCC: Triangular fibrocartilage complex \*Geissler Classfication, \*\*Palmer Classification

Table 2: Stable and unstable non-union criteria								
Patient no	Fractured disreplacement (mm)	Lateral intrascaphoid angle	Radiolunat angle					
1	<1 mm	52°	8°					
2	<1 mm	50°	14°					
3	<1 mm	48°	8°					
4	<1 mm	46°	12°					
5	<1 mm	48°	14°					
6	<1 mm	52°	11°					
7	<1 mm	46°	12°					
8	<1 mm	48°	14°					
9	<1 mm	54°	12°					

Table 3a: Alnot's Scaphoid Non-union Classification								
Stage 1	Linear pseudarthrosis							
Stage 2								
2A	Slight bone resorption no displacement							
2B	Unstable Pseudoarthrosis, Palmar flexion and adaptive DISI, Palmar bone loss							
Stage 3								
3A	Unstable pseudarthrosis, Palmar bone loss, Radioscaphoid arthritis							
3B	Radiocarpal arthritis							

Table 3b: Scapho	id nonunion classification according to Slade and Geissler
Grade 1	Late diagnosed acute fractures
Grade 2	Non-union with fibrous union
Grade 3	Non-unions that do not develop deformity but have a gap <1 mm
Grade 4	Non-unions with cystic changes (1-5 mm)
Grade 5	The type in which deformity develops and structural bone graft is required

Scaphoid serial radiographs and CT images were used for evaluation of the postoperative time to union. In the clinical measurement evaluation, the pre and postoperative visual analog scale (VAS) (0=no pain, 10= the worst pain), Mayo wrist score (MWS), and the disability of the arm shoulder and hand (DASH) scores were used. The total wrist flexion-extension range was measured with a goniometer preoperatively and in the postoperative follow-up period in both the operated wrist and the non-operated wrist, and the values were recorded. The grip strength of both hands was measured with a JAMA hydraulic dynamometer (Asimov Engineering, Los Angeles, CA, USA).

#### **Statistical Analysis**

Data obtained in the study were analyzed statistically using SPSS for Windows vn. 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were stated as mean  $\pm$  standard deviation values for continuous data showing normal distribution and as median (minimum-maximum) values for data not showing normal distribution. Categorical variables were stated as number (n) and percentage (%).

Table 4: Bad prognostic factors										
Patient no	Proximal pole fracture	Proximal pole AVN	>5 year non- union	Story of failed surgery	Smoking	Chronic disease	Bad prognostic factors	Union time		
1	Yes	Yes	Yes	No	Yes	No	+4	Non-union		
2	Yes	No	No	No	No	No	+1	5 weeks		
3	Yes	Yes	No	No	Yes	No	+3	Non-union		
4	Yes	Yes	No	No	Yes	No	+3	Non-union		
5	No	No	Yes	No	Yes	No	+2	10 weeks		
6	No	No	No	No	No	No	0	9 weeks		
7	Yes	No	No	No	No	No	+1	8 weeks		
8	No	No	No	No	Yes	No	+1	8 weeks		
9	Yes	No	No	No	Yes	No	+2	11 weeks		

AVN: Avascular necrosis



**Figure 1:** A) Arthroscopic image of scaphoid non-union, B) Debridement of fibrous tissue at the non-union line, C) Spot hemorrhages showing that we have reached the living bone tissue in the debridement procedure, D) Placing the cancellous graft taken from the iliac orest into the cavity, E) Tisseel [(Greenplast Kit, Green Cross) on the graft, Yongin Korea] tightening procedure, F) AP direct X-ray showing the stabilization of the fracture fragments and midcarpal (scacocapitate) with 3 K-wires, G) lateral direct X-ray

## Results

Evaluation was made of 9 patients, comprising 7 males and 2 females with a mean age of 31 years (range, 20-45 years). When the cause of trauma was questioned retrospectively, the fracture was caused by a fall in 8 patients and as a result of assault in 1 patient. The mean time from trauma to operation was 56.5 months (range, 6-252 months). The postoperative follow-up period in our clinic was mean 22.5 months (range,

17-30 months). According to the Alnot fracture classification system, type 2A non-union was observed in 4 patients, type 2B in 3, and type 3A in 2. Union in the scaphoid was observed in 6 patients and this method was not successful in 3 patients. No complications related to arthroscopy were seen in any patient.

Radiologically, the time to union was mean 8.5 weeks (range, 5-10 weeks). The mean VAS score decreased from preoperative mean 6.5 (range, 1-10) to 1.7 (range, 1-3) at the final follow-up examination. In the scoring applied for the functional



**Figure 2:** A) Radiographic images showing the bone bridges in the 10<sup>th</sup> week postoperatively in the middle 1/3 of the scaphoid bone A) AP radiograph B) AP radiograph in ulnar deviation, C) Lateral X-ray, D) CT image in the coronal plane, E) CT image in the sagittal plane, F) CT image in the axial plane CT: Computed tomography

Table 5: Postoperative clinical and radiological results of the patients											
Patient no	Preop VAS	Postop VAS	DASH	MWS	Grip strength (kg)	Functional hand grip (kg)	Preoperative flexion- extension arc (degree)	postoperative flexion- extension arc (degree)	Contralateral flexion- extension arc (degree)	Preop SL angle	Postop SL angle
1	3	2	0 (Perfect)	95 (Perfect)	36.5	45.5	80	95	140	51	43
2	9	1	0 (Perfect)	85 (Good)	33	42	75	110	135	37	46
3	6	2	6.25 (Good)	85 (Good)	34.5	44	85	100	135	50	57
4	7	3	6.25 (Good)	85 (Good)	33.5	40	80	105	130	28	48
5	9	1	25 (Satisfactory)	85 (Good)	34	38.5	85	100	135	35	44
6	7	1	10 (Good)	95 (Perfect)	35	48	80	105	140	70	57
7	7	1	33.3 (Satisfactory)	70 (Satisfactory)	37	47.5	90	110	135	35	40
8	10	3	32.5 (Satisfactory)	75 (Satisfactory)	36.5	44.5	80	95	130	51	55
9	1	2	20 (Satisfactory)	75 (Satisfactory)	35.5	45	75	90	140	52	50

DASH: Disabilities of the arm, shoulder and hand, MWS: Mayo modified wrist score, SL: Scapholunate ligament, VAS: Visual analogue scale

evaluation, the mean MWS was 83.5 (range, 75-95), with 2 patients evaluated as excellent, 4 as good, and 3 as satisfactory. In the DASH evaluation, the mean value of all the patients was 15 (range, 0-33.5), with the results evaluated as excellent in 2 patients, good in 3, and satisfactory in 4 (Table 5).

The wrist flexion-extension range of the patients was measured as mean 81° (range, 75-90°) preoperatively, and mean 101° (range, 90-110°) postoperatively. A 20° increase was obtained in the wrist flexion-extension range. This range of movement was up to 75% of the contralateral side, which was measured as mean 135° (range, 130-140°). The grip strength value of the patients was measured as mean 35 kg (range, 33-37 kg). This value was 78% of the contralateral, non-operated side value, which was measured as 45 kg (range, 42-48 kg). The SL angle measured on direct radiographs was mean 45° (range, 28-70°) preoperatively, and 49° (range, 40-57°) in the early postoperative period (Table 5).

#### Discussion

Many surgical treatment methods have been described for scaphoid non-union, but as yet no ideal surgical method has been developed for all non-unions (11). The advantage of open surgery methods is that reduction is easily obtained with direct visualisation of the region of non-union. However, opening the joint capsule causes disruption to the blood flow of the scaphoid. This method lost popularity because of the decrease in scaphoid vascularity with open reduction and this has driven surgeons to develop new methods (6). One of these is the arthroscopy-assisted percutaneous minimally invasive surgery method, which has become increasingly used in recent years (12). The advantages of this surgical technique are that open capsulotomy is not performed, the weak blood flow of the scaphoid is preserved, and the carpal ligaments are not damaged (13,14). Preservation of the scaphoid vascularity provides more rapid and better bone healing compared to open surgery (4,10). In literature, this method has been reported to have been applied in cases of non-union of distal third, midthird, and proximal third fractures together with acute fractures (15,16). In the current study, the factors affecting the success of this method were examined by evaluating the postoperative clinical results of 9 patients applied with percutaneous K-wire fixation using arthroscopy-assisted cancellous bone grafting.

In a study by Slade and Gillon (4) arthroscopy-assisted percutaneous minimally invasive surgery was performed on 234 patients, and the time to union in acute scaphoid fractures was seen to be shorter than in cases operated on because of non-union. It has been reported that there is a higher risk of avascular necrosis development in proximal third fractures in particular and there could be non-union (2,16,17). Inoue et al. (18) examined the factors affecting prognosis in scaphoid nonunion and showed that vascularisation of the proximal fragment, instability, and delayed surgery were associated with non-union. In the current study, the time to union was mean 8.5 weeks, which was consistent with the literature (19). In the 3 patients of the current study where union was not obtained, the fracture region was in the proximal third. In one case the operation was 21 years after the time of the fracture. Vascularised bone graft can be considered a good alternative in delayed operations for scaphoid non-union with impaired vascularity. Microvascular bone grafts both transferred free and with pedicle have been used successfully in the treatment of scaphoid non-union (20). In cases where points of bleeding cannot be obtained from the proximal bone, it may be logical to prefer vascularised bone operations.

In the arthroscopy-assisted percutaneous minimally invasive surgery technique, fixation of the scaphoid bone is extremely important. This fixation is usually made with headless screws and sometimes with K-wires (21). The tightening force of a headless screw on the fracture line is significantly greater than that of a K-wire. Moreover, it is not necessary to remove a headless screw and it can remain in the bone for longer than a K-wire (17). Close to 100% bone healing has been reported in literature in stabilisations made with K-wires using corticocancellous bone graft (5,22). The use of these wires has been shown not to affect the blood flow of the bone and to have a positive effect on healing (23). In addition, K-wires cause less bone loss than screws and preserve the biology (23). However, it has also been shown that compared with screws, K-wires can only create tightening of the fracture line of up to a third of the force exerted by a screw (24). Placement of K-wires passing through the centre of the scaphoid reduces the bending and shear forces loaded onto the scaphoid. If it is wished to reduce the effects of these forces on the fracture line, the K-wire can be placed to pass from the scaphoid to the adjacent carpal bones (lunate, capitate) (Figure 3) (25). In this way, the fixation also provides better stabilisation (5,25). Especially in proximal third fractures of the scaphoid, the tension over the K-wires increases greatly and the fracture line is exposed to greater bending and shear forces. The fixation of these fractures is more difficult compared to other regions. Therefore, in these types of fractures, by adding scaphocapitate fixation with K-wires, the midcarpal joint is locked, and these wires are embedded subcutaneously, then removed at 6-8 weeks (Figure 4) (17,26). In the current study, the K-wires were removed from all the patients in the 8th week. This 8-week period may be shorter than the period needed for healing of the scaphoid bone. In a study by Wong and Ho (27), a union rate of 91% (62/68) was obtained with this method, and the mean radiographic time to union was reported to be 12 weeks. In 2 of the 3 patients where union was not obtained in the current study, the midcarpal locking procedure with the K-wire was not applied. This can be considered to have caused increased tension

over the K-wires and have exposed the fracture line to strong bending and shear forces. In the cases where healing was not obtained, micro-movement formed in the fracture line had a negative effect on scaphoid union (Figure 5).

Other poor prognostic signs of scaphoid non-union include the presence of the fracture in the proximal region, the observation of avascular necrosis during surgery in the proximal region, a history of unsuccessful surgery, non-union lasting for longer than 5 years, smoking, and an accompanying chronic disease (9).

When the functional scores of the current study patients were compared with those of open surgery in literature, it



Figure 3: K-wire fixation radiographs between the scaphoid fracture ends and the scapholunate joint in the early postoperative period of the patient who was operated for non-union in the middle 1/3 of the scaphoid bone A) AP X-ray, B) AP X-ray in the ulnar deviation, C) Lateral X-ray

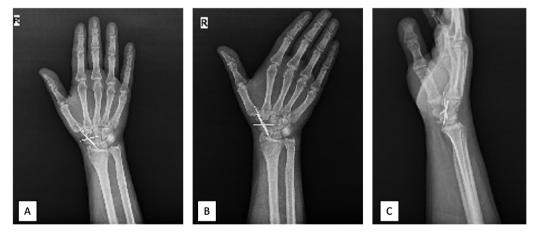


Figure 4: Early postoperative radiographs of the patient who was operated for non-union in the proximal 1/3 of the scaphoid bone. Fixation with K-wire between the scaphoid fracture ends and in the scacocapitate joint A) AP X-ray, B) AP X-ray in ulnar deviation, C) Lateral X-ray

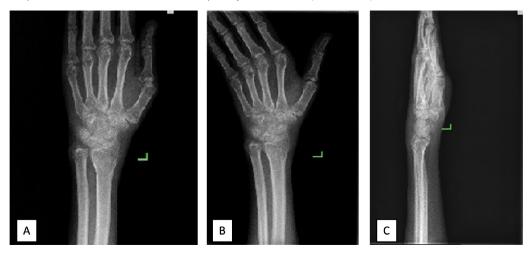


Figure 5: Non-union in the proximal 1/3 of the scaphoid bone A) AP X-ray, B) AP X-ray in ulnar deviation, C) Lateral X-ray

was seen that better wrist function was obtained with arthroscopy-assisted repair of scaphoid non-union than with open surgery (3,28). In a study by Lamon et al. (29), the pain scores fell from 7 preoperatively to 1 postoperatively, and postoperative grip strength was seen to have reached 83% of the non-operated side. Similarly in the current study, the pain scores of the patients significantly decreased compared to the values in the preoperative period, and the mean VAS score was 1.7 postoperatively. The wrist flexion-extenson range of the patients showed a 20° increase after surgery, and the postoperative grip strength reached 79% of the non-operated side. These results suggest that with minimally invasive surgery, less joint stiffness developed and rapid bone healing was due to better preservation of the scaphoid blood flow compared to open surgery.

#### **Study Limitations**

There were some limitations to this study, primarily that it was retrospective in design and was conducted with a small patient group. In addition, the MWS and DASH scores were not evaluated preoperatively. Finally, only direct radiographs and CT images were used for the measurement of avascular necrosis, and MRIs, which are more sensitive and specific, could not be included as they were not available for all the patients. Nevertheless, this study can be considered of value in drawing attention to the factors for success in the surgical technique of arthroscopy-assisted percutaneous K-wire fixation using bone grafting in the treatment of scaphoid non-union.

#### Conclusion

Arthroscopy-assisted percutaneous K-wire fixation using autologous bone graft is an extremely effective treatment method for scaphoid non-union. However, the main reasons for failure are not observing bleeding points in the fracture ends with debridement of the non-union area and removal of the fixation made with K-wires after 8 weeks with a second operation. The use of headless screws instead of K-wires in this technique may increase the rates of surgical success.

#### Ethics

**Ethics Committee Approval:** The study was approved by Ankara University Faculty of Medicine, Human Research Ethics Committee (date: 19.12.2022, approval no: İ11-675-22).

Informed Consent: Single-center retrospective study.

Peer-reviewed: Externally peer-reviewed.

#### **Authorship Contributions**

Concept: U.B., M.C.G., Design: M.A., Y.Y., Data Collection and Processing: M.C.G., Y.Y., Analysis or Interpretation: U.B., Y.Y., Literature Search: M.C.G., Y.Y., Writing: U.B., Y.Y., M.C.G., M.A. **Conflict of Interest:** The authors declared that there was no conflict of interest during the preparation and publication of this article.

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