Intrinsic and extrinsic risk factors for nonunion after nonoperative treatment of midshaft clavicle fractures

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ABSTRACT

Background: The optimal treatment of midshaft clavicle fractures remains controversial. Nonunion is usually considered to be an uncommon complication following a nonoperatively treated clavicle fracture. Hypothesis: Not every midshaft clavicular fractures shares the same risk of developing nonunion after nonoperative treatment. The present study was performed to identify the intrinsic and extrinsic independent factors that are independently predictive of nonunion in patients with midshaft clavicular fractures after nonoperative treatment.

Materials and methods: We performed a retrospective study of a series of 804 patients (391 men and 413 women with a median age of 51.3 years) with a radiographically confirmed midshaft clavicle fracture, which was treated nonoperatively. There were 96 patients who underwent nonunion. Putative intrinsic (patient-related) and extrinsic (injured-related) risk factors associated with nonunion were determined with the use of bivariate and multivariate statistical analyses.

Results: By bivariate analysis, the risk of nonunion was significantly increased by several intrinsic risk factors including age, sex, and smoking and extrinsic risk factors including displacement of the fracture and the presence of comminution (P < 0.05 for all). On multivariate analysis, smoking (OR = 4.16, 95% CI: 1.01–14.16), fracture displacement (OR = 7.81, 95% CI: 2.27–25.38) and comminution of fracture (OR = 3.86, 95% CI: 1.16–13.46) were identified as independent predictive factors.

Conclusion: The risk factors for nonunion after nonoperative treatment of midshaft clavicle fractures are multifactorial. Smoking, fracture displacement and comminution of fracture are independent predictors for an individual likelihood of nonunion. Further studies are still required to evaluate these factors in the future.

Level of evidence: Level III, case-control study.

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1. Introduction

Clavicular fractures accounts for 5% of all fractures in adults. A large number of these fractures, about 69–82%, are located in the midshaft of the clavicle [1–5]. Most midshaft clavicular fractures are caused by a direct axial compression to the shoulder after a sudden stop or fall during sports, such as cycling and horse riding [5,6]. To date, the optimal treatment of midshaft clavicular fractures is still in controversy. Although many forms of nonoperative treatment have been described, the most widely accepted treatment involves the provision of a simple sling for support during the initial phase of treatment, with early mobilization of the shoulder as the pain subsides.

Nonunion is usually considered to be an uncommon complication following a clavicular fracture. Between five and 20% of patients with midshaft clavicular fractures develop nonunion if treated by nonoperative intervention [7–10]. Patients who undergo primary fixation have a lower rate of nonunion and report better functional outcomes than those treated nonoperatively [11]. Outcomes following primary fixation are also better than outcomes following secondary fixation in patients who develop nonunion following nonoperative treatment [7]. This has resulted in the growing support for a policy of primary fixation for midshaft clavicular fractures in adult patients [7]. However, a blanket surgical approach would exert potential complications of surgery on huge numbers of patients who would have healed without surgical intervention. Despite the risk of nonunion after these fractures, most are still treated nonoperatively. Therefore, it is imperative to identify the
patient who is at higher risk of nonunion if they will be treated by nonoperative intervention. In addition, identification of patients with relative risk factors of nonunion is desirable at the time of the initial treatment to improve patient counseling and enable targeted surgical treatment.

Several studies have attempted to evaluate the risk factors of nonunion in patients after nonoperative intervention. A wide range of factors have been hypothesized to contribute to the risk of nonunion after injury. These include intrinsic factors, such as the age and gender of the patient, and extrinsic factors, such as the location and extent of displacement of the fracture [12–15]. However, these studies have included participants in children [14], fractures of the medial and lateral ends of the clavicle [9], or only displaced midshaft fractures of clavicle [16]. Thus, the models in these previous studies are limited in their ability to predict nonunion in adult patients with midshaft fractures of clavicle [9]. Therefore, we take a hypothesis that not every midshaft clavicular fractures shares the same risk of developing nonunion. In the present study, we intend to identify the intrinsic and extrinsic factors that are independently predictive of nonunion through a retrospective cohort study.

2. Materials and methods

2.1. Study design

A database was compiled of patients who were treated nonoperatively in an academic hospital – a university-based medical center from 1st February 2008 to 31st January 2013 following a midshaft clavicular fracture. We performed a retrospective analysis of the data that included only patients who were 18 years of age or older.

2.2. Inclusion criteria

Patients who were at least 18 years of age were included in the study if they had:

- a fracture in the middle three-fifths of the clavicle;
- no fracture in other parts of body;
- nonoperative treatment (brace or sling) until either confirmed fracture-healing or the development of nonunion;
- adequate documentation of demographic details and clinical and radiographic follow-up until fracture-healing or the development of nonunion.

2.3. Patients excluded from study

1059 patients identified as having a midshaft clavicular fracture were treated nonoperatively. Of the 1059 patients, 804 satisfied the above inclusion criteria and were consider further. 34 patients were excluded because of no demographic data could be gained during the follow-up study. Moreover, 51 patients were excluded for incomplete clinical or demographic data. 63 patients were excluded because they were lost to follow-up before fracture union was determined. 80 patients were excluded because they underwent operative treatment after nonoperative treatment (within two weeks of injury). The surgery was performed as a result of skin or neurovascular compromise in 13; pathological fracture, floating shoulder, or other multifocal shoulder girdle injury in 20; a request by the patient in 24; and a decision of the treating surgeon in 23. 27 patients were excluded for the patients underwent early operative treatment from two to 24 weeks after injury before the development of definite nonunion.

2.4. Assessment of fracture union

The union of midshaft clavicle fracture was evaluated by two authors (W.D.L and Y.X). Fracture union was judged as the absence of mobility or pain on stressing the site of the fracture and evidence of bridging callus on radiographs. On each radiograph, the cortices were evaluated for the amount of bridging. Healing time was set as the time when the fracture was bridged, defined by the disappearance of the cortical interruption at the fracture site as a result of callus formation. Nonunion was judged as a fracture that remained unhealed according to these above criteria at 24 weeks after the injury. Eighty-three patients with nonunion were offered operative open reduction and plate fixation after 24 weeks unless they were unfit for surgery. 16 patients who was uncertainty in fracture union underwent exploratory operation, and three were found to be united; the remaining 13 had a definite nonunion, which was treated with plate fixation and bone-grafting. These 13 patients were considered to be nonunion at 24 weeks. All patients with nonunion were united following surgery.

2.5. Putative intrinsic (patient-related) and extrinsic (injured-related) risk factors

All demographic and outcome data were gathered by two authors (W.D.L and Y.D.H). The displacement of fracture was defined as at least one residual cortical not contact between bone ends. The intrinsic (patient-related) information recorded at age, gender, with or without medical comorbidities (including rheumatoid disease, immunocompromise, renal failure and etc), tobacco consumption, alcohol consumption, employment status insurance or medicolegal claim pending and mental status. The extrinsic (injured-related) information included mechanism of injury, displacement of fracture (including translation, angulation and shortening of the fracture which was recorded from the initial anteroposterior radiographs made after the injury), comminution of fracture, presence of neurological deficit.

2.6. Statistical analysis

Factors associated with nonunion after nonoperative treatment of midshaft clavicular fractures were identified using univariate analysis. The data analysis was performed using SPSS version 19.0 (Chicago, IL, USA). Continuous data were compared between the 2 groups using the Student’s t-test, whereas discontinuous data were analyzed using the Chi-squared test. Fisher’s exact test was used for small data subsets (n < 5). All significance tests were 2-tailed, with P<0.05 representing statistical significance. In addition, a multivariate logistic regression analysis was performed to identify which independent factors helped predict the probability of nonunion.

3. Results

3.1. Demographic data

Of the 804 patients, 96 underwent nonunion, representing a risk of 11.9%. A summary of the demographic data of union group and nonunion group is presented in Table 1. The data about putative extrinsic risk factors is present in Table 2.

3.2. Bivariate analysis

Age, sex, smoking are the intrinsic risk factors for nonunion after nonoperative treatment for midshaft clavicular fractures on bivariate analysis. While, for the extrinsic risk factors, overall fracture displacement, including presence of complete displacement of fracture, shortening of an off-ended fracture, translation of fracture, and angulation of fracture and comminution of fracture were associated with increased risk of nonunion on bivariate analysis.
Table 1
Baseline intrinsic (patient-related) characteristics of the two groups with or without nonunion.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Union (n = 708)</th>
<th>Nonunion (n = 96)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55.3 ± 7.3</td>
<td>49.1 ± 6.4</td>
<td>0.049</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>335 (47.3%)</td>
<td>56 (58.3%)</td>
<td>0.043</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173.1 ± 13.1</td>
<td>169.8 ± 15.7</td>
<td>0.818</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.5 ± 11.7</td>
<td>77.4 ± 15.3</td>
<td>0.798</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.5 ± 2.5</td>
<td>20.7 ± 3.1</td>
<td>0.799</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td>125 (17.7%)</td>
<td>30 (31.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Alcohol, n (%)</td>
<td>212 (30.0%)</td>
<td>21 (21.9%)</td>
<td>0.102</td>
</tr>
<tr>
<td>Comorbidty, n (%)</td>
<td>25 (3.5%)</td>
<td>4 (4.2%)</td>
<td>0.754</td>
</tr>
<tr>
<td>Employment, n (%)</td>
<td>493 (69.6%)</td>
<td>60 (62.5%)</td>
<td>0.157</td>
</tr>
<tr>
<td>Mental disorder, n (%)</td>
<td>6 (0.8%)</td>
<td>1 (1.0%)</td>
<td>0.848</td>
</tr>
</tbody>
</table>

Table 2
Baseline extrinsic (injured-related) characteristics of the two groups with or without nonunion.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Union (n = 708)</th>
<th>Nonunion (n = 96)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple fall</td>
<td>220 (31.1%)</td>
<td>25 (26.0%)</td>
<td>0.315</td>
</tr>
<tr>
<td>Fall from a height</td>
<td>165 (23.3%)</td>
<td>23 (24.0%)</td>
<td>0.887</td>
</tr>
<tr>
<td>Sports</td>
<td>133 (18.8%)</td>
<td>16 (16.7%)</td>
<td>0.616</td>
</tr>
<tr>
<td>Traffic accident</td>
<td>79 (11.2%)</td>
<td>13 (13.5%)</td>
<td>0.491</td>
</tr>
<tr>
<td>Direct violence</td>
<td>76 (10.7%)</td>
<td>11 (11.5%)</td>
<td>0.830</td>
</tr>
<tr>
<td>Other</td>
<td>35 (4.9%)</td>
<td>8 (8.3%)</td>
<td>0.166</td>
</tr>
<tr>
<td>Displacement of fracture</td>
<td>186 (26.3%)</td>
<td>55 (57.3%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Complete displacement of fracture</td>
<td>35 (5.9%)</td>
<td>11 (11.5%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Translation of fracture</td>
<td>58 (8.2%)</td>
<td>15 (15.6%)</td>
<td>0.038</td>
</tr>
<tr>
<td>Angulation of fracture</td>
<td>32 (4.5%)</td>
<td>10 (10.4%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Shortening of fracture</td>
<td>61 (8.6%)</td>
<td>19 (19.8%)</td>
<td>0.033</td>
</tr>
<tr>
<td>Comminution of fracture</td>
<td>170 (24.0%)</td>
<td>38 (39.6%)</td>
<td>0.039</td>
</tr>
<tr>
<td>Presence of neurological deficit</td>
<td>35 (4.9%)</td>
<td>6 (6.3%)</td>
<td>0.585</td>
</tr>
</tbody>
</table>

Table 3
Independent risk factors for nonunion in patients after nonoperative treatment for midshaft clavicular fracture.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Odds ratio value</th>
<th>95% confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>4.16</td>
<td>1.01-14.16</td>
<td>0.031</td>
</tr>
<tr>
<td>Fracture displacement</td>
<td>7.81</td>
<td>2.27-25.38</td>
<td>0.001</td>
</tr>
<tr>
<td>Comminution of fracture</td>
<td>3.86</td>
<td>1.16-13.46</td>
<td>0.035</td>
</tr>
</tbody>
</table>

3.3. Logistic regression analysis

These above parameters were entered into the logistic regression model. By multivariate logistic regression analysis, several independent factors were identified to be related to a higher risk of nonunion. Smoking, fracture displacement and comminution of fracture are independently predictive. The results were presented in Table 3.

4. Discussion

The present study confirms that the nonunion after nonoperative treatment for midshaft clavicular is an uncommon occurrence. The prevalence is higher than the previously reported in other retrospective studies [4,17]. The present findings support the increased prevalence of nonunion reported in contemporary studies [7]. In the present study, nonunion occurred in 96 (11.9%) of the 804 patients who were at least 18 years of age. Although this prevalence is twice that observed by Nowak et al. [6], the previous study did not report the treatment of midshaft clavicular fracture. The differences in nonunion frequency might be partly related to the chosen definition of a nonunion and different treatment.

Although age and sex were identified as the risk factors in the bivariate analysis, age and sex no longer represented an independently significant predictor of nonunion in multiple logistic regression analysis. Only three factors, namely smoking, comminution of fracture and overall fracture displacement, were independently predictive of nonunion. Using a multivariate regression model that takes the three identified risk factors into account, estimates of the risk of nonunion after nonoperative management can be produced.

Several studies have included children and the lateral and medial ends of the clavicle fracture [9,18], which place an influence on the stability of the results. We, therefore, only investigate midshaft fractures in adults in the present study, aiming to reduce the confounding effects of age and anatomical location.

A young patient predominantly male has a higher risk to have a clavicle nonunion than an old one in the bivariate analysis. The reason is that these fractures occurred in young patient and male population may be caused by high-energy injury such as a sports injury or a traffic accident. The severity of the fracture may influence the healing progression of fracture. Smoking is the only one intrinsic risk factor for nonunion after nonoperative treatment for midshaft clavicular fracture. Previously, several clinical and experimental studies have confirmed the association between the fracture union and smoking [19,20]. However, several studies reported that smoking was not a risk factor for clavicular nonunion [8,18]. Although smoking was identified as an independent risk factor for nonunion in the present study, the strength of association cannot be concluded to establish whether heavier smokers were at great risk.

As extrinsic risk factors, overall displacement and comminution of fractures are identified as the two independent risk factors for nonunion. The above two factors place more attention to the reduction and fracture morphology on healing. Communion and displacement of fractures may be associated with higher-energy trauma and, therefore, add to the severity of underlying osseous and soft tissue injuries. Several studies also argued that fracture comminution was associated with poorer outcome [8–10]. Previous studies demonstrated that high nonunion rates (up to 29%) have been observed in displaced fractures [8,9,21,22]. Bernstein [7] reported that a direct relationship existed between increased displacement and worse functional outcome scores. Hill et al. [8] argued that there was a significant association between initial shortening and the development of nonunion. It has also been reported that displaced midshaft fractures were 18.5 times more likely to result in delayed union or nonunion compared with nondisplaced fractures [5].

The present confirm the need for consideration of all three variables when identifying patients at greatest risk of nonunion. Although three independent risk factors are associated with nonunion in patients with midshaft clavicular, the ability to accurately predict nonunion in individual patients may be poor, because of the relatively low prevalence of nonunion. Although it is possible to determine whether patients have the above-mentioned risk factors, it is less certain that patients with one or more independent risk factors will develop nonunion. Many patients at high-predicted risk of nonunion will heal without nonunion, and a number of patients with few risk factors will nevertheless develop nonunion.

The limitations of the present study include the following: although X-ray allows a qualitative assessment of callus formation and cortical bridging, doubt has been cast over its reliability for the assessment of fracture-healing [23]. The complex three-dimensional configurations of fractures are not fully appreciated on radiographs, limiting the accuracy of judgments of shortening,

translation, and angulation. Therefore, the potential false-positive rate may affect the stability of the results of the present study. Three-dimensional computed tomography would improve the interpretation of fracture morphology and provide a more accurate assessment of healing in future studies [24], but its use was limited in the present study by its cost. Patients who underwent operative treatment before the last follow-up for reasons including skin infection, patient request, or a decision of the surgeon were excluded. It is almost certain that some of these patients were at high risk of nonunion, which will affect the external validity of the present study. The present study has not recorded the specific smoking consumption for individual patients. Thus, we cannot determine the threshold of risk level of smoking for nonunion. According to the above limitation, it is significant that the results of the present study will be validated in independent samples. Moreover, the specific nonoperative treatments, including brace and sling, were not evaluated, which may influence the stability of the results. The proportion of patients were lost to follow-up before the final assessment. We were unable to confirm whether these fractures had united, and it could be argued that many of these patients probably failed to return for the follow-up examination because they were asymptomatic, with a healed fracture. This limitation, therefore, could overestimate the risk of nonunion in the present study.

Although several putative intrinsic and extrinsic risk factors for nonunion were evaluated in the present study, other risk factors such as interposition of soft tissue between fragments and genetic predisposition were not identified. Moreover, risk factors of low prevalence may influence the development of nonunion in individual cases. In particular, comorbidities, including rheumatoid disease, immunocompromise, renal failure, epilepsy, and use of drugs (corticosteroids and those interfering with vitamin-D metabolism), may increase the risk of nonunion. Because of insufficient frequency of these comorbidities, they cannot investigate their identification as statistically significant risk factors.

It is better that these independent risk factors should be used to guide clinicians in counseling patients. In addition, patients with these risk factors does not imply that their outcome would always be improved by primary operative intervention. Primary fixation of midshaft clavicular fractures has been advocated in recognition of the increased rate of nonunion and inferior functional outcomes associated with nonoperative treatment of fractures of this type [7]. The present study aims to improve awareness of which patients are at greatest risk of nonunion while minimizing the number of patients undergoing unnecessary surgery.

5. Conclusion

The risk factors for nonunion after nonoperative treatment in midshaft clavicular fractures are multifactorial. Multivariate logistic regression analysis suggests that smoking, fracture displacement and comminution of fracture are independently predictions for an individual likelihood of nonunion. We believe that the predicted risk factors of nonunion should be used to guide clinicians in counseling patients. Primary fixation of midshaft clavicular fractures may be advocated in patients with above-mentioned risk factors. In summary, we hope to improve awareness of which patients are at greatest risk of nonunion while minimizing the number of patients undergoing unnecessary surgery by providing current estimate of risk factors of nonunion. High-quality, randomized, controlled trials are still required to evaluate these factors in the future.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References