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FACTORS ASSOCIATED WITH PATIENT-REPORTED OUTCOMES FOLLOWING A HUMERAL SHAFT FRACTURE: NONUNION RESULTS IN A POORER OUTCOME DESPITE UNION AFTER SURGICAL FIXATION

William M. Oliver, LLB(Hons), MBBS(Hons), MRCSEd – william.m.oliver@doctors.org.uk

Henry K. C. Searle, MBChB – henry.searle@doctors.org.uk

Samuel G. Molyneux, MSc, FRCSEd(Tr&Orth) – sgmolyneux@gmail.com

Timothy O. White, MD, FRCSEd(Tr&Orth) – twhite@rcsed.ac.uk

Nicholas D. Clement, FRCSEd(Tr&Orth), PhD – nickclement@doctors.org.uk

Andrew D. Duckworth, MSc, FRCSEd(Tr&Orth), PhD – andrew.duckworth@ed.ac.uk

All authors affiliated with:

Edinburgh Orthopaedics – Trauma, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, Midlothian, EH16 4SA, UK

ADD also affiliated with: Centre for Population Health Sciences, Usher Institute, University of Edinburgh, 49 Little France Crescent, EH16 4SB, UK

Corresponding author:

William M. Oliver, Orthopaedic Trauma Research Fellow

Address: Edinburgh Orthopaedics – Trauma, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, Midlothian, EH16 4SA, UK

Email: william.m.oliver@doctors.org.uk

Telephone: +44 131 242 3459

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ABSTRACT

Objectives: The primary aim was to assess patient-reported outcomes ≥1yr following a humeral diaphyseal fracture. The secondary aim was to compare outcomes of patients who united after initial management (operative/non-operative) with those who united after nonunion fixation (NU-ORIF).

Design: Retrospective.

Setting: University teaching hospital.

Patients and intervention: From 2008-2017, 291 patients (mean age 55yrs [17-86], 58% [n=168/291] female) were available to complete an outcomes survey. Sixty-four (22%) were initially managed operatively and 227 (78%) non-operatively. After initial management, 227 (78%) united (n=62 operative, n=165 non-operative), two had a delayed union (both non-operative) and 62 (21%) a nonunion (n=2 operative, n=60 non-operative). Fifty-two patients (93%, n=52/56) united after NU-ORIF.

Main outcome measurements: QuickDASH, EuroQol-5 Dimension (EQ-5D)/Visual Analogue Scale (EQ-VAS), 12-item Short Form Physical (PCS) and Mental Component Summary (MCS).

Results: At a mean of 5.5yrs (1.2-11.0) post-injury, the mean QuickDASH was 20.8, EQ-5D 0.730, EQ-VAS 74, PCS 44.8 and MCS 50.2. Patients who united after NU-ORIF reported worse function (QuickDASH 27.9 vs. 17.6, p=0.003) and health-related quality of life (HRQoL; EQ-5D 0.639 vs. 0.766, p=0.008; EQ-VAS 66 vs. 76, p=0.036; PCS 41.8 vs. 46.1, p=0.036) than those who united primarily. Adjusting for confounders, union after NU-ORIF was independently associated with a poorer QuickDASH (difference 8.1, p=0.019) and EQ-5D (difference -0.102, p=0.028).

Conclusions: Humeral diaphyseal union after NU-ORIF resulted in poorer patient-reported outcomes compared to union after initial management. Targeting early operative intervention to at-risk patients may mitigate the potential impact of nonunion on longer-term outcome.

Level of evidence: III – Case-control study.

Word count 250/250

Keywords: Humerus; diaphysis; shaft; fracture; long-term; patient-reported outcomes; nonunion

INTRODUCTION

Humeral diaphyseal fractures constitute one percent of adult fractures[1], with an annual incidence of 12 per 100,000[2]. Non-operative management using a functional brace[3] remains the default position in many centres, with historic union rates reported between 87% and 98%[4–10] and minimal impairment of shoulder and elbow function[5,8,11]. Although recent studies have suggested union rates between 67% and 83% following non-operative management[12–15], surgical fixation remains an effective option for nonunion[16].

Existing studies reporting functional outcomes after non-operatively managed humeral shaft fractures are heterogeneous[6,8,10,11], but excellent results may only occur in around half of patients[17]. Studies presenting validated patient-reported outcomes after a humeral diaphyseal fracture either involve fewer than 100 patients[10,15,18,19], or do not extend beyond 12 months post-injury[15,18,20]. Longer-term patient-reported outcomes after a humeral diaphyseal fracture and the legacy of humeral shaft nonunion surgery are incompletely understood. The authors are aware of only two smaller studies assessing factors associated with functional outcome[18,19], and neither examines the effect of nonunion in the longer-term.

The primary aim of this study was to assess patient-reported outcomes at a minimum of one year following a humeral diaphyseal fracture. The secondary aim was to compare the outcomes of patients who united after initial management (operative or non-operative) with those who united after nonunion surgery.

MATERIALS AND METHODS

Study cohort

Patients were retrospectively identified from an established trauma database held at the study centre[2]. After applying our inclusion and exclusion criteria, 749 patients were potentially eligible for follow-up (**Figure 1**). Of these, 235 patients were unavailable due to death (n=158), incapacity (n=42) or having no valid contact details (n=35). Ten further patients had incomplete radiographic follow-up and were therefore omitted. The remaining 504 patients were sent an outcomes survey by post. Nineteen patients declined to complete the survey and 194 failed to respond. The study cohort comprised 291 patients who completed the survey; the rate of survey completion was 58% (n=291/504). With the exception of body mass index (BMI), social deprivation and mechanism of injury, no differences were observed in patient or injury characteristics between the study cohort and those who were unavailable or lost to follow-up (**Table 1**). The study was assessed by the NHS Research Ethics Service (NR/161AB6) and registered with the local musculoskeletal quality improvement committee.

Patient and injury characteristics

Patient demographics and injury details were determined from medical records and radiographs. A fall from height was defined as any height greater than six feet[21]. Fractures were classified based upon location within the humeral diaphysis (proximal, middle or distal) and according to the *Arbeitsgemeinschaft für Osteosynthesefragen*-Orthopaedic Trauma Association (AO-OTA) classification[22]. Open injuries were classified using the Gustilo and Anderson classification[23].

Management

Of the study cohort, 22% (n=64/291) were initially managed operatively (within 12 weeks of injury) and 78% (n=227/291) were managed non-operatively. Over the 10-year study period, treatment was determined by 13 consultant orthopaedic trauma surgeons. Seven had level III expertise (experienced), four had level IV expertise (highly experienced) and two had level V expertise (expert)[24]. Indications for operative management were patient preference (47%, n=30/64), polytrauma (13%, n=8/64), loss of closed reduction (8%, n=5/64), open fracture (6%, n=4/64), progressive radial nerve deficit (6%, n=4/64), involvement in an *in vivo* research study of an intramedullary implant (5%, n=3/64) and delayed progression to union after six weeks of non-operative management (16%, n=10/64). Mean time from injury to primary fixation was 16 days (range 0 to 83). The method of surgical fixation was at the treating surgeon's discretion and involved either open reduction and internal fixation (92%, n=59/64) or intramedullary nailing (8%, n=5/64). Similarly, the postoperative treatment protocol was at the treating surgeon's discretion, but generally consisted of a short period of rest in a sling with early shoulder and elbow range of motion encouraged thereafter.

Standard non-operative management involved application of a plaster of Paris 'U-slab' in the Emergency Department, which was replaced by a functional brace in the fracture clinic. The timing of conversion to a brace was at the treating surgeon's discretion, but study centre protocol is that this normally occurs within the first two weeks following injury. Pendular shoulder exercises and range of motion exercises at the elbow, wrist and hand were commenced immediately after brace application. Physiotherapy was not used routinely, but referral was made in select cases at the treating surgeon's discretion and/or patient preference.

Complications and radiographic outcomes

All patients were followed-up in the outpatient clinic until fracture union. Any documented treatment-related complications were recorded. Radiographic follow-up was through review of medical records and radiographs. Union was defined clinically as reduced/absent pain at the fracture site, and radiographically as bridging callus across all fracture cortices/obliteration of all cortical fracture lines, prior to clinic discharge[25,26]. Nonunion was defined as a failure of the fracture to unite within six months of non-operative treatment[20,27] and/or where the treating surgeon considered that nonunion surgery was required beyond 12 weeks post-injury[12,15]. Both definitions are recognised within the literature. Delayed union was defined as radiographic union occurring spontaneously after more than six months of non-operative management and without further intervention.

Final coronal and sagittal angulation were measured on the most recent orthogonal radiographs for all patients who achieved eventual union. Malunion was defined as a coronal plane deformity $\geq 30^{\circ}$ or sagittal plane deformity $\geq 20^{\circ}$[28]. Radiographic alignment was not assessed for patients with residual nonunion at final follow-up.

Patient-reported outcomes

Longer-term patient-reported outcomes were obtained via a postal survey. The primary outcome measure was the abbreviated Disabilities of the Arm, Shoulder and Hand score (QuickDASH)[29] which has been validated for the assessment of upper limb function following an upper extremity fracture[30]. Secondary outcome measures included indicators of health-related quality of life (HRQoL) – the EuroQol Five-Dimension Three-Level Health Outcome score (EQ-5D) and Visual Analogue Scale (EQ-VAS)[31], and the 12-item Short Form Health Survey score (SF-12)[32] – pain and satisfaction with treatment. The SF-12 consists of a physical (PCS) and mental component summary score (MCS), which were reported separately[32].

Patients were asked to rate the severity of pain at their previous fracture site (none, mild, moderate, severe). The survey also stated 'A normal arm, that allows you to carry out all functions such as washing, lifting, carrying, dressing, brushing your hair, and reaching behind your back, is considered 100% function' – patients were then asked to respond to the question 'What percentage of normal has your arm been over the past week?' by entering a number from 0 to 100. Finally, patients were asked to indicate overall satisfaction with their treatment outcome on a five-point scale (very satisfied, satisfied, neutral, dissatisfied, very dissatisfied).

Statistical analysis

Odds ratios (OR) were calculated for contingency tables. The relationship between categorical variables was assessed using a chi-squared test (CS) or Fisher exact test (FE, where the value of any cell was <5). The relationship between continuous non-parametric data was assessed using the Mann-Whitney U test (MWU) for two groups and the Kruskal-Wallis test for three or more groups. Significance was set at $p<0.05$, 95% confidence intervals (CIs) and two-tailed p-values were reported. A multiple regression model was used to assess the independent influence of multiple factors upon the QuickDASH and EQ-5D.

RESULTS

Patient and injury characteristics

The mean age at injury was 55 years (range 17 to 86) and 58% (n=168/291) were female (**Table 1**). Two-thirds of patients (68%, n=197/291) had documented medical comorbidities. A fall from standing was the most common injury mechanism (73%, n=211/291). Middle-third diaphyseal fractures were most common (49%, n=144/291), followed by proximal- (30%, n=86/291) and distal-third (21%, n=61/291). Sixty-three percent (n=183/291) were AO-OTA type A fractures, 35% (n=102/291) type B and 2% (n=6/291) type C. Four patients (1.4%) sustained an open fracture and associated injuries were documented in 22% (n=63/291).

Sixteen patients (6%) had a concomitant radial nerve palsy at presentation, of which four were progressive and underwent surgical exploration alongside fracture fixation; the radial nerve was intact in all cases. Fifteen patients (94%) recovered spontaneously at a mean of 30 weeks post-injury (range 0.1 to 73.6). The remaining patient, whose radial nerve was not explored surgically, had not recovered at the time of clinic discharge (16 weeks post-injury); the patient sought a private referral to the regional peripheral nerve injuries unit and the final outcome was unknown.

Complications and radiographic outcomes

Mean outpatient clinic follow-up was 8.2 months (range 1.4 to 73.5). Overall, 18% (n=51/291) of the study cohort developed at least one treatment-related complication. These included radial nerve palsy (2%, n=5/291), brace-related skin breakdown (11%, n=32/291) and superficial infection (4%, n=13/291). Specific operative complications included radial nerve palsy (2%, n=1/64), deep infection (2%, n=1/64) and fixation failure (3%, n=2/64).

After initial management, 78% (n=227/291; n=62 operative, n=165 non-operative) of patients united and 21% (n=62/291; n=2 operative, n=60 non-operative) developed a nonunion

(**Figure 2**). Eight percent of patients (n=24/291) required a CT scan to confirm fracture union: 5% (n=3/64) of those treated operatively and 9% (n=21/227) of those treated non-operatively (p=0.310, FE). Two patients, both managed non-operatively throughout, had a delayed union at seven months and 15 months post-injury. Both were excluded from subsequent comparisons of union and nonunion. Of the 62 patients with a nonunion, six opted for no further treatment and 56 underwent surgery at a mean of 34 weeks post injury (range 12.4 to 93.6), comprising 3% (n=2/64) of the operative group and 24% (n=54/227) of the non-operative group. Fifty-two of these 56 patients (93%) united after nonunion surgery, with four having a persistent nonunion. The remaining 10 patients (3%) had a residual nonunion at final study follow-up.

For patients who achieved eventual union (97%, n=281/291), final mean coronal angulation was 6° varus (95% CI 7° to 5° varus, range 45° varus to 15° valgus) and the median sagittal angulation was 3° procurvatum/apex-anterior (95% CI 3° to 2° procurvatum, range 31° procurvatum to 13° recurvatum/apex-posterior). One patient had a varus malunion and seven (2%) had a malunion in procurvatum. Although operative fixation (either primary or nonunion surgery) resulted in less angular deformity than non-operative management, there was no difference in malunion rate (**Table 2**).

Patient-reported outcomes

Mean survey follow-up was 5.5 years (range 1.2 to 11.0). The overall mean QuickDASH was 20.8 (95% CI 18.3 to 23.3, range 0 to 95). The mean EQ-5D was 0.730 (95% CI 0.697 to 0.764, range -0.540 to 1) and EQ-VAS 74 (95% CI 72 to 76, range 10 to 100). The mean SF-12 PCS was 44.8 (95% CI 43.4 to 46.1, range 16 to 63.4) and MCS 50.2 (95% CI 49.1 to 51.4, range 16.6 to 67.7).

Forty-nine percent of patients (n=144/291) reported some degree of pain during normal activity; 30% (n=87/291) mild, 16% (n=46/291) moderate and 4% (n=11/291) severe. Patients rated their arm as 82% of normal (95% CI 80% to 85%, range 0% to 100%), and 82% (n=239/291) were satisfied or highly satisfied with their outcome.

Union after initial management versus *union after nonunion surgery*

Compared with patients who united after initial operative or non-operative management, patients who united after nonunion surgery reported poorer upper limb function (mean QuickDASH 27.9 vs. 17.6; p=0.003, MWU) and HRQoL (mean EQ-5D 0.639 vs. 0.766, p=0.008; mean EQ-VAS 66 vs. 76, p=0.036; mean SF-12 PCS 41.8 vs. 46.1, p=0.036, all MWU; **Table 3** and **Figure 3**). Union after nonunion surgery was also associated with increased pain (**Figure 4**) and increased dissatisfaction with outcome (31% vs. 13%; p=0.002, CS). Compared with union after initial management, multiple regression indicated that union after nonunion surgery was independently associated with an 8.1-point reduction in QuickDASH (beta = 8.123, 95% CI 1.342 to 14.904; p=0.019; **Table 4)** and a 0.109-point reduction in EQ-5D (beta = -0.109, 95% CI -0.192 to -0.011; p=0.028; **Table 5**).

Other findings

Radiographic alignment and malunion were not associated with functional outcome (**Table 6**). Other factors independently associated with a poorer QuickDASH on multiple regression were the presence of an associated injury (p=0.010), alcohol abstinence (p=0.037) and being unemployed/retired (p=0.006; **Table 4)**. Other factors independently associated with a poorer EQ-5D were being unemployed/retired (p=0.002) and not being involved in sport at final follow-up (p=0.001; **Table 5**).

DISCUSSION

This study of patient-reported outcomes at a minimum of one year (mean five years) following a humeral shaft fracture demonstrated that overall upper limb function and HRQoL were comparable to the general population. However, patients uniting after nonunion surgery had worse upper limb function and HRQoL when compared to those uniting after primary operative or non-operative management. This challenges the suggestion that union after nonunion surgery results in equivalent outcomes to initial union. The potential longer-term sequelae of nonunion, even when union is subsequently achieved following nonunion surgery, highlight the importance of achieving union with primary management. An approach whereby early operative fixation is targeted to those most at risk of nonunion may confer longer-term benefits to patients.

The average QuickDASH for the study cohort was consistent with published values for similar populations in the United States[33] and Europe[34], and the mean EQ-5D and EQ-VAS for the cohort were similar to other age-matched populations[35]. The SF-12 PCS and MCS were also commensurate with the presumed average score of 50 in the general population[36]. Moreover, we observed no significant differences in patient-reported outcomes between patients who achieved union after either primary operative or non-operative management. These findings support the view that, irrespective of whether patients are treated operatively or non-operatively[6,8,10,11,18,19], as long as their initial management results in union most can expect to achieve satisfactory upper limb function and HRQoL in the longer-term.

Non-operative management remains the default position in many centres, despite the increased risk of nonunion compared to operative fixation[13,20,37–39]. One possible explanation is that undergoing successful nonunion surgery after failed non-operative management is felt to result in an outcome equivalent to that of patients who achieve initial union. During two-year follow-up of 49 patients managed non-operatively, Ekholm *et al.*[10] identified a trend towards inferior everyday function in patients who united after nonunion surgery compared with those who united primarily. Broadbent *et al.*[18] also observed humeral diaphyseal nonunion was associated with a worse Neer score up to one-year post-injury. Our results add to this growing body of evidence that poorer function and HRQoL may persist for years following a humeral shaft nonunion. Surgeons should counsel patients on the potential benefits and risks of non-operative management, being mindful of the risk factors associated with developing a nonunion, and the longer-term functional implications even if union nonunion surgery is successful.

The reason why nonunion should impair longer-term outcomes, even when union is achieved following nonunion surgery, is difficult to elucidate and likely multifactorial. In this study, patients uniting after nonunion surgery reported increased levels of pain and dissatisfaction than those achieving primary union. One explanation may be that nonunion has an impact on the mental health of patients, which has been reported in fractures of the femur[40] and tibia[41], and that this emotional setback manifests as longer-term functional impairment. Depression, catastrophic thinking, anxiety and emotional attitudes to pain have been identified as factors most strongly associated with disability after upper extremity injuries, and may be more important than patient and injury characteristics or objective measures such as range of motion[42]. Pre-existing psychiatric illness has been identified as a risk factor for poor functional outcome following humeral shaft fracture[19]. However, in the present study there was no difference in the SF-12 MCS between patients who united after primary management and those who developed nonunion requiring fixation.

Unlike some other upper limb fractures, such as the lateral clavicle[43], olecranon[44] or proximal radius[45], humeral diaphyseal nonunion is almost universally symptomatic and thus more likely to require intervention. The fact that a quarter of patients may develop nonunion following a non-operatively managed humeral shaft fracture[13,46], and that long-term functional outcome may be impaired even if union is subsequently achieved, emphasise the importance of achieving union with initial management. Surgical fixation is associated with a lower rate of nonunion, although offering fixation to all patients in order to reduce nonunion risk would likely represent over-treatment[38]. A targeted approach, in which early fixation is selectively offered to 'at-risk' patients with known clinical[18,47,48] or radiographic[49,50] risk factors for nonunion, may be the most appropriate strategy.

In keeping with previous studies[18,51], we did not identify a relationship between humeral shaft malunion and functional outcome. However, the presence of an associated injury, alcohol abstinence, not being in employment and not participating in sport at longer-term follow-up were found to impair outcomes. Shields *et al.*[19] found that associated injuries did not influence upper limb function or HRQoL at a mean of four years following humeral shaft fracture. Moderate alcohol consumption may have beneficial effects upon pain[52] and psychological wellbeing[53], thereby improving self-reported functional outcome and HRQoL. The benefits of employment upon upper limb function[54–56] and quality of life[57] are recognised, but returning to work after a humeral shaft fracture may be both a cause and a consequence of improved patient-reported outcomes. Similarly, sports participation appears to be a significant contributor to HRQoL[58]. The factors underpinning these phenomena are beyond the scope of this study but an interesting avenue for future research.

The primary limitation was the loss to follow-up (42% of the 'available' cohort, n=213/504), despite multiple attempts to contact every patient by post and over the telephone. However, to the best of the authors' knowledge, this series is the largest in the literature documenting outcomes beyond one year after humeral shaft fracture, and the baseline patient and injury characteristics of the study cohort (n=291) were representative of the cohort as a whole. Second, although final humeral angulation was retrospectively assessed using the most recent AP and lateral radiographs available, it was not possible to standardise X-ray projections. This introduces the potential for measurement error. Third, although union after nonunion surgery was found to impair functional outcome, we acknowledge the difference in the QuickDASH was lower than the published minimal clinically-important difference[59] and thus the clinical significance of this finding is uncertain. Finally, we attempted to control for confounding variables in our regression analysis but recognise the possibility of residual confounding. We also acknowledge there was a spectrum of follow-up length, although we did not find any relationship between follow-up length and outcome.

CONCLUSIONS

At a minimum of one year following a humeral diaphyseal fracture, patient-reported upper limb function and HRQoL were satisfactory and comparable to the general population. Nonunion appears to impair patient-reported outcomes, even when union is achieved after surgical fixation. Achieving union with initial management, irrespective of the treatment method, may benefit patients for years after their injury. Targeting early fixation to patients at risk of nonunion may have an important role.

Word count 3,084

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TABLES

Table 1: Baseline patient and injury characteristics for the study cohort *versus* unavailable or lost to follow-up (LTFU)

	Study cohort (n=291)	**Unavailable/LTFU (n=458)**	**p-value (test)**
Sex (n, %)			
Male	123, 42.3%	217, 47.4%	.171 (CS)
Female	168, 57.7%	241, 52.6%	
Age at injury (years)			
Mean ± SD	55.7 ± 16.7	55.6 ± 22.1	.794 (MWU)
95% CI	53.8 to 57.6	53.5 to 57.6	
Median (IQR)	57.6 (45.3 to 68.4)	57.6 (35.0 to 74.4)	
Comorbidities (n, %)			
None	94, 32.3%	125, 27.3%	.142 (CS)
≥1	197, 67.7%	333, 72.7%	
BMI (kg/m^2)			
Mean ± SD	28.7 ± 6.9	27.2 ± 6.6	**.007* (MWU)**
95% CI	27.8 to 29.6	26.4 to 27.9	
Median (IQR)	27.4 (24.5 to 32.1)	26.2 (22.6 to 30.7)	
SIMD quintile (n, %)			
1 (most deprived)	32, 11.0%	75, 16.4%	**.005* (CS)**
2	57, 19.6%	118, 25.8%	
3	57, 19.6%	83, 18.1%	
4	50, 17.2%	82, 17.9%	
5 (least deprived)	95, 32.6%	100, 21.8%	
Injury mechanism (n, %)			
Fall from standing	211, 72.5%	326, 71.2%	**.032* (CS)**
Fall from height	11, 3.8%	16, 3.5%	
Sport	33, 11.3%	32, 7.0%	
Road traffic accident	16, 5.5%	28, 6.1%	
Other	16, 5.5%	53, 11.6%	
Unknown	4, 1.4%	3, 0.7%	
Injury energy (n, %)			
Low	252, 86.6%	410, 89.5%	.324 (CS)
High	35, 12.0%	45, 9.8%	
Unknown	4, 1.4%	3, 0.7%	
Side of injury (n, %)			
Right	141, 48.5%	220, 48.0%	.528 (CS)
Left	150, 51.5%	236, 51.5%	
Bilateral	0	2, 0.4%	
Fracture location (n, %)			
Proximal	86, 29.6%	126, 27.5%	.598 (CS)
Middle	144, 49.5%	222, 48.5%	
Distal	61, 21.0%	110, 24.0%	

AO-OTA type (n, %)				
	A	183, 62.9%	300, 65.5%	.202 (CS)
	B	102, 35.1%	155, 33.8%	
	C	6, 2.1%	3, 0.7%	
AO-OTA group (n, %)				
	A1	121, 41.6%	184, 40.2%	.334 (CS)
	A2	16, 5.5%	34, 7.4%	
	A3	45, 15.5%	82, 17.9%	
	B2	87, 29.9%	131, 28.6%	
	B3	16, 5.5%	24, 5.2%	
	C2	3, 1.0%	3, 0.7%	
	C3	3, 1.0%	0	
Open fracture (n, %)				
	No	287, 98.6%	444, 96.9%	.220 (FE)
	Yes	4, 1.4%	14, 3.1%	
Radial nerve palsy (n, %)				
	No	275, 94.5%	423, 92.4%	.256 (CS)
	Yes	16, 5.5%	35, 7.6%	
Associated injury (n, %)				
	No	226, 77.7%	342, 74.7%	.271 (CS)
	Yes	63, 21.6%	116, 25.3%	
	Unknown	2, 0.7%	0	
Associated injury, minor (n, %)				
	No	16, 25.4%	31, 26.7%	.847 (CS)
	Yes	47, 74.6%	85, 73.3%	
Associated injury, major (n, %)				
	No	37, 58.7%	70, 60.3%	.833 (CS)
	Yes	26, 41.3%	46, 39.7%	

AO-OTA, *Arbeitsgemeinschaft für Osteosynthesefragen*-Orthopaedic Trauma Association; BMI, body mass index; CI, confidence interval; CS, chi-squared test; FE, Fisher exact test; IQR, interquartile range; MWU, Mann-Whitney 'U' test; SD, standard deviation; SIMD, Scottish Index of Multiple Deprivation; ***significant at the p<0.05 level**

NB. The Scottish Index of Multiple Deprivation (SIMD) is a measure of socioeconomic deprivation, assessed according to the patient's postcode at the time of injury[60].

NB. Associated minor injuries included uncomplicated head injuries, simple soft tissue injuries (contusions, lacerations, abrasions, incised wounds with no underlying structural injury) and ligament sprains; associated major injuries included other skeletal fractures or dislocations, soft tissue injuries with underlying neurovascular or tendon damage or any solid organ injury.

Table 2: Final angulation and malunion for operative management (initial/nonunion surgery) *versus* non-operative management (primary/delayed union)

	Operative (n=114)	**Non-operative (n=167)**	**p-value (test)**
Coronal angulation (degrees)			
Mean ± SD	1.5º varus ± 4.8º	9.1º varus ± 7.9º	**<.001* (MWU)**
95% CI	2.4º to 0.6º varus	10.3º to 7.9º varus	
Median (IQR)	0º (4.2º varus to 0º)	9º varus (14º to 4º varus)	
Sagittal angulation (degrees)			
Mean ± SD	1.0º pro ± 4.9º	3.8º pro ± 7.0º	**<.001* (MWU)**
95% CI	1.9º to 0.1º pro	4.9º to 2.7º pro	
Median (IQR)	0º (1.2º pro to 0º)	4º pro (8º pro to 0º)	
Varus malunion (n, %)			
No	114, 100%	166, 99.4%	1 (FE)
Yes	0	1, 0.6%	
Procurvatum malunion (n, %)			
No	112, 98.2%	162, 97.0%	.705 (FE)
Yes	2, 1.8%	5, 3.0%	

CI, confidence interval; FE, Fisher exact test; IQR, interquartile range; MWU, Mann-Whitney 'U' test; pro, procurvatum; rec, recurvatum; SD, standard deviation; ***significant at the p<0.05 level**

Table 3: Relationship between union outcome and patient-reported outcomes following a humeral diaphyseal fracture (n=289)

	Union after initial operative management (n=62)	**Union after initial non-operative management (n=165)**	**Union after nonunion surgery (n=52)**	**Any management, residual nonunion (n=10)**	**p-value (test)**
QuickDASH					
Mean ± SD	19.0 ± 19.6	17.0 ± 18.8	27.9 ± 24.5	48.4 ± 27.5	**<.001***
95% CI	14.1 to 24.0	14.1 to 19.9	21.1 to 34.7	28.7 to 68.1	**(KW)**
Median (IQR)	11.4 (6.8 to 27.8)	9.1 (2.3 to 26.1)	22.7 (6.8 to 47.7)	51.1 (25.6 to 65.9)	
EQ-5D					
Mean ± SD	0.764 ± 0.252	0.767 ± 0.265	0.639 ± 0.337	0.507 ± 0.369	**.004***
95% CI	0.700 to 0.828	0.726 to 0.808	0.545 to 0.733	0.243 to 0.771	**(KW)**
Median (IQR)	0.796 (0.691 to 1)	0.796 (0.691 to 1)	0.735 (0.533 to 0.848)	0.674 (0.109 to 0.735)	
EQ-VAS					
Mean ± SD	76 ± 18	76 ± 17	67 ± 26	68 ± 17	.078
95% CI	71 to 81	74 to 79	59 to 74	56 to 80	(KW)
Median (IQR)	80 (64 to 90)	80 (68 to 90)	80 (46 to 85)	70 (58 to 80)	
SF-12 PCS					
Mean ± SD	46.2 ± 11.0	46.0 ± 11.3	41.8 ± 13.0	33.8 ± 9.7	**.004***
95% CI	43.4 to 49.0	44.3 to 47.8	38.2 to 45.4	26.9 to 40.8	**(KW)**
Median (IQR)	51.4 (40.3 to 55.1)	50.0 (37.3 to 55.4)	44.7 (30.4 to 54.3)	33.0 (28.4 to 39.4)	
SF-12 MCS					
Mean ± SD	51.7 ± 9.9	50.4 ± 9.2	48.5 ± 11.2	49.5 ± 13.4	.238
95% CI	49.2 to 54.2	49.0 to 51.9	45.4-51.6	40.0 to 59.1	(KW)
Median (IQR)	55.1 (48.2 to 57.8)	52.5 (45.5 to 57.8)	52.6 (42.5 to 56.0)	53.6 (40.3 to 59.1)	

CI, confidence interval; EQ-5D, EuroQol Health Outcome score; EQ-VAS, EuroQol Visual Analogue Scale; IQR, interquartile range; MCS, mental component summary; MWU, Mann-Whitney 'U' test; PCS, physical component summary; QuickDASH, abbreviated Disabilities of the Arm, Shoulder and Hand score; SD, standard deviation; SF-12, 12-item Short Form Health Survey score; ***significant at the p<0.05 level**

Table 4: Multiple regression model for predictors of functional outcome (QuickDASH) following humeral diaphyseal fracture (R^2=0.278, adjusted R^2=0.161; p<0.001)

Predictors in the model			**95% CI**		
		B	**Lower**	**Upper**	**p-value**
Associated injury					
	No	Ref			
	Yes	8.977	2.203	15.750	**.010***
Union type					
	After initial management	Ref			
	After nonunion surgery	8.123	1.342	14.904	**.019***
Current alcohol intake					
	Teetotal	6.919	.419	13.419	**.037***
	Social				
	Moderate	5.087	-1.645	11.818	.138
	Excess	-8.164	-35.088	18.760	.550
Current employment status					
	Employed	Ref			
	Unemployed/retired	9.178	2.635	15.721	**.006***

B, regression coefficient; CI, confidence interval; ***significant at the p<0.05 level**

NB. The following variables were entered into the model: Patient sex; age at injury (yrs); medical comorbidities; body mass index classification; Scottish Index of Multiple Deprivation quintile; injury energy; closed/open injury; injury side (dominant/non-dominant); fracture location; AO-OTA classification; radial nerve palsy; associated injuries; primary management; complications; union type, excluding delayed union (n=2) and residual nonunion (n=10); malunion; length of follow-up (yrs); current smoking status; current alcohol intake; current employment status; current sports participation

Table 5: Multiple regression model for predictors of health-related quality of life (EQ-5D) following humeral diaphyseal fracture (R^2=0.290, adjusted R^2=0.175; p<0.001). All variables were entered into the model; data for variables significantly associated with EQ-5D are presented

Predictors in the model	**B**	**95% CI Lower**	**95% CI Upper**	**p-value**
Union type				
After initial management	Ref			
After nonunion surgery	-0.102	-0.192	-0.011	**.028***
Current employment status				
Employed	Ref			
Unemployed/retired	-0.140	-0.227	-0.052	**.002***
Current sports participation				
Plays sport	Ref			
Does not play sport	-0.143	-0.223	-0.063	**.001***

B, regression coefficient; CI, confidence interval; ***significant at the p<0.05 level**

NB. The following variables were entered into the model: Patient sex; age at injury (yrs); medical comorbidities; body mass index classification; Scottish Index of Multiple Deprivation quintile; injury energy; closed/open injury; injury side (dominant/non-dominant); fracture location; AO-OTA classification; radial nerve palsy; associated injuries; primary management; complications; union type, excluding delayed union (n=2) and residual nonunion (n=10); malunion; length of follow-up (yrs); current smoking status; current alcohol intake; current employment status; current sports participation

Table 6: Influence of radiographic alignment upon upper limb function (QuickDASH) following humeral diaphyseal fracture (n=281)

	Median QuickDASH (IQR)	**p-value (test)**
Coronal alignment		
Varus (n=197)	11.4 (2.3 to 27.4)	.281 (MWU)
Anatomical (n=49) – reference	11.4 (5.7 to 28.4)	
Valgus (n=35)	18.2 (9.1 to 45.5)	.221 (MWU)
Sagittal alignment		
Procurvatum (n=142)	11.4 (4.5 to 31.8)	.714 (MWU)
Anatomical (n=80) – reference	11.4 (2.3 to 27.3)	
Recurvatum (n=59)	18.2 (2.3 to 31.8)	.518 (MWU)
Malunion		
No (n=274)	11.4 (2.3 to 29.5)	.245 (MWU)
Yes (n=7)	13.6 (11.4 to 40.9)	

IQR, interquartile range; MWU, Mann-Whitney 'U' test; QuickDASH, abbreviated Disabilities of the Arm, Shoulder and Hand score

FIGURES

Figure 1: Identification of the study cohort

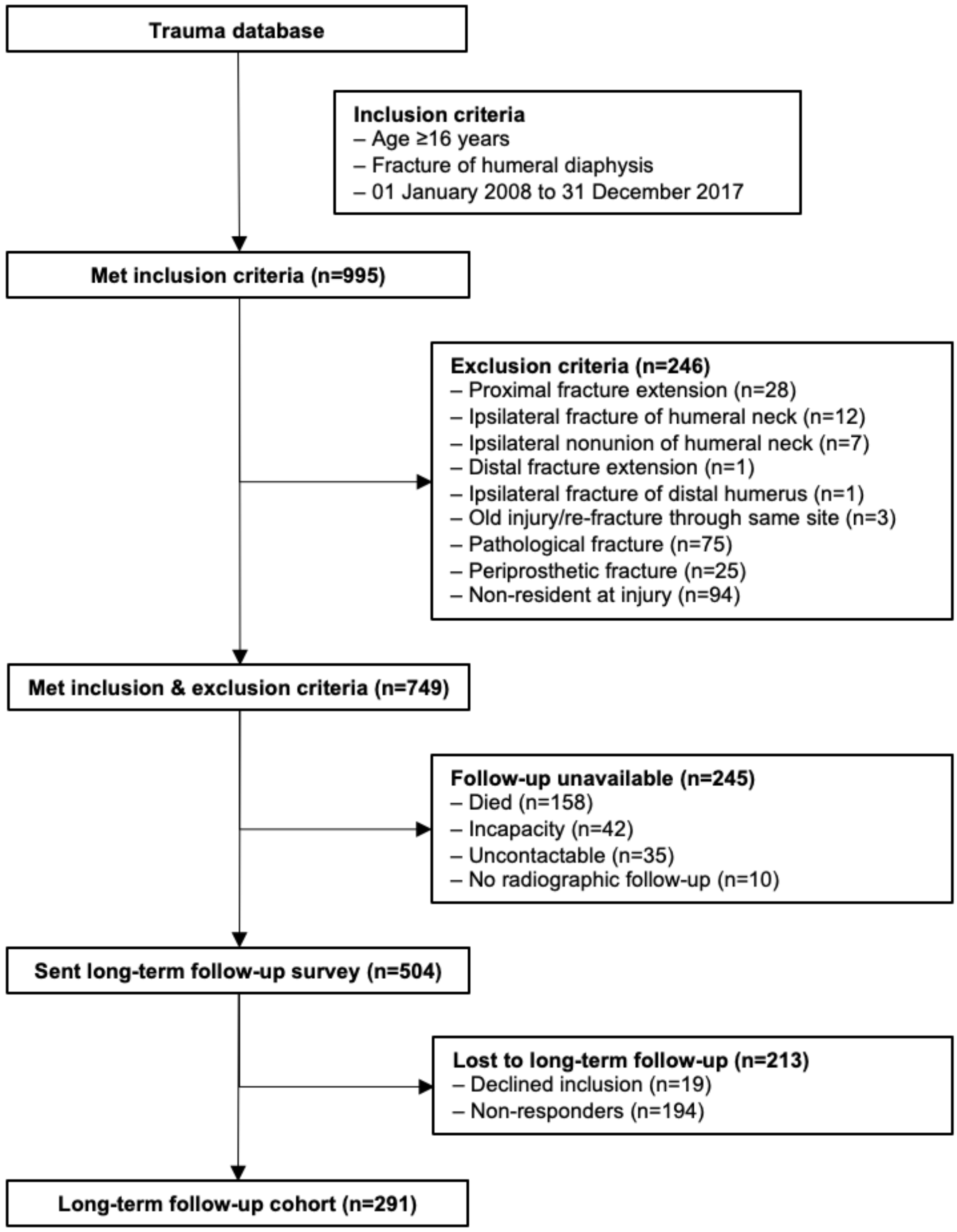

Figure 2: Overview of management and union outcome for the study cohort

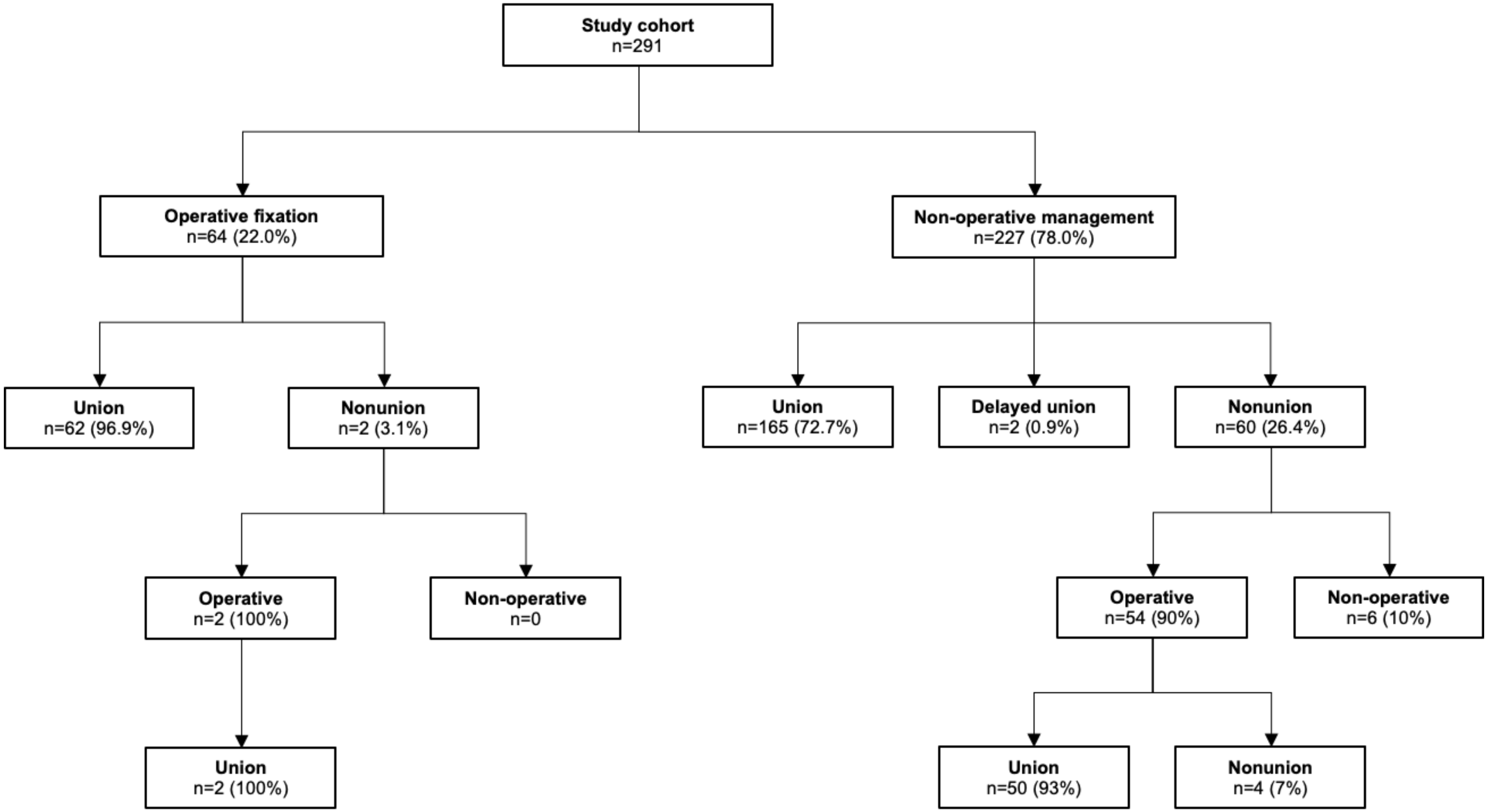

Figure 3: Patient-reported outcomes following a humeral diaphyseal fracture, comparing union after initial management (operative or non-operative) and union after nonunion surgery; A, QuickDASH; B, EQ-5D; C, EQ-VAS; D, SF-12 PCS; E, SF-12 MCS; MWU, Mann-Whitney 'U' test; ***significant at the p<0.05 level**

Figure 3A

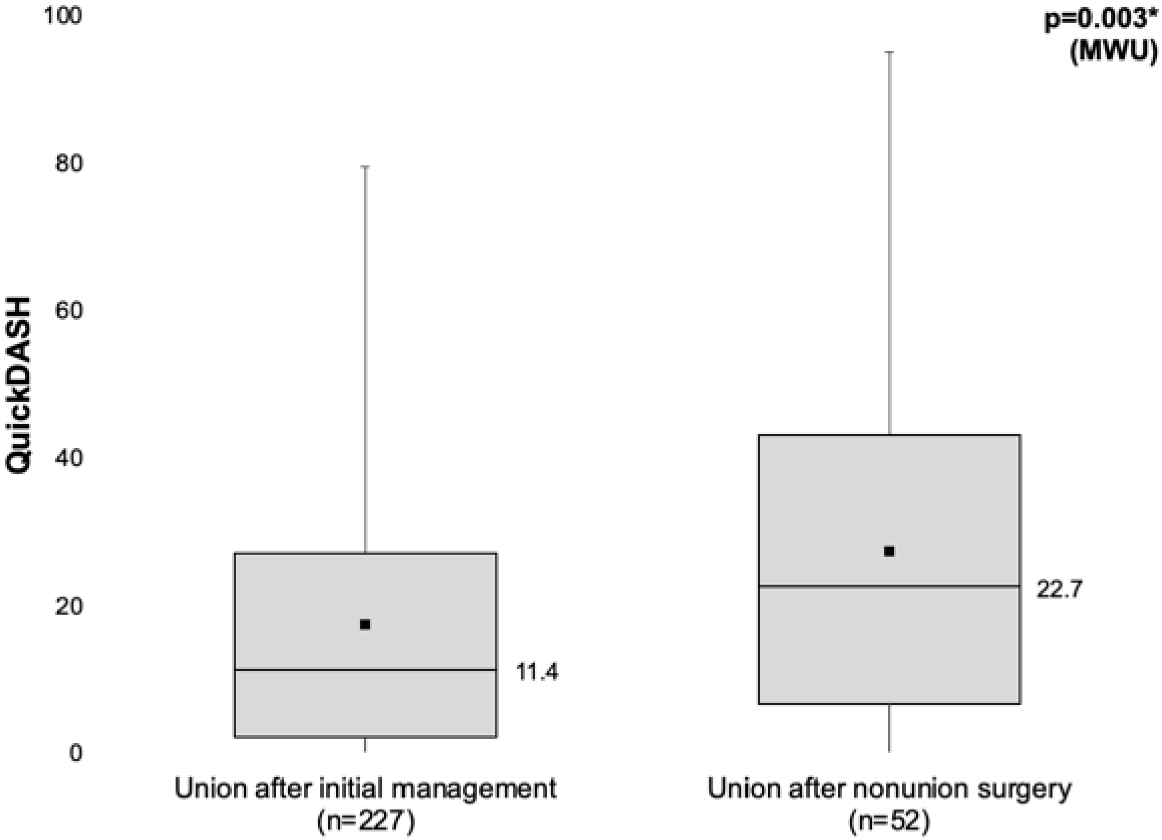

Figure 3B

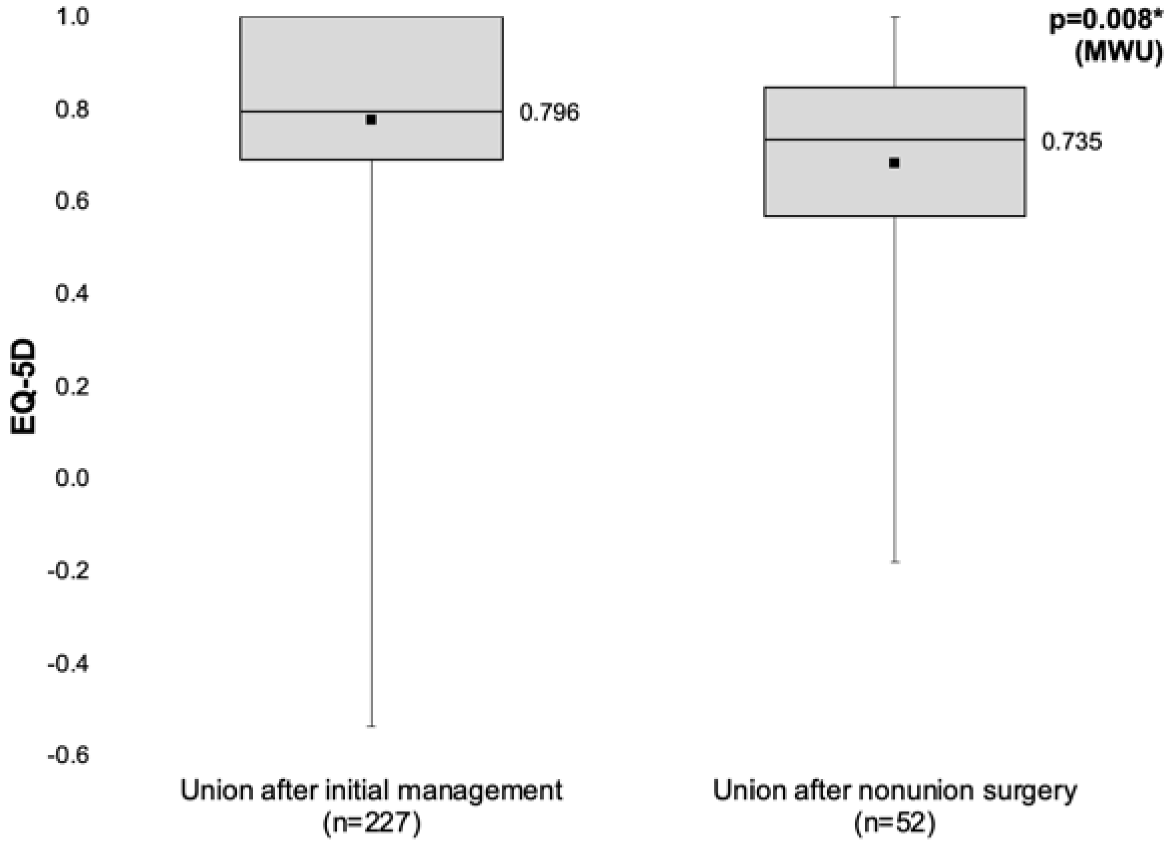

Figure 3C

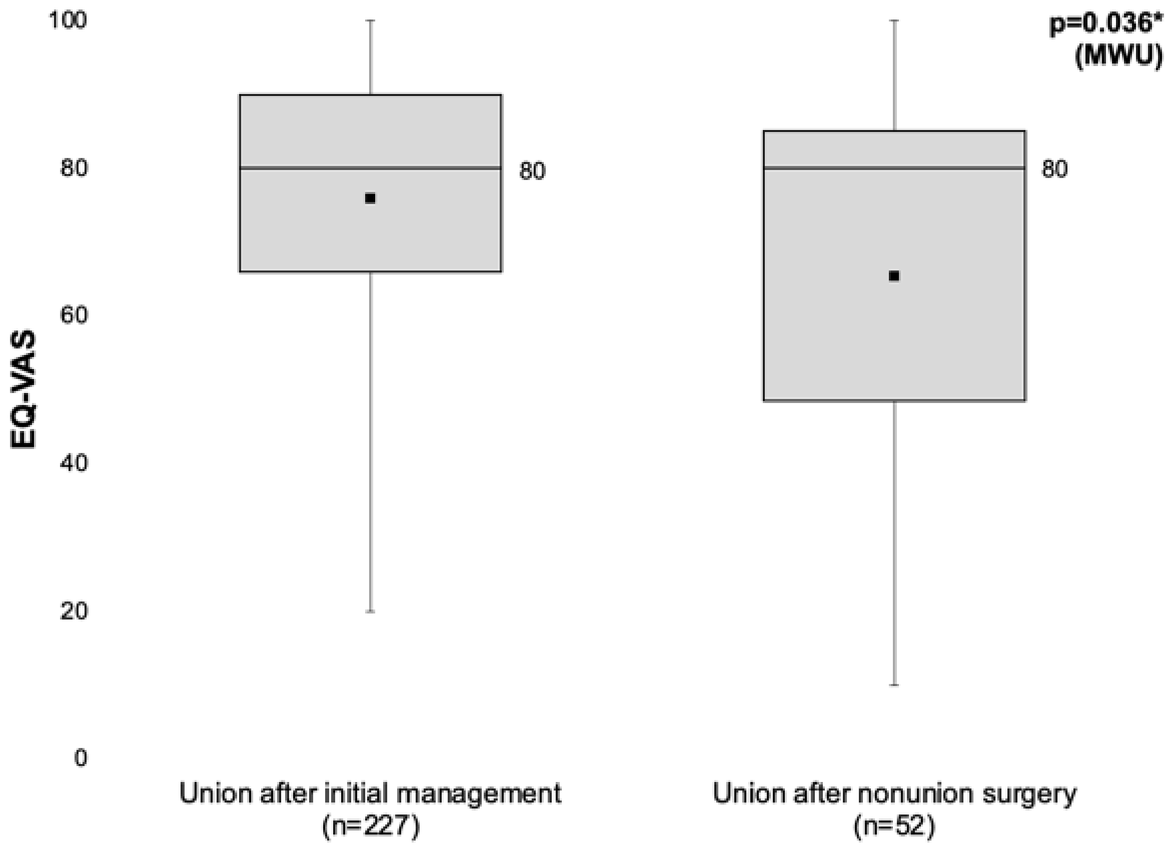

Figure 3D

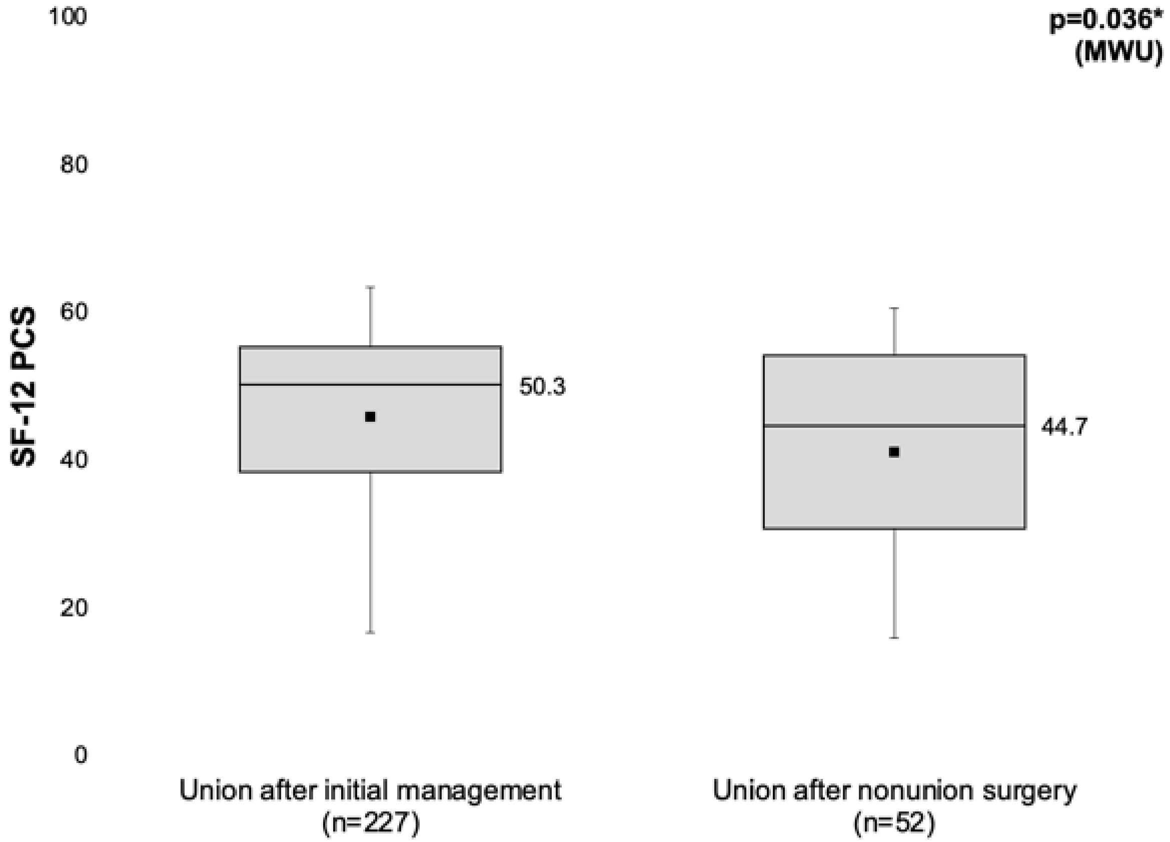

Figure 3E

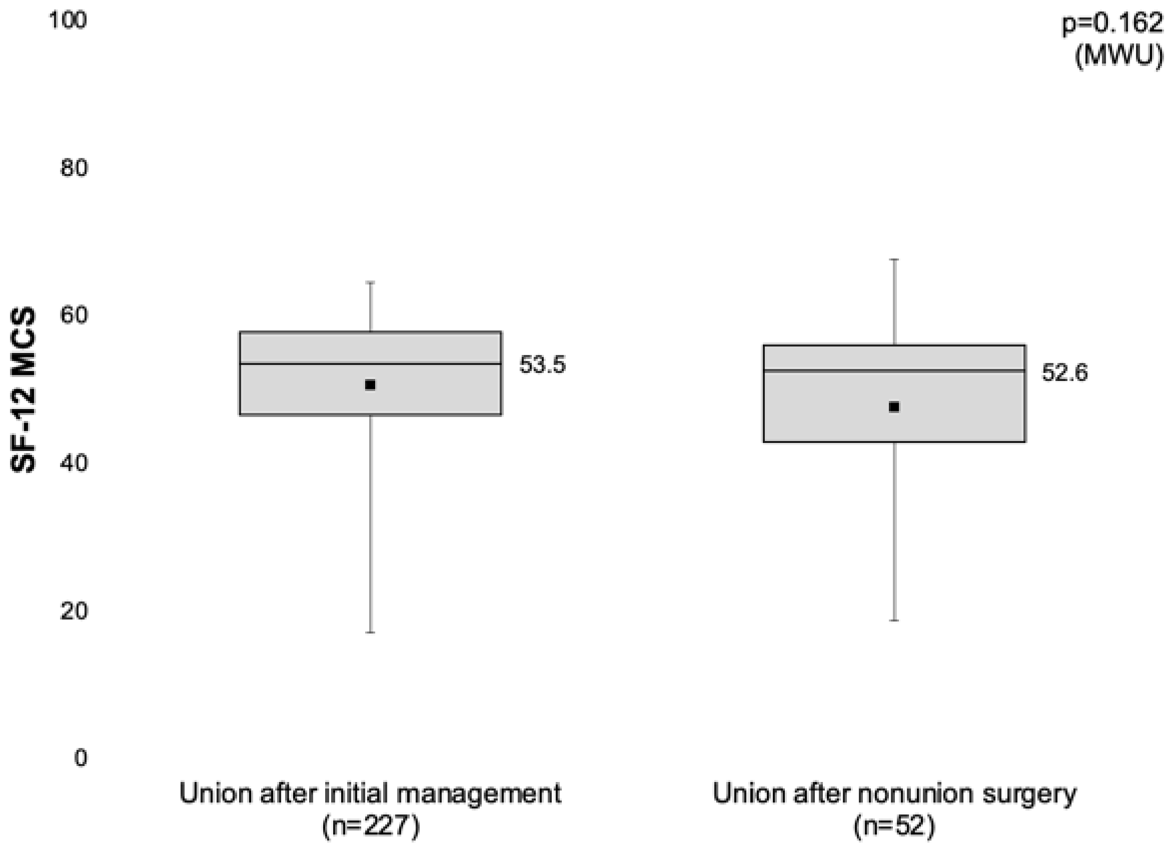

Figure 4: Comparison of pain at the site of a humeral diaphyseal fracture, by primary or secondary union; CS, chi-squared test; ***significant at the p<0.05 level**