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Non-union in lateral locked plating for distal femoral fractures: A systematic review

Michael Tianfeng Wang[a,b,*], Vincent V.G. An[c,d], Brahman Shankar Sivakumar[e]

[a] Department of Surgery, Austin Health, Heidelberg, Victoria, Australia
[b] Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Australia
[c] Department of Surgery, Royal Prince Alfred Hospital, Australia
[d] Faculty of Medicine and Health, Sydney University, New South Wales, Australia
[e] Department of Hand Surgery & Microsurgery, Liverpool & Fairfield Hospitals, New South Wales, Australia

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ABSTRACT

Introduction: This study aims to identify patient and intra-operative factors that contribute to non-union in locked lateral plating for distal femoral fractures.

Methods: Systematic searches of English-language articles in Ovid Medline, PubMed, Embase, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews were undertaken in February 2018 according to the PRISMA guidelines. The search terms were (fracture or fracture*) AND (distal femur or distal femoral) AND (malunion or non-union). Eligible studies published at any time reported non-union rates and compared patient and intraoperative factors in patients who underwent locked lateral plating for traumatic distal femoral fractures. The quality of included papers was assessed using The Journal of Bone and Joint Surgery levels of evidence (Wright et al., 2003), and further appraised using the Downs and Black score (Downs and Black, 1998).

Results: Eight studies investigating 1380 distal femoral fractures were found to satisfy the inclusion and exclusion criteria. These studies analysed a variety of patient and intra-operative factors that may contribute to non-union. These include high BMI, open fracture, comminution, fracture infection, stainless steel plate material, shorter working length, open reduction and internal fixation when compared with minimally invasive plate osteosynthesis, high construct rigidity scores and purely locking screw constructs.

Conclusion: This review has identified multiple factors which potentially contribute to non-union including stainless steel plate material, high construct rigidity scores and purely locking screw constructs. These findings may reflect that overly rigid plating constructs can contribute to non-union. However, they should be taken in the context of heterogeneity amongst included studies, with further research necessary to support these findings.

Introduction

Distal femoral fractures account for 3–6% of adult femoral fractures and 0.4% of all fractures, with a bimodal distribution typically comprising of younger patients with high energy injuries and older patients sustaining fractures from minimal trauma [3]. For elderly patients, distal femoral fractures are associated with a five year mortality of up to 48.8% [4]. Studies show that operative management produces superior outcomes in fracture union compared to non-operative options [5–7]. The most commonly employed surgical techniques are sub-muscular plating or retrograde intramedullary nail fixation. Lateral locked plating (LLP) has become increasingly popular, with concerns of non-locking plates leading to an increased incidence of late varus displacement [8].

Reported rates of non-union in LLP vary widely, with some early studies demonstrating rates less than 6% [9] and more recent studies up to 17–21% [10,11]. This increase may be attributable to variations in operative technique, as well as broader acceptance and a lower threshold for utilization of LLP. Patient factors including age and comorbidities may impact the likelihood of non-union [12]. Clinical uncertainty exists regarding the optimal technical specifications including plate working length, proximal screw density, screw configuration and implant material.

* Corresponding author at: Austin Hospital, 145 Studley Road, Heidelberg, Victoria, Australia.
E-mail addresses: TMichaelWang@gmail.com (M.T. Wang), Vian2424@uni.sydney.edu.au (V.V.G. An), Brahma.Sivakumar@health.nsw.gov.au (B.S. Sivakumar).

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Thus, the aim of this systematic review is to identify patient and intra-operative factors that contribute to non-union in LLP for distal femoral fractures, including patient demographics, comorbidities and fracture characteristics in addition to plate and screw variables.

Methods

Literature search strategy

A systematic review of the literature was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. Electronic searches were performed during February 2018 using Ovid Medline, PubMed Embase, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews databases for the following search terms: (fracture or fracture*) AND (distal femur or distal femoral) AND (malunion or non-union). The reference lists of all review articles were assessed to identify additional studies for inclusion based on the inclusion and exclusion criteria outlined below. Fig. 1 summarises the literature search strategy and results.

Studies eligible for this systematic review included English language studies published at any time, that reported non-union rates and patient and intraoperative factors in patients who underwent locked lateral plating for traumatic distal femoral fractures. Studies investigating intramedullary nails, simultaneous arthroplasty and non-operative treatment were excluded, as were studies that failed to analyse the non-union group compared with the union group. Case reports, abstracts and conference proceedings were also excluded.

Quality assessment

The quality of included papers was assessed using The Journal of Bone and Joint Surgery levels of evidence [1]. Additionally, the studies were appraised using the Downs and Black score [2], with the final point regarding power analysis excluded from the checklist, leaving a score out of 26.

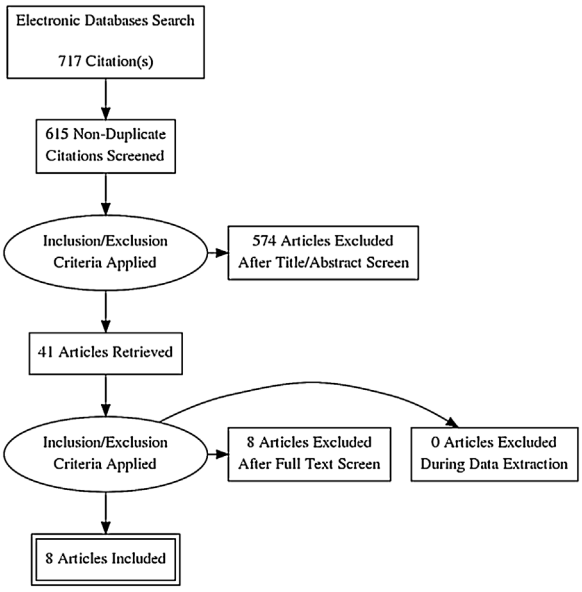

Fig. 1. PRISMA flowchart of our search strategy.

Data extraction and synthesis

Due to heterogeneity in study designs and reporting methods, meta-analysis of outcomes could not be performed. The included studies were divided into three main categories based on the factors investigated: patient demographic factors, fracture characteristics and intra-operative factors. Intra-operative factors included plate and screw variables.

Results

The initial search yielded 717 articles, with 615 articles remaining after duplicates were removed. Title and abstract screening left 41 articles for full-text review. After applying the inclusion and exclusion criteria, 8 studies were retained for further analysis (Fig. 1).

Included studies employed a variety of designs, with the sample size investigated ranging from 34 to 339 as demonstrated in Table 1. There was a total pooled sample of 1380 distal femoral fractures between 2011 and 2017. Statistical analysis techniques varied widely, spanning from t-tests to multivariate logistic regression. The majority of included studies were retrospective, with only one study prospective in nature. The median Downs and Black score was 18.5 out of a possible 26 points (17 to 20). The components of the Downs and Black score most poorly satisfied were related to:

- Item 9: Have the characteristics of patients lost to follow-up been described?
- Item 14: Was an attempt made to blind study subjects to the intervention they had received?
- Item 15: Was an attempt made to blind those measuring the main outcomes of the intervention?
- Item 23: Were study subjects randomised to intervention groups?
- Item 24: Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?
- Item 26: Were losses of patients to follow-up taken into account?

Findings of studies

Patient related factors (Demographics)

All studies investigated patient demographic characteristics including age, sex, bone mineral density, body mass index, diabetes, steroid use, dialysis and smoking status.

BMI (>30) was significantly associated ($p = 0.03$) with increased risk of non-union by one high quality paper [14] - however this association was not found in a geriatric population [15]. Other patient demographics were not significantly associated with non-union in the included studies.

Associated injury characteristics

Out of six papers examining the relationship between open fractures and non-union, two papers [14,16] demonstrated a statistically significant positive association. Additionally, Hoffman et al [17] showed a near-association between open fractures and non-union ($p = 0.057$) and demonstrated that Gustilo/Anderson type III open fractures are significantly ($p = 0.042$) associated with non-union compared to closed and minimally open (Gustilo/Anderson types I and II) fractures, although the external validity of this finding may be limited by classification ambiguity in practice. The remaining three papers demonstrated high rates of non-union amongst patients with open fractures, although these findings were not statistically significant.

Table 1
Paper details, quality (JBJS level of evidence and Downs and Black scores) and study design of the 8 included papers.

Paper	Published	Level of evidence	D&B score	n	Modelling used	Factors investigated
Rodriguez [14]	2014	3	20	283	Student t-test, Fisher's exact test, Pearson Chi-square, Wilson's method, Multivariable logistic regression	Age, sex, BMI, diabetes, steroid use, dialysis, smoking status, open vs closed fracture, periprosthetic fracture, AO/OTA classification, infection, metal alloy, screw density, plate length
Harvin [22]	2017	3	20	96	Fisher's exact test	Age, sex, mechanism of injury diabetes, smoking, open vs closed fracture, AO/OTA classification, infection, metal alloy, proximal screw construct, working length, coronal alignment, proximal segment screws, proximal segment cortices, proximal screw density
Rodriguez [20]	2016	3	19	271	Multivariable logistic regression, Student t test, Fisher exact test	Age, periprosthetic fracture, AO/OTA classification, metal alloy, rigidity score, proximal segment screws, proximal screw density, screw density, average number of unfilled holes adjacent to fracture, total filled screws, distal screws, plate length, plate total holes, fixation crossing fracture line
Moloney [15]	2016	3	18	176	t-test, chi square test	Age, BMI, TKA, Diabetes, smoking status, open vs closed fracture, comminution, AO/OTA classification, infection
Hoffmann [17]	2013	3	18	111	Chi square, t test, Wilcoxon two-sample test, ANOVA	Previous TKR, open vs closed fracture, length of comminution, metal alloy, plating technique, working length, proximal screw density, additional lag screws
Molina [16]	2016	3	17	339	Chi square test, Fisher exact test, bivariate analysis, multivariate analysis	Mechanism of injury, diabetes, steroid use, smoking status, open vs closed fracture, intraarticular vs extra-articular fracture, periprosthetic fracture, bone graft, periosteal stripping, comminution, plating technique
Henderson [19]	2011	3	17	70	Fisher's exact test, Student's t test ANOVA	Age, diabetes, smoking, open vs closed fracture, AO/OTA classification, infection, metal alloy, average number of unfilled screws adjacent to fracture, average bridge span length (working length), plate length, bridge span to plate length ratio
Yoo [32]	2017	2	17	34	Wilcoxon rank-sum test, Fisher's exact test	Age, sex, BMD, angulation, plating technique, proximal screw density, screw density, total filled screws, plate length

From five studies directly comparing the significance of AO/OTA fracture classification, [18] only Henderson et al [19] demonstrated a statistically higher rate of non-union in the more comminuted OTA fracture classification group (33A3, C2, C3) compared with the less comminuted group ($p = 0.01$). Additionally, Molina et al [16] demonstrated a significant association between comminution and non-union ($p = 0.026$) but did not specifically classify fractures based on the AO/OTA system, and did not demonstrate a statistically significant association between intra-articular fractures and non-union. Studies were not specific regarding comparison techniques for AO/OTA classification, which may explain the variation in results.

Peri-prosthetic fractures were not significantly associated with increased rates of non-union in four studies [14–16,20]. However, Hoffman et al [17] demonstrated a statistically greater rate of failed implants amongst fractures proximal to total knee arthroplasties.

Fracture infection was strongly associated with non-union in two studies [14,15] ($p < 0.01$), despite not demonstrating statistical significance in Henderson et al. [19] Additionally, fracture angulation was not shown to be significantly associated with non-union [21].

Surgical variables

All eight studies examined operative factors and their association with non-union, including plate characteristics, screw density and construction, working length, metal alloy and plating technique.

Metal alloy

Five studies compared the impact of stainless steel and titanium plates. Two papers by Rodriguez et al [14,20] with data drawn from the same patient population demonstrated a strong association between stainless steel plate material and non-union ($p < 0.001$). However, three studies [17,19,22] demonstrated no statistical difference between the two metals. Henderson et al [19] demonstrated an increase in callus formation for patients treated with titanium plates compared to steel plates at 6 and 12 weeks post-operatively ($p = 0.03$). This callus formation difference at 24 weeks did not retain statistical significance (0.09).

Plate factors

Plate length was not shown to have a statistically significant association with non-union in four studies [14,19–21]. Amongst a low-energy fracture population utilising the MIPO technique, longer plate lengths trended towards a lower rate of non-union, however this did not reach statistical significance ($p = 0.075$). Total plate holes [20], average bridging length, [19] bridging length to plate length ratio [19] and fixation crossing fracture line [20] were not shown to be significantly associated with non-union.

Minimally invasive plate osteosynthesis (MIPO) was compared to the traditional LCP in Molina et al [17] and Hoffman et al. [16] Hoffman et al [17] demonstrated a significant reduction in non-union in the MIPO group compared to the open reduction group ($p = 0.024$). Molina et al [17] showed no significant differences in post-operative complications.

Screw factors

Rodriguez et al [20] demonstrated a significant association between higher rigidity scores and non-union ($p < 0.001$). This rigidity score included the variables of proximal screw density, plate material and number of screws crossing the fracture plane. Additionally, all-locking screw constructs were strongly associated with a higher rate of non-union when compared with hybrid constructs [22]. Increased proximal screw density and total screw density was significantly associated with higher non-union rates only in the low-energy fracture population [15]. This association was not demonstrated in other studies assessing the same parameters [14,17,20,22].

Working length of a plate construct is defined as the distance between the first screws on either side of the fracture, with a

longer working length hypothesised to reduce non-union rates. Henderson et al [19] demonstrated a significant association between higher working length and lower rates of non-union as measured by the average number of unfilled holes adjacent to the fracture ($p = 0.01$). However, this association was not demonstrated in Henderson et al [19] when measured in millimetres. Harvin et al [22] and Hoffman et al [17] did not demonstrate a significant association between working length and non-union.

The total number of unfilled holes, [20] number of distal screws [20], total screws [20,21], proximal segment screws [20,22], and proximal segment cortices [22] were not shown to be significantly associated with non-union.

Other operative factors that did not demonstrate a significant association with non-union in any study include the use of additional lag screws, [17] coronal alignment [22], periosteal stripping [16] and planned bone graft [16] (after controlling for other variables).

Discussion

Distal femoral fractures are a relatively common occurrence, and are associated with significant morbidity and mortality. Non-union rates of up to 21% have been demonstrated in the literature [10,11]. Understanding the contributing factors are crucial to establishing best practice.

As shown in this study, BMI is the only patient demographic significantly associated with increased risk of non-union [14]. Other analysed patient demographic factors were not significantly associated with an increased risk of non-union. This is in contrast to previously published literature not specific to distal femoral fractures, demonstrating elevated non-union risk associated with male gender, osteoporosis, diabetes and smoking [23].

Fracture characteristics associated with higher rates of non-union include open fractures, [14,16,17] comminution, [16,19] fracture infection [14,15] and previous total knee arthroplasty [17]. These findings are reflective of the prior literature for both distal femoral fractures and other fractures. [24–26]

Surgical variables associated with increased rates of non-union include stainless steel plate material, [14,20] open reduction and internal fixation when compared with minimally invasive plate osteosynthesis [17], higher construct rigidity scores, [20] purely locking screw constructs [20] and a lower average number of unfilled holes adjacent to the fracture [19].

Plate material selection remains a key surgical decision for distal femoral fracture repair. Although stainless steel is typically cheaper than titanium, it is a much stiffer material with approximately twice the density of titanium [27]. Whilst Rodriguez et al demonstrated a significantly higher rate of non-union associated with stainless steel plate material ($p < 0.01$), the authors were unable to eliminate the impact of confounding, with the study utilising primarily Synthes LISS titanium plates accepting only locking screws compared with stainless-steel locking compression plates allowing cortical screws. No significant difference in union rates associated with plate material were found in other studies. [17,19,22]. Whilst theoretical and in-vivo evidence exists that the stiffness of stainless steel contributes to decreased callus formation, [19] the practical ramifications of plate material on femoral non-union remains uncertain.

Minimally invasive plate osteosynthesis has become an increasingly popular method of treating distal femoral fractures, which in theory enables the increased preservation of blood supply, fracture haematoma and a reduction in soft tissue damage. Hoffman et al demonstrated a significant reduction in non-union in the MIPO group compared with the open reduction group. The evidence surrounding MIPO in other long bone fractures remains mixed, [28–30] with further research necessary to delineate the potential benefits of MIPO.

Higher construct rigidity scores were significantly associated with increased rates of non-union ($p < 0.01$) in Rodriguez et al, 2016. This rigidity score awarded points for increasing proximal screw density, if a screw crossed the main fracture plane and the use of a stainless steel plate. Whilst significant, the authors concede that the score likely reflects the predominant effect of plate material and design over the other included variables, with its external validity highly limited.

Proximal screw constructs comprised of all locking screws were strongly associated with higher rates of non-union when compared with hybrid proximal screw constructs (OR 2.9 [1.2–7.0], $p = 0.01$) [22]. This may reflect the current evidence that stiff locked plating constructs may prevent adequate callus formation [10]. Interestingly, increased proximal screw density and total screw density was only associated with higher non-union rates in a low-energy fracture cohort [21].

Henderson et al [19] showed a significant association between longer working length and lower rates of non-union as measured by the average number of unfilled holes adjacent to the fracture ($p = 0.01$). No significant association was demonstrated when measured in millimetres – however, the average working length in the non-union group trended lower than the healed fracture group (64.4 mm vs 69.8 mm, $p = 0.59$), with no evidence of adequate study power provided. These contrasting findings suggest that while a correlation between longer working length and lower rates of non-union may exist, further appropriately powered studies are necessary to confirm this conclusion. Whilst these findings were not supported in other studies [17,19,22], this may reflect different comparison groupings as in Harvin's [22] comparison of 'Short (<90.5 mm)' vs 'Long (>90.5 mm)' and Hoffman's [17] unclear comparative grouping.

The above associations between surgical variables and non-union may support the hypothesis that overly rigid constructs increase non-union rates. However, plate length [14,19–21] and the use of additional lag screws [17] were not found to be significantly associated with non-union rates. The contrasting results in included studies may be influenced by the majority of studies providing no evidence of obtaining an appropriately powered sample size to limit the potential for type II errors.

Clinicians should note factors identified in the present review as potential contributors to non-union for distal femoral fractures. However, there is insufficient evidence at this time to develop conclusive guidelines for optimal surgical intervention. The findings are constrained by methodological limitations within the included studies such as marked heterogeneity, varied definitions, mixed population samples, limited controlling for confounding variables, absence of randomised controlled trials and sub-optimal reporting of results.

For example, Rodriguez et al, 2014 [14] was the only included study appropriately powered to analyse all endpoints, with Hoffman et al, [17] Molina et al [16] and Rodriguez et al, 2016 [20] underpowered in at least one aspect, and the other studies making no reference to a power analysis. Heterogeneity of patient population was evident with varied inclusion and exclusion criteria, with some studies analysing solely a geriatric population, and others examining low energy fractures exclusively. Similarly, the definition of non-union displayed marked variability across the included papers. Most studies implemented univariate analysis with little or no ability to control for confounding variables or selection bias.

Whilst this systematic review synthesises important information, the findings must be interpreted in light of the review limitations. However, the surgical variables associated with higher rates of non-union are consistent with the increasing body of literature suggesting overly rigid constructs are detrimental to fracture union in the setting of distal femoral fractures [20]. The wide

variety of factors influencing fracture union after LLP may account for the variance in the estimated prevalence of non-union associated with this technique when compared with other techniques including retrograde nailing and angled blade plate [10,11]. Whilst the optimal surgical configurations remain unclear, controlling surgical variables to prevent overly rigid fixation constructs in LLP, and creation of 'absolutive stability,' [31] may contribute to reduced non-union rates in the management of distal femoral fractures.

Indeed, surgeons are faced with a difficult balance between preventing overly rigid fixation constructs and enabling callus formation, without creating an unstable fixation, with further research necessary to determine the optimal balance of intraoperative variables. It is crucial that future studies examine homogenous data properly powered for analysis purposes, with confounding variables minimised ideally through the use of randomised control trials, or otherwise accounted for in analysis of surgical cohorts.

Conclusion

This systematic review has identified a variety of patient factors, fracture characteristics and surgical variables which influence the union rates in distal femoral fractures. Whilst evidence suggests that overly rigid constructs may increase the risk of non-union, the inconsistency in study methodology and reporting limits the development of definitive conclusions. Future large-scale randomised controlled trials or appropriately powered cohort studies are necessary to examine the optimal LLP techniques for management of distal femoral fractures.

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