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The outcome of bone graft surgery for nonunion of fractures of the scaphoid

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Abstract:	Data on 806 patients undergoing bone graft surgery for a scaphoid fracture nonunion were retrospectively collected at 19 centres in the United Kingdom. Each centre contributed at least 30 cases. 462 cases had sufficient data to study factors which influenced the outcome of surgery. The overall union rate was at least 69%, and the nonunion rate was at least 22%, with 9% of cases having “uncertain union status”. The union rate appeared to be adversely influenced by smoking and time between acute scaphoid fracture and nonunion surgery with adjusted odds ratios of 1.8 and 2.4 respectively, but neither achieved the pre-determined significance level of 0.003. Type of bone graft (vascular v non-vascular; iliac crest v distal radius) did not appear to influence outcome. Further large multicentre prospective studies with clear definitions of “union” and other factors are needed to clarify whether modification of surgical technique can influence the union rate.

The outcome of bone graft surgery for nonunion of fractures of the scaphoid

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ABSTRACT

Data on 806 patients undergoing bone graft surgery for a scaphoid fracture nonunion were retrospectively collected at 19 centres in the United Kingdom. Each centre contributed at least 30 cases. Sufficient data were available in 462 cases to study factors which influenced the outcome of surgery. Overall union occurred in at least 69%, and nonunion in at least 22%, with 9% of cases having "uncertain union status". Union appeared to be adversely influenced by smoking and the time between acute scaphoid fracture and nonunion surgery, with adjusted odds ratios of 1.8 and 2.4 respectively, but neither achieved the pre-determined significance level of 0.003. The type of bone graft (vascular vs non-vascular; iliac crest vs distal radius) did not appear to influence outcome. Further large multicentre prospective studies with clear definitions of "union" and other factors are needed to clarify whether modification of surgical technique can influence union.

Level of evidence: IV

INTRODUCTION

Symptomatic scaphoid fracture nonunion is typically treated operatively with bone grafting and internal fixation, unless significant wrist arthritis has developed as a consequence of the nonunion. Previous small studies suggest that the outcome of bone grafting and fixation of scaphoid fracture nonunion is affected by patient factors including smoking (Little et al., 2006), fracture factors such as the site of fracture (proximal pole or waist), the time interval between the acute fracture and the nonunion surgery (Inoue et al., 1997; Merrell et al., 2002; Nakamura et al., 1993; Trezies et al., 2000) and bone graft factors including the donor site and graft vascularity (Braga-Silva et al., 2008; Goyal et al., 2013).

Two recent systematic reviews have investigated factors which affect the outcome of scaphoid fracture nonunion surgery and how successful it is in achieving union. One (Pinder et al., 2015) found high frequencies of union with both vascularized and non-vascularized bone grafts but did not consider confounding factors. The other (Ferguson et al., 2016) resolved that it was difficult to draw any conclusions because most studies contained few cases, confounding factors were rarely considered and there were inconsistencies between studies, including the definition of union and variable length of follow-up after surgery which sometimes was only a few weeks.

This retrospective study investigated the outcome of the treatment of scaphoid fracture nonunion by bone grafting in 19 centres within the United Kingdom.

METHODS

This study was defined as a multicentre retrospective evaluation of service by the Research and Innovation Department of the Nottingham University Hospitals NHS Trust, and thus did not require ethical committee approval. This definition of the study was confirmed at each recruiting centre. Surgeons at 19 centres throughout the United Kingdom agreed to provide data on patients with scaphoid fracture nonunions treated with surgery to achieve union and thus improve wrist function. A trainee surgeon at each centre identified patients who had undergone such surgery before October 2014 by searching hospital records starting in September 2014 and working backwards in time, until a minimum of 30 cases were identified. Cases of revision bone grafting and fixation after a previous failed bone graft procedure were excluded. Relevant data on these cases were extracted from the hospital case notes and radiographs during October to December 2016. Thus, the minimum time between surgery and data collection from the medical records was 2 years. For this study a nonunion was defined as a fracture which had not united within 12 weeks of the acute injury based on plain radiographs or computed tomography (CT) scans. It was also decided that a minimum radiological follow-up of 12 weeks after the nonunion was required to determine whether a scaphoid fracture had, or had not, united.

Eligibility

Data was collected on 806 cases. Specific cases were excluded for the following reasons:

- patient age <16: (*n*=27);
- age at surgery not recorded (*n*=10);
- nonunion part of a trans-scaphoid perilunate dislocation (*n*=2);
- site (waist, distal or proximal pole) was not recorded (*n*=8);
- type of bone graft not recorded (*n*=11);
- was treated with synthetic bone graft (*n*=1);

- time from acute fracture to nonunion surgery could not be calculated (*n*=93);
- bone graft surgery occurred within 12 weeks of the acute fracture (*n*=65);
- time from surgery to last radiological follow-up not recorded (*n*=17);
- less than 12 weeks postoperative radiological follow-up (*n*=120).

This left 462 cases as some had more than one reason for exclusion. These 462 fracture nonunions were categorized as proximal if within the proximal 20% of the length of the scaphoid and distal if within the distal 20% of the length of the scaphoid. Those in the central 60% of the scaphoid were categorized as nonunion of the waist of the scaphoid.

The outcome of the "nonunion" surgery was union status. This was categorized as united, persistent nonunion or "uncertain whether united", based on the impressions of the treating surgical team as recorded in the medical notes. The trainee assessor at each of the 19 centres also assessed the last available postoperative radiographs, CT or magnetic resonance imaging (MRI) of each patient and categorized the outcome as united, persistent nonunion or "uncertain whether united". This was according to the absence or presence of adverse features such as: a gap at the fracture site or graft interface; lucency around, or movement (backing out) of, the implant; and displacement of the graft or the fracture (Dias, 2001).

Analysis

This study was designed as hypothesis-generating research, so no sample size calculation was done. Descriptive statistics are provided as frequencies with percentages (%). Age was skewed so the geometric mean and 95% confidence intervals (CI) are reported and compared using natural-log transformed data in a one-way ANOVA with Bonferroni correction. Proportional differences were examined using the chi-squared or Fisher's exact tests as appropriate. Agreement between the surgeon and the trainee assessor was determined using Cohen's kappa.

Union as diagnosed by the treating surgeon was the outcome of interest. Uncertain cases were classified as persistent nonunion. Logistic regression was used to estimate the odds ratio (OR) and 95% CI for persistent nonunion after surgery. To adjust for known confounders, multivariable logistic regression was used with the pre-selected co-variables of age as a continuous measure, and smoking, fracture pattern, method of fixation and time from acute fracture to nonunion surgery as categorical co-variates. We chose to examine the type of bone graft used through effect modification. Separate logistic regressions were also used to estimate the outcomes for patients with proximal pole and waist fracture nonunions; there was insufficient data to model distal pole fractures separately. All models were internally validated by lossless non-parametric bootstrapping by resampling with replacement, with 1000 iterations (Collins et al., 2015). All tests were two-sided. To improve the reliability of our results, the family-wise error rate was revised from $p<0.05$ to $p<0.003$ (Sidak, 1967).

RESULTS

The baseline characteristics of the patients and their nonunions, treatments and outcomes are summarized in Table 1. The surgery was unsuccessful, leaving persistent nonunion in 22% per cent of patients (n=104). In another 41 (9 %) of cases there was uncertainty as to whether the nonunion had united or not. Non-vascularized bone graft was the most common method of grafting for every type of scaphoid fracture and was used with increasing frequency from the proximal pole (51%) to the waist (77%) to the distal pole (89%).

Plain radiographs were the most commonly employed test for union (n=321, 60%). Comparison of assessments of postoperative union by the treating surgical team and the trainee assessors in this study showed excellent agreement (90%, k=0.8, p<0.001).

Descriptive statistics of the variables associated with persistent nonunion are reported in Table 2. Table 3 shows the unadjusted (univariable) and adjusted (multivariable) ORs which suggest that smoking and delays to nonunion surgery are associated with a worse outcome. Smoking at the time of surgery nearly doubled the odds of a persistent nonunion (i.e. treatment failure); this association remained strong in our multivariable modelling which was also independent of age, time from injury to surgery and the method of fixation. Similarly, delay of 1-2 years from injury to nonunion surgery was independently associated with 40% higher odds of persistent nonunion, whereas a delay of more than 2 years increased the odds by 140%. The variability of these estimates suggests that the longer the delay, the lower the probability of achieving union. Using effect modifiers in our multivariable model, the use of vascularized bone (as either a local or free flap) did not significantly alter the odds of achieving union for smokers (p=0.5), proximal pole nonunion (p=0.2) or nonunion treated more than 1 year after the acute fracture (p=0.2). Resampling did not change any of these estimates. We recommend caution in interpreting these models because, whilst they appear clinically significant, they are not statistically significant according to the family-wise error rate of p<0.003.

When examining the different fracture patterns individually, we again identified smoking and delays to nonunion surgery as potentially significant factors. Concerning proximal pole fractures, our bootstrapped multivariable logistic regression identified the patient's smoking status as the only factor potentially associated with persistent nonunion (OR 4.3 [95% CI 1.2 to 15]; re-sampled p=0.03). Similarly, concerning waist fractures, our bootstrapped multivariable logistic regression suggested that the time between acute fracture and nonunion surgery was independently associated with treatment failure whereby a delay of 1-2 years increased the odds by 110% (OR 2.1 [95% CI 1.5 to 13]) and delays over 2 years increased the odds by 440% (OR 4.4 [95% CI 1.5 to 13]; re-sampled p=0.007). However, these estimates should be interpreted with caution because they are not statistically significant with respect to the family-wise error rate of p<0.003.

DISCUSSION

Shortcomings of the existing evidence on outcomes of scaphoid fracture nonunion surgery include the lack of large prospective studies and a multitude of small studies which have used different criteria to define union and nonunion, failed to consider the impact of confounders such as smoking, and used different types of bone graft according to characteristics of the nonunion such as site, deformity and vascularity. This has resulted in different studies coming to different conclusions about which factors influence the success of bone graft surgery. This study also has many of these shortcomings as it was a retrospective survey of practice in 19 centres within the United Kingdom. However, 462 of the 806 collected cases satisfied our preselected definitions of nonunion (fracture not united after 12 weeks), and had sufficient follow-up (more than 12 weeks) to analyse the influence of factors such as smoking and time since acute fracture on outcome with adjustment for confounders.

Union occurred in 69% of cases after bone graft surgery in the 19 centres overall. This is lower than reported in many single centre studies and less than the 79% union recently reported for low-intensity pulsed ultrasound (LIPUS) (Seger et al., 2017). It is also lower than the overall frequency of union in over 80% reported by two systematic reviews (Ferguson et al., 2016; Pinder et al., 2015). This might indicate surgical failings, but all the 19 centres regularly manage this clinical problem. It could also be an underestimate due to us categorizing some fractures as having "uncertain union status". If all these fracture nonunions had actually united, then overall 78% would have been classed as united. It is perhaps surprising that other studies have not reported difficulties determining whether union had, or had not, occurred in some instances. Other possible explanations are the use of different criteria for defining union (Dias, 2001), different lengths of follow-up, or even reporting bias, in which only case series with high percentages of unions have been submitted for publication.

A recent meta-analysis found that smokers have twice the risk of experiencing a nonunion after a number of trauma and elective orthopaedic operations (Pearson et al., 2016). Its mechanism for inhibiting fracture healing is not known but could be due to nicotine (Feitelson et al., 2003; Gaston and

177 Simpson, 2007) or carbon monoxide (Sorensen et al., 2009) within the inhaled smoke. Two studies
178 reported 82% and 88% union after bone graft surgery for scaphoid fracture nonunion in non-smokers
179 compared with 40% and 57% in smokers respectively (Dinah and Vickers, 2007; Little et al., 2006).
180 Our data suggest that smoking is probably associated with a doubling of the odds of persistent
181 nonunion after bone graft surgery, which is consistent with these two studies.
182 Separate analysis of proximal pole and waist fractures suggested that smoking may particularly affect
183 the outcome of proximal pole fracture nonunion (non-smokers vs smokers: 77% vs 43%; p=0.01).
184 However this finding is not significant, given the revision of our family-wise error rate (p<0.003).
185 Also, it was based on univariate analyses which do not take into account confounding factors such as
186 time since the acute fracture.
187 Merrell et al. (2002) reported union of scaphoid fracture nonunions in 90% after surgery within a year
188 and 80% after surgery more than 1 year after injury. Another study of 160 patients found that one of the
189 factors associated with poorer outcomes was delay before surgery (Inoue et al., 1997). Nakamura et al.
190 (1993) found delays to surgery of over 5 years were associated with poorer outcomes after nonunion
191 surgery, as did Inaparthy and Nichol (2008). However, others have found no impact from delay
192 (Trezies et al., 2000). Our data suggest that the outcome of bone graft surgery is time dependant, with
193 patients with a delay of 1-2 years having 40% and those with a delay of more than 2 years having a
194 140%, higher odds of treatment failure than those who underwent surgery 3 to 6 months after the acute
195 fracture. We recommend that future researchers measure time on a continuous scale (e.g. in days,
196 weeks or months) rather than categorizing data into time blocks. This will allow a more accurate
197 estimation of the impact of specific delays on the likelihood of union.
198 The type of bone graft used for scaphoid fracture nonunion surgery remains a subject of debate and
199 may depend on characteristics of the nonunion, including the vascularity of the proximal fracture
200 fragment and deformity at the nonunion. Current reports show tendencies to use tricortical wedge
201 (corticocancellous) bone grafts for unstable nonunion, vascularized bone grafts for nonunion with

evidence of avascular necrosis of the proximal fragment, and cancellous bone graft for stable nonunion (Merrell et al., 2002; Munk and Larsen, 2004; Uesato et al., 2017). Our study did not distinguish between different corticocancellous and cancellous non-vascularized grafts, but a recent review by Sayegh and Strauch (2014) suggested the former resulted in better restoration of the height of the scaphoid and carpal alignment, and significantly better Mayo wrist scores. They found that cancellous grafts were associated with shorter time to union, but there was no difference in the overall percentages of union between these grafts. Our data suggest that non-vascularized iliac crest bone graft is the most common choice for scaphoid nonunion surgery in the United Kingdom. Vascularized bone grafts appear to be used most frequently for proximal pole (32%), rather than waist (17%) nonunions. Our univariate analyses suggested that vascularized local bone graft may influence the union of proximal pole (vascularized vs non-vascularized: 82% and 58%; p=0.04) but not waist fracture nonunion, though again these findings were not statistically significant. Also, analysis of the whole group of 462 scaphoid fractures (distal pole, waist and proximal pole) revealed no benefit to vascularized bone grafts. This is in agreement with the findings of recent systematic reviews which reported similar union results for vascularized and non-vascularized bone grafts (92% and 88%, respectively) (Ferguson et al., 2016; Pinder et al., 2015). We did not however independently assess the preoperative rationale for the use of vascularized grafting or any preoperative imaging for evidence of avascular necrosis (AVN). This therefore may introduce a risk of selection bias affecting any benefit of vascularized grafting in the setting of AVN.

We also found no benefit of iliac crest bone graft over a graft from the distal radius, which concurs with one systematic review (Pinder et al., 2015). Harvest of iliac crest bone graft may cause complications, and for this reason, use of non-vascularized bone from the distal radius might be the preferred choice when restoration of scaphoid height restoration is not required, or the nonunion is within the proximal pole (Arrington et al., 1996; Goulet et al., 1997). However, we accept our study

analyses are probably underpowered to detect differences in outcomes between the different types of bone grafts.

Avascular necrosis of the proximal fracture fragment is thought to increase the failure rate of bone graft surgery although ischaemia alone, without AVN of the proximal fragment, may not influence the success of grafting (Rancy et al., 2018). The reference standard to assess vascularity is intra-operative assessment of punctate bleeding from the proximal fracture fragment (Green, 1985). It can be assessed preoperatively with MRI, but its value in predicting the outcome of surgery is uncertain (Cerezal et al., 2000; Singh et al., 2004). AVN of the proximal fragment was not studied in this evaluation of service as the presence of punctate bleeding is frequently not recorded in the operation notes and MRI is not normally used preoperatively in the United Kingdom. Also, cases of avascular necrosis causing collapse and fragmentation of the proximal pole would have been excluded from our study as they are not suitable for bone graft reconstruction of the scaphoid.

There is no consensus on the definition of a scaphoid nonunion, which makes comparisons between published papers impossible. A recent systematic review (Ferguson et al., 2016) looked at 144 studies of scaphoid nonunion and found that only 17 defined the time since the acute fracture after which a failure of union indicated a nonunion. The time intervals suggested ranged from 12 weeks to 1 year. In this study we required a minimum period of 12 weeks after acute fracture, in keeping with current practice and other researchers (Murase et al., 2005; Schuind et al., 1999). Many surgeons feel that union is unlikely to occur 12 weeks or more after injury, either spontaneously or with further immobilization of the wrist in plaster, and patients are reluctant to tolerate long periods in a cast. Every case that was included in our study had the diagnosis of nonunion confirmed at the time of surgery.

There is also no consensus on the definition of radiological union after scaphoid fracture nonunion surgery. One systematic review found that the radiological features used to diagnose a nonunion, such as absence of bridging trabeculae, both before or after bone graft surgery, were not described in any of 144 studies (Ferguson et al., 2016). Plain radiographs are most commonly used and the absence of a

complete gap between the fracture fragments on any image, as well as no evidence of loosening of the fixation screw or wires (if present) suggest union, such that nonunion is a diagnosis by exclusion (Dias, 2001). Persistent nonunion may give the appearance of bridging trabeculae due to overlap of the distal and proximal fracture fragments unless the X-ray beam for at least one view is in the plane of the fracture. The timing of the radiographs is also important as graft resorption may make a nonunion evident at 12 weeks after surgery, whereas radiographs taken at 6 weeks (before bone graft resorption) may suggest union. It was for this reason we excluded all cases with a radiological follow-up of less than 12 weeks from our analyses. CT scanning probably allows a more reliable assessment of union, but the presence of a metallic fixation device (screw or wires) may distort the images and make this assessment difficult.

This study was a retrospective service evaluation, and thus has several failings, including a high percentage of case exclusions (344/806 = 43%) for the reasons previously given. A systematic review of scaphoid fracture nonunion surgery revealed that the outcome of bone graft surgery had been reported in 5464 cases in 144 studies of ten or more cases published in peer reviewed journals before 2015 (Ferguson et al., 2016). Therefore, despite the number of exclusions, our 462 cases are equal to 7.8% of the previously reported outcomes of scaphoid fracture nonunion surgery.

Another issue with the present study is the possibility that the different centres involved used different criteria for determining whether the surgery had succeeded in achieving union because the primary outcome in this study was the conclusion of the treating surgical team. Despite the potential for bias, this outcome was selected as it allowed consideration of the clinical, as well as the radiographic, presentation. An assessment of the postoperative imaging of the scaphoid fracture nonunions by the trainee assessors in each centre which used defined criteria (Dias, 2001) demonstrated 95% agreement with the conclusions of the treating surgical team. Although the trainee assessors were not blinded to the treating surgical team's assessment of union when making their assessments, this instils some confidence in the accuracy of the assessments of union, especially as we included an additional,

"uncertain", category of "union state" for cases where the observers felt unable to categorize the outcome as "united" or "not united" with reasonable certainty. Future prospective studies should be designed to allow longer follow-up or further imaging with CT scans to elucidate the outcome of these cases.

In conclusion this study suggests that the previously published values for union (>80%) after bone grafting of scaphoid fracture nonunions may not reflect the outcome of current practice in the United Kingdom. It supports the hypotheses that both smoking and the time interval between acute fracture and nonunion surgery influence the outcome of bone graft surgery. Both these factors are often beyond the control of the surgeon and will act as confounders during data analysis. Any conclusions regarding the impact of variations of surgical technique on the outcome of bone graft surgery for scaphoid nonunion must be considered unsound, and potentially incorrect, if these factors are not considered. Future studies of the outcome of bone graft surgery for scaphoid fracture nonunion should be prospective to allow complete data collection and sufficiently large to allow for the management of potential confounders such as smoking. They should also report their definitions of a nonunion and union after surgery and have a standardized imaging protocol for assessing union and nonunion. Ideally these definitions and imaging requirements should be standardized for all future studies as previously suggested (Ferguson et al., 2016). Only when the results of such studies are available will we know whether surgical techniques can be modified to improve the outcome of bone graft surgery for scaphoid fracture nonunion.

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Conflict of Interest

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Table 1

Table 1. Summary of patient characteristics**.**

		Total (*n*=462)	Proximal pole (*n*=119)	Waist (*n*=316)	Distal pole (*n*=27)
Mean age (95% CI)		26 (26 to 28)	26 (24 to 27)	26 (25 to 26)	26 (23 to 29)
Sex (%)	Female	33 (7)	5 (4)	24 (8)	4 (15)
	Male	427 (93)	114 (96)	290 (92)	23 (85)
Smoker at the time of surgery (%)	Yes	125 (27)	30 (25)	90 (29)	5 (19)
	No	185 (40)	40 (41)	125 (40)	12 (44)
	Unable to ascertain from notes	152 (33)	41 (34)	101 (32)	12 (44)
Time from acute fracture to nonunion surgery (%)	3-6 months	99 (22)	25 (21)	68 (21)	6 (22)
	6-12 months	135 (29)	40 (34)	91 (29)	4 (15)
	1-2 years	125 (27)	30 (25)	86 (27)	9 (33)

	More than 2 years	103 (22)	24 (20)	71 (23)	8 (30)
Type of bone graft used (%)	None	36 (8)	18 (15)	18 (6)	0 (0)
	Non-vascularized distal radial graft/ulnar graft	136 (29)	36 (30)	89 (28)	11 (41)
	Non-vascularized iliac crest graft	193 (42)	25 (21)	155 (49)	13 (48)
	Vascularized local bone flap (pedicle)	91 (20)	38 (32)	50 (16)	3 (11)
	Free vascularized bone flap	6 (1)	2 (2)	4 (1)	0
Type of fixation (%)	No fixation	4 (1)	0	4 (1)	0
	Kirschner wires	35 (8)	1 (1)	32 (10)	2 (7)
	Cannulated screw	422 (91)	117 (98)	280 (89)	25 (93)
	Non-cannulated screw	1 (0)	1 (1)	0	0
Postoperative follow-	3-6 months	179 (39)	38 (32)	127 (41)	14 (52

up (%)	6-12 months	149 (32)	39 (33)	104 (33)	6 (22)
	1-2 years	91 (20)	27 (23)	58 (18)	6 (22)
	More than 2 years	43 (9)	15 (13)	27 (9)	1 (4)
Union as stated in the medical records, (%)	Not United	104 (22)	32 (27)	65 (21)	7 (26)
	Uncertain	41 (9)	8 (7)	31 (10)	2 (7)
	United	317 (69)	79 (66)	220 (69)	18 (67)
	Radiographs unavailable	1 (0)	1 (0)	0 (0)	0 (0)
Union as assessed by trainee (%)	Not United	114 (25)	36 (23)	72 (25)	6 (22)
	Uncertain	29 (6)	6 (7)	23 (6)	0 (0)
	United	306 (66)	73 (68)	214 (66)	19 (70)
	Radiographs unavailable	13 (3)	4 (2)	7 (3)	2 (7)

Imaging technique used to diagnosis postoperative union	Plain radiographs	331 (72)	83 (70)	288 (72)	20 (74)
	CT scan	120 (26)	32 (27)	82 (26)	6 (22)
	MR scan	6 (1)	3 (3)	3 (1)	0 (0)
	Uncertain	5 (1)	1 (0)	3 (1)	1 (4)

CI: confidence interval; CT: computed tomography; MR: magnetic resonance.

Table 2. Postoperative union and baseline factors (*n*=462).

		Union (*n*=317)	Persistent nonunion (*n*=104)	Uncertain (*n*=41)	*p*-value
Mean age (95% CI)		25 (24 to 26)	27 (26 to 28)	25 (22 to 28)	0.3
Sex (%)	Male	287 (91)	100 (96)	40 (98)	0.13
	Female	28 (9)	4 (4)	1 (2)	
Smoker at the time of surgery (%)	No	134 (43)	39 (38)	12 (29)	0.01
	Unable to tell	106 (34)	24 (23)	17 (42)	
	Yes	73 (23)	40 (39)	12 (29)	
Fracture pattern (%)	Proximal pole	79 (25)	32 (31)	8 (20)	0.6
	Waist	220 (69)	65 (73)	31 (76)	
	Distal pole	18 (6)	7 (7)	2 (5)	
Time from	3-6 months	72 (23)	19 (18)	8 (20)	0.05

acute fracture to nonunion surgery (%)	6-12 months	104 (33)	23 (22)	8 (20)	
	1-2 years	82 (26)	29 (28)	14 (34)	
	>2 years	59 (19)	33 (32)	11 (26)	
Type of bone graft used (%)	No bone graft	23 (7)	9 (9)	4 (10)	
	Non-vascularized distal radius/ulna bone graft	92 (29)	30 (29)	14 (34)	
	Non-vascularized iliac crest bone graft	129 (41)	43 (41)	21 (51)	0.3
	Pedicled (local) vascularized bone flap	69 (22)	20 (19)	2 (5)	
	Free vascularized bone flap	4 (1)	2 (2)	0 (0)	
Type of fixation (%)	None	2 (1)	2 (10)	0 (0)	
	Kirschner wire(s)	24 (8)	7 (7)	4 (10)	0.7
	Screw	291 (92)	95 (91)	37 (90)	
Imaging technique to	Plain radiographs	221 (71)	76 (73)	34 (83)	
	CT	87 (28)	26 (25)	7 (17)	0.4

diagnose	MRI	4 (1)	2 (2)	0 (0)
postoperative union (%)	6-12 months	116 (37)	22 (21)	11 (27)
	1-2 years	61 (19)	28 (27)	2 (5)
	>2 years	19 (6)	22 (21)	2 (5)

CI: confidence interval; CT: computed tomography; MRI: magnetic resonance imaging.

Table 3

Table 3. Risk factors for persistent nonunion after surgery (*n*=462).

		Univariable OR (95% CI)	Adjusted OR (95% CI)	*p*-value*
Age		1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	0.3
Male		2.4 (0.8 to 7.1)	2.3 (0.8 to 7.1)	0.1
Current smoker	No	1 (referent)	1 (referent)	0.01
	Unclear	0.8 (0.4 to 1.4)	0.7 (0.4 to 1.3)	
	Yes	1.9 (1.1 to 3.2)	1.8 (1.0 to 3.1)	
Time from injury to surgery	3-6 months	1 (referent)	1 (referent)	0.01
	6-12 months	0.8 (0.4 to 1.6)	0.9 (0.4 to 1.7)	
	1-2 years	1.3 (0.7 to 2.6)	1.4 (0.7 to 2.8)	
	>2 years	2.1 (1.1 to 4.1)	2.4 (1.2 to 4.8)	
Fracture location	Distal pole	1 (referent)	1 (referent)	0.3
	Waist	0.8 (0.3 to 1.9)	0.7 (0.3 to 1.9)	
	Proximal pole	1.0 (0.4 to 2.7)	1.1 (0.4 to 3.0)	
Fixation	Screw	1 (referent)	1 (referent)	0.4
	Kirschner Wires	0.9 (0.4 to 2.1)	0.8 (0.3 to 2.1)	
	None	3.0 (0.4 to 22)	4.0 (0.5 to 31)	

*Derived from multivariable logistic regression. CI: confidence interval; OR: odds ratio.

Dear Editor,

All the authors have approved the final contents of the submission, been actively involved in the planning and enactment of the study, and have also assisted with the preparation of the submitted article. The article has not been submitted elsewhere. The references have been checked and are correct. The authors have read the Submission Guidelines and the paper conforms to this Guide in all respects.

We, the authors of this submission confirm that we have not published the same or a very similar study with the same or very similar results and major conclusions in any other journals. These include English or non-English language journals and journals that are indexed or not indexed in PubMed, regardless of different words being used in the article titles, introduction and discussion. The authors of this submission understand that dual submission refers to publication in any language and that dual submission will result in academic sanctions which will include the blocking of all authors to prevent their future submissions to the JHS-E.

Yours sincerely,

Professor Tim Davis

Dear Geoff,

I have been through this all. I was uncertain about some of your bracketing and have left comments to highlight this. Also I have made a few tweaks in tracked changes.

I hope this is OK

BW

Tim

Title Page

Title

The outcome of bone graft surgery for nonunion of fractures of the scaphoid

Authors

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