Health Outcomes of Delayed Union and Nonunion of Femoral and Tibial Shaft Fractures

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A thesis submitted in fulfilment of the requirements for the degree of Master of Surgery

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July 2015
For my daughter and wife,
Isabel and Tiana,
and my parents,
Lena and Ben.
INTRODUCTION
Knowledge about the functional consequences of lower limb long bone fractures is helpful to inform patients, clinicians and employers about their recovery process and prognosis. This study aims to describe the epidemiology and health outcomes of femoral and tibial shaft fractures treated at two level I adult trauma centres, by comparing the differences between patients with delayed union or nonunion and patients with normal union.

PATIENTS AND METHODS
An analysis of registry data over two years, supplemented with medical record review, was conducted. Fracture healing was retrospectively assessed by clinical and radiological evidence of union, and the need for surgical intervention. SF-12 scores, and work and pain status were prospectively recorded at 6 and 12 months post injury.

RESULTS
285 fractures progressed to union and 138 fractures developed delayed union or nonunion. There was a significant difference between the two cohorts with regards to the mechanism of injury, association with multitrauma, open fractures, grade of Gustilo classification, patient fund source, smoking status and presence of comorbidities. The SF-12 physical component score was less than 50 in both groups at 6 and 12 months, but significantly better in the union cohort. 72% of patients with union and 59% of patients with delayed union or nonunion had returned to work at 12 months. 54% of patients with union and 72% of patients with delayed union or nonunion continued to have pain at one year. These differences in outcomes were also significant.

DISCUSSION
Even patients whose fractures unite in the expectant time frame will have residual physical disability. Patients with delayed union or nonunion have still poorer outcomes, including ongoing problems with returning to work and pain. It is important to educate patients about their injury and prognosis so that they have
realistic expectations. This is particularly relevant given that the population most likely to sustain femoral or tibial shaft fractures are working-age healthy adults, and up to one third of these fractures will develop delayed union or nonunion.

**CONCLUSION**

Despite modern treatment, the patient-reported outcomes of lower limb long bone shaft fractures do not return to normal at one year. Patients with delayed union or nonunion can expect poorer health outcomes.
DECLARATION

I, Wei-Han Tay, declare that all work contained in this thesis is my own original work, except where due acknowledgement is given. And, to the best of my knowledge, this thesis does not contain material that has been previously published or written by any other person, except where appropriate reference is made in the text.

Signature: [Signature]
Date: 17th September 2014
# TABLE OF CONTENTS

ABSTRACT .................................................................................................................. III
DECLARATION .............................................................................................................. V
PUBLICATION .............................................................................................................. VI
TABLE OF CONTENTS .............................................................................................. VII
LIST OF FIGURES ...................................................................................................... IX
LIST OF TABLES ......................................................................................................... X
ABBREVIATIONS ....................................................................................................... XI

SECTION ONE – AN OVERVIEW ................................................................................. 1

CHAPTER 1: INTRODUCTION .................................................................................. 1

CHAPTER 2: BACKGROUND ...................................................................................... 2
  2.1. Epidemiology .................................................................................................... 2
  2.2. Classification .................................................................................................. 4
  2.3. Treatment ....................................................................................................... 5
  2.4. Delayed Union and Nonunion ...................................................................... 7
  2.5. Outcomes Assessment ................................................................................... 9

SECTION TWO – THE EVIDENCE ............................................................................ 11

CHAPTER 3: LITERATURE REVIEW ......................................................................... 11
  3.1. Background and Objective .......................................................................... 11
  3.2. Methods ......................................................................................................... 12
  3.3. Results .......................................................................................................... 14
  3.4. Discussion .................................................................................................... 16
  3.5. Conclusion ................................................................................................... 18

SECTION THREE – THE STUDY ............................................................................. 19

CHAPTER 4: OBJECTIVES ...................................................................................... 19

CHAPTER 5: PATIENTS AND METHODS ................................................................. 20

CHAPTER 6: RESULTS ............................................................................................. 24
  6.1. Fracture Outcomes ....................................................................................... 24
  6.2. Follow-up ..................................................................................................... 25
  6.3. Patient Demographics ................................................................................. 26
6.4. Injury Profile.............................................................................................................27
6.5. SF-12 Physical and Mental Health.................................................................28
6.6. Return to Work and Pain...................................................................................29
CHAPTER 7: DISCUSSION ..........................................................................................30
CHAPTER 8: CONCLUSION .....................................................................................35
SECTION FOUR – REFERENCES........................................................................37
APPENDICES ..............................................................................................................i
A.1. AIS 90 codes used to search the VOTOR database.................................i
A.2. ICD-10-AM codes used to search the VOTOR database ......................ii
LIST OF FIGURES

Figure 1: Search strings using Medical Subject Headings................................. 12
Figure 2: Search strings not using Medical Subject Headings.......................... 13
Figure 3: Flowchart of article selection process ............................................ 14
Figure 4: Flowchart of patient inclusion process ............................................. 21
Figure 5: Flowchart of fracture outcome review ............................................. 24
LIST OF TABLES

Table 1: Summary of articles selected for methodological review ...............15
Table 2: Follow-up rates (%) of health outcomes ........................................25
Table 3: Patient demographics .................................................................26
Table 4: Injury profile..............................................................................27
Table 5: Linear regression of effect of DU/NU on SF-12 median scores ........28
Table 6: Logistic regression of effect of DU/NU on return to work and pain ......29
ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIS 90</td>
<td>Abbreviated Injury Scale 1990 Revision</td>
</tr>
<tr>
<td>AO</td>
<td>Arbeitsgemeinschaft für Osteosynthesefragen</td>
</tr>
<tr>
<td>CCI</td>
<td>Charlson Comorbidity Index</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>DU</td>
<td>Delayed union</td>
</tr>
<tr>
<td>ICD-10-AM</td>
<td>International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>MCS</td>
<td>Mental Component Summary</td>
</tr>
<tr>
<td>MeSH</td>
<td>Medical Subject Headings</td>
</tr>
<tr>
<td>NU</td>
<td>Nonunion</td>
</tr>
<tr>
<td>PCS</td>
<td>Physical Component Summary</td>
</tr>
<tr>
<td>RTW</td>
<td>Return to work</td>
</tr>
<tr>
<td>SF-12</td>
<td>Medical Outcomes Study Short Form 12-Item Health Survey</td>
</tr>
<tr>
<td>SF-36</td>
<td>Medical Outcomes Study Short Form 36-Item Health Survey</td>
</tr>
<tr>
<td>VOTOR</td>
<td>Victorian Orthopaedic Trauma Outcomes Registry</td>
</tr>
</tbody>
</table>
CHAPTER 1: INTRODUCTION

Femoral and tibial shaft fractures are major limb injuries that can lead to significant physical impairment [1]. Because they usually result from high energy trauma, delayed union and nonunion are common occurrences of these fractures [2].

Fracture nonunion is a chronic condition associated with pain, and functional and psychosocial disability [3] that has been shown to have a greater negative impact on the quality of life than patients with end stage congestive heart failure, and patients receiving renal dialysis or chemotherapy for cancer [4, 5]. In addition to the considerable economic costs to society [6], delayed union and multiple surgeries cause patients to have ongoing pain, swelling, stiffness and inability to bear weight on their affected limb [7].

The assessment of fracture healing using traditional parameters, such as time to union or range of motion for adjacent joints, does not necessarily correlate with the patient’s experience of their injury or recovery [8]. While patient-reported outcomes have now been studied for several orthopaedic conditions [9-11], review of the literature confirms a paucity of comparable data on fracture nonunion. In particular, a direct comparison of the health status of patients with delayed union or nonunion and with normal fracture healing has yet to be documented. The exact determination of the burden of delayed union and nonunion of lower extremity long bone fractures is important to inform patients and their families, clinicians, employers and insurers about their recovery process and functional prognosis. This could also guide the design of more focused research in this area and provide relevant information to potential funding bodies.

The aim of this thesis is to describe the epidemiology and health outcomes of femoral and tibial shaft fractures treated at two level I adult trauma centres, by comparing the differences between patients with delayed union or nonunion and patients with normal union.
CHAPTER 2: BACKGROUND

2.1. Epidemiology

Femoral Shaft Fractures
The annual incidence of femoral shaft fractures has been reported to be 21 fractures per 100,000 people in New South Wales, Australia [12]. Higher incidences have been documented among males in their third decade of life and females greater than 75 years old [13-15].

The causes of femoral shaft fractures vary depending on the demographics of the population under study [13-15]. Femoral shaft fractures sustained by males and in younger patients frequently result from high energy trauma, such as road traffic accidents, falls from significant height and firearm injuries [15-17]. They may also be due to osteoporosis in menopausal females or in the elderly, or result from a pathological fracture secondary to malignancy or infection [15].

Because of their high energy nature, femoral shaft fractures are commonly a marker for other significant injuries in young adults [18]. They are associated with ipsilateral fractures of the femoral neck in 2.5-6% of cases [19], and are open injuries in 12-27% of presentations [13, 14, 20]. Polytrauma patients with bilateral femoral shaft fractures have a higher mortality rate of 5.6% compared to 1.5% in isolated injuries [21]. Bleeding of up to 1.5 litres into the thigh can occur from a closed femoral shaft fracture [18].
**Tibial Shaft Fractures**

The annual incidence of tibial shaft fractures has been reported to be between 50 and 200 fractures per 100,000 people in Sweden [22], and is the most common long bone fracture [23, 24]. These injuries are most frequent among males and in patients aged in their second and third decades of life [25, 26].

Similar to the femur, most tibial shaft fractures are caused by high energy mechanisms associated with motor vehicle accidents [27]. Lower energy trauma secondary to simple falls and sporting injuries are also common mechanisms in the elderly and in younger patients, respectively [27, 28]. Other causes include work-related accidents, assault and firearm injuries [27].

Because of the tibia’s subcutaneous location in the leg, 13-46% of tibial shaft fractures are open injuries [29], accounting for almost half of all open long bone fractures [24]. 80% of tibial shaft fractures have an ipsilateral fibular shaft fracture [27]. In addition, 16-41% of patients are associated with multiple injuries [29].
2.2. Classification

Femoral Shaft Fractures

The Müller Arbeitsgemeinschaft für Osteosynthesefragen (AO) classification system defines the femoral shaft as the segment between the inferior margin of the lesser trochanter and the upper border of a square containing the distal end of the femur [30, 31]. For descriptive purposes, the shaft is divided into proximal, middle and distal thirds [31]. The proximal third is also referred to as the subtrochanteric region [18, 31]. Femoral shaft fractures are classified as located in bone 3 and segment 2, or 32 [18, 30]. Their morphology is further described as type A (simple), B (wedge) or C (complex) depending on the number of fragments and degree of cortical contact after reduction, and as group 1 (spiral), 2 (oblique or bending or segmental) or 3 (transverse or multifragmentary or irregular) according to the pattern of force or fracture line configuration [18, 30].

Tibial Shaft Fractures

The Müller AO classification system describes tibial shaft fractures as located in bone 4 and segment 2, or 42 [30, 32]. Comparable to the classification of femoral shaft fractures, the morphology of the fracture is further classified as type A, B or C, and as group 1, 2 or 3 [30, 32].

Open Fractures

The most widely used method to classify fractures associated with soft tissue injury is the system devised by Gustilo and Anderson [33-35]. The original classification described open fractures as type I, II or III according to the severity of the associated soft tissue damage [33]. Clinical application led Gustilo to further subdivide the classification of the severe or type III injuries into subgroups A, B or C based on the extent of loss of soft tissue coverage and the presence of a vascular injury [34].
2.3. Treatment

**Femoral Shaft Fractures**

The treatment of femoral shaft fractures includes nonoperative and operative management [31]. Nonoperative management involves skin or skeletal traction, either as temporary or definitive stabilisation [31]. Immobilisation in a spica cast is usually reserved for young paediatric patients [31].

Today, the most common treatment method of adult femoral shaft fractures is operative fixation by intramedullary nailing [18, 31]. The fracture is reduced by closed or open technique, and the fixation device is inserted via an antegrade or retrograde approach into a reamed or unreamed intramedullary canal [18, 31]. Other operative options include open reduction and internal fixation by compression plating, bridge plating using a percutaneous technique, and temporary or definitive stabilisation with an external fixateur [18, 31].

The rate of union has historically been reported at 97-100% in closed fractures treated with traction [36]. The overall union rate using plate fixation is 90-95% [37-39], with healing occurring at approximately 17.2 weeks post injury [40]. Fractures treated with antegrade reamed nailing have a union rate of 95-99% [41]. Clinical and radiological union ranges from 12 to 24 weeks after closed intramedullary nailing [42, 43]. With regards to the outcomes of specific intramedullary nailing techniques, unreamed and smaller diameter nails have a statistically higher rate of nonunion compared to reamed intramedullary nails at 7.5% versus 1.6%, respectively [44]. In an Australian cohort of femoral shaft fractures treated by intramedullary nailing, 23% of patients required further surgery for delayed union or nonunion [45].
Tibial Shaft Fractures

The treatment of tibial shaft fractures likewise includes nonoperative and operative management [32]. Fractures in children or that have a stable pattern can be treated nonoperatively in a long leg plaster cast, followed by early weight bearing in a patellar tendon bearing cast [32].

Similar to the femur, the most common treatment method of tibial shaft fractures is an intramedullary nail, which is inserted antegrade into a reamed or unreamed canal [46-51]. Fractures of the proximal and distal shaft with articular extension can be suitably fixed with specific contoured locking plates [32]. In severe soft tissue or contaminated injuries, temporary or definitive stabilisation with an external fixateur is a reasonable option [32].

Because of its poorer blood supply, tibial shaft fractures are slower to unite than other long bone fractures [52]. The mean duration to radiological union ranges from 18 to 28 weeks [48, 53-56]. Fractures associated with severe soft tissue injuries may require up to 44 weeks [56, 57]. Clinical union or the ability to bear full weight without restriction is usually achieved between 12 and 22 weeks post injury [58, 59], and is normally reached before radiological union [46, 60].

Delayed union and nonunion of tibial shaft fractures is more frequent compared to other long bone fractures [52, 61]. The overall incidence of delayed union and nonunion of tibial shaft fractures is reported at 3-33% [54, 62], but may be as high as 47% of Gustilo type I injuries [59] or up to 60% of fractures with extensive comminution [63]. In a recent multicentre randomised trial in Canada, the reoperation rate (including autodynamisation) after intramedullary nailing was reported at 13.7% and 26.5% for closed and open fractures, respectively [64]. This study also favoured the use of reamed nailing for closed fractures [64]. The overall revision rate for nonunion and infection was 35.8% at a major trauma centre in Australia [65].
2.4. Delayed Union and Nonunion

Despite advances in the knowledge of fracture healing, definitions of delayed union and nonunion continue to be subject to variable interpretation [66-71]. In a survey of 444 orthopaedic surgeons from North America and Europe, Bhandari et al concluded a lack of consensus in the assessment of fracture healing among practising clinicians [72]. For example, surgeons’ temporal criteria for delayed union ranged as widely as 1 to 8 months after the initial injury, while definitions of nonunion varied from 2 to 12 months post fracture [72]. Furthermore, the proportion of surgeons who always used a particular criterion to assess fracture healing and who occasionally or never used the criterion was less than one half and less than one third of clinicians, respectively [72].

Traditional definitions of delayed union and nonunion are based on the clinical experience that most fractures will unite within 3 to 4 months [73]. Generally, union is considered delayed when healing has not advanced at the average rate, usually 3 to 6 months, depending on the location, type of fracture and the patient’s age [2, 66, 68, 69, 74]. Failure to unite by a further set time limit, usually 6 to 8 months post fracture, is said to constitute nonunion [66, 68, 69, 75]. Clinical signs of delayed union and nonunion include motion and tenderness at the fracture site, limb swelling and pain on weight bearing [68, 71, 73, 74, 76-80]. Radiological signs include sclerosis and rounding of the edges at the fracture ends, a gap, absent or hypertrophic callus, and lack of cortical continuity or a persistent radiolucent line on serial radiographs [74, 81, 82]. Persistent motion at a fracture site may result in the formation of a false joint or pseudoarthrosis [2, 73, 74]. This may take years to develop after the original injury [2, 73, 74].

For the purposes of clinical research, the United States Food and Drug Administration defines nonunion as “established when a minimum of 9 months has elapsed since injury and the fracture shows no visible progressive signs of healing for 3 months” [83]. Using the tibia as a reference, Müller describes nonunion as failure of a fracture to unite after 8 months of nonoperative treatment [84]. Conversely, others contend that any temporal-dependent criterion is inherently subjective and cannot be arbitrarily set, because they rely on the speculation of future events based on clinical and radiological findings by the
clinician [2, 73, 85]. As such, Brinker defines nonunion as “a fracture that, in the opinion of the treating physician, has no possibility of healing without further intervention” [85]. He further distinguishes delayed union as “a fracture that, in the opinion of the treating physician, shows slower progression to healing than was anticipated and is at substantial risk for becoming a nonunion without further intervention” [85]. In a similar vein, Einhorn proposed definitions that were independent of a time line [67]. Einhorn describes nonunion as a fracture whereby “all healing processes have ceased and union has not occurred” [67]. He defines delayed union as present when “healing processes continue”, but “union has not occurred in the expected time and the outcome is uncertain” [67].

For practicality, this thesis defines delayed union and nonunion as a fracture that has required unplanned reoperation for impaired fracture healing at less than 6 months and greater than 6 months post injury, respectively.
2.5. Outcomes Assessment

The use of subjective measurements to evaluate patient outcomes is expanding in modern research [86]. The interpretation of laboratory or clinical data is enhanced by information derived from the patient’s perspective of a disease or treatment and their subsequent state of health [86]. Like many other fields in medicine, this is relevant in orthopaedics, given that the theoretical implications do not always match the patient’s concerns or functional outcome. It is also analogous to the old adage, “treat the patient, not the x-ray”.

The physician-patient interview for history-taking is the oldest method of assessing subjective or qualitative descriptions of a patient’s condition [86]. Because of the difficulties in translating individual qualitative reports into quantifiable data to test a research hypothesis, the use of subjective measurements was not popularised until the advent of standardised survey instruments [86]. These surveys are typically structured questionnaires that use a formula, which combines the patient’s responses to estimate an analysable value [86]. In addition, these questionnaires can be generic or disease-specific [86]. Generic instruments are used to describe the general population regardless of their health status or disease [86]. Disease-specific instruments are used to differentiate patients with the same condition [86]. While more sensitive to within-individual changes, disease-specific surveys do not allow comparison across populations with different conditions [86].

The Medical Outcomes Study Short Form 36-Item Health Survey (SF-36) is a commonly employed generic questionnaire that was designed for use in clinical practice and research, and general population studies [4]. The desire for a briefer survey led to the development of the Medical Outcomes Study Short Form 12-Item Health Survey (SF-12) [86]. Consisting of only 12 of the original 36 items, the SF-12 exclusively focuses on the physical and mental health components of the SF-36 [86]. Through comparison with the normal population, these surveys can help identify disability within population groups.

In an age of increasing insurance claims and litigation, distinguishing the difference between impairment and disability is a further recent challenge for
medical practitioners, governing bodies and insurance companies. According to the Guides to the Evaluation of Permanent Impairment, the American Medical Association defines impairment as “a significant deviation, loss, or loss of any body structure or body function in an individual with a health condition, disorder, or disease” [87]. In contrast, they define disability as “activity limitations and or participation restrictions in an individual with a health condition, disorder, or disease” [87]. This distinction proposes that a person can be impaired considerably but have no disability, while another individual can be significantly disabled with only limited impairment [87]. Although beyond the scope of this thesis, it is reasonable to assume that most patients with an uncomplicated femoral or tibial shaft fracture will at least have both temporary partial impairment and disability.
CHAPTER 3: LITERATURE REVIEW

3.1. Background and Objective
The outcomes of delayed union and nonunion have traditionally been assessed by objective parameters, including time to clinical and radiological union, range of motion for adjacent joints and reoperation rate [88-90]. The functional recovery, such as the patients’ ability to perform everyday tasks and their mental state, as reported by the patient have not been well documented [8].

An understanding of the existing evidence about the health outcomes of patients with delayed union or nonunion would help to identify deficiencies in our knowledge and guide further research. The aim of this literature review was to examine published data about the impact on patient-reported outcomes of delayed union or nonunion of femoral and tibial shaft fractures in adult patients.

This chapter is based on information current at the time of the literature review.
3.2. Methods

To examine previous research findings, a structured literature review was performed. The databases, MEDLINE, PubMed, EMBASE, the Cochrane Library, Web of Science and Scopus, were navigated using the search engines, Ovid, Entrez, Ovid, Wiley InterScience, ISI Web of Knowledge and Elsevier, respectively. In addition, reference lists of eligible articles were manually checked to identify other relevant papers.

**Figure 1: Search strings using Medical Subject Headings**

<table>
<thead>
<tr>
<th>Fractures, Ununited <strong>or</strong> Pseudarthrosis <strong>or</strong> Fracture Nonunion</th>
</tr>
</thead>
<tbody>
<tr>
<td>and</td>
</tr>
<tr>
<td>Femoral Fractures <strong>or</strong> Femur Shaft Fracture <strong>or</strong> Femur Fracture <strong>or</strong> Femur Shaft <strong>or</strong> Femur <strong>or</strong> Tibial Fractures <strong>or</strong> Tibia Shaft Fracture <strong>or</strong> Tibia Fracture <strong>or</strong> Tibia Shaft <strong>or</strong> Tibia <strong>or</strong> Diaphysis <strong>or</strong> Diaphyses</td>
</tr>
<tr>
<td>and</td>
</tr>
<tr>
<td>Health Status <strong>or</strong> Functional Status <strong>or</strong> Quality of Life <strong>or</strong> Prognosis <strong>or</strong> Treatment Outcome <strong>or</strong> Outcome Assessment (Health Care) <strong>or</strong> Health Status Indicators <strong>or</strong> Short Form 8 <strong>or</strong> Short Form 12 <strong>or</strong> Short Form 20 <strong>or</strong> Short Form 36</td>
</tr>
</tbody>
</table>

For the search strategy framework, three search strings were used to include relevant citations. This is summarised in Figures 1 and 2. In the first search string, descriptive terms for “delayed union” and “nonunion” were included. Synonyms for “femoral shaft fracture” and “tibial shaft fracture” were applied for the second search string. Employed in the third search string were phrases that represent “health status” and “functional outcome”. Terms were mapped to Medical Subject Headings (MeSH) in MEDLINE, PubMed, EMBASE and the Cochrane Library. For MEDLINE, both terms not using MeSH keywords and mapped to MeSH were included. A modified search combination was used for Web of Science and Scopus which did not use MeSH. All texts on record up to 20th August 2009 were searched for each database. Non-English language articles were also included in the review.
All retrieved citations were collected into an EndNote reference library. Duplicate citations detected by EndNote were eliminated. The title and abstract for each citation were manually examined to exclude irrelevant articles. Eligible papers were studies in which:

1. The primary aim was to investigate the health outcomes of delayed union or nonunion of femoral and tibial shaft fractures in adult patients;
2. The study utilised an appropriate and recognised patient-reported outcomes measurement to assess health or functional outcomes.

The full papers of these studies and any citation, whose eligibility for inclusion remained ambiguous after review of its abstract, were examined to obtain a final shortlist of relevant papers for discussion. Information about the study design, sample population, fracture type, definition of nonunion used to establish cases, treatment intervention, method of outcomes assessment, follow-up and significant results of patient-reported outcomes were extracted from eligible articles and evaluated in a narrative format.
3.3. Results
A total of 3,347 citations, including duplicates not identified by EndNote, were retrieved. Figure 3 outlines the article selection process. The most frequent reasons for exclusion of citations were paper not about femoral or tibial fractures, paper about non-diaphyseal fractures or with reference to arthroplasty, paper about congenital pseudoarthrosis or paediatric patients, paper primarily a discussion on the disease or a surgical technique, paper primarily an investigation of risk factors, paper primarily a laboratory-based study or with non-human subjects, and duplicate citations not detected by EndNote. One citation for which the abstract or full text could not be obtained was also eliminated.

Figure 3: Flowchart of article selection process

| Medical databases searched: **6 databases** |
| Titles and abstracts examined: **3,347 citations** |
| Excluded: **3,318 citations** |
| Not specific to femoral or tibial shaft fractures in adult patients, or the assessment of patient-reported outcomes |
| Full papers retrieved and examined: **29 citations** |
| Excluded: **22 citations** |
| Not focused on delayed union or nonunion: 13 citations |
| Unrecognised health outcomes measurement: 9 citations |
| Papers assessed for methodological quality: **7 citations** |

The seven papers selected for evaluation comprised all case series. The details and results of these papers are presented in Table 1. There were no studies about delayed union. There were no additional relevant articles identified from the reference lists of these papers.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Study design</th>
<th>n</th>
<th>Sample: Age Gender</th>
<th>Fracture</th>
<th>Definition of Nonunion</th>
<th>Intervention</th>
<th>Patient-Reported Outcomes Measurement</th>
<th>Follow-up: Duration Rate</th>
<th>Results of Patient-Reported Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brinker et al [91]</td>
<td>2007</td>
<td>Prospective case series</td>
<td>23</td>
<td>61-92 (72) 8M, 15F</td>
<td>23T</td>
<td>Previous treatment and no probability of healing without further intervention as per treating doctor</td>
<td>Ilizarov</td>
<td>Medical Outcomes Study Short Form, 12-Item Health Survey (SF-12), American Academy of Orthopaedic Surgeons Lower Limb Core Scale (AAOS LLC), Brief Pain Inventory (BPI), Time Trade-Off (TTO)</td>
<td>18-61 (38) months post discharge from care 16/23</td>
<td>Improvement in SF-12, AAOS LLCS and BPI scores at follow-up; TTO ratings post intervention equivalent to gaining 5.3 quality-adjusted life years per patient</td>
</tr>
<tr>
<td>Złowodzki et al [8]</td>
<td>2005</td>
<td>Prospective case series</td>
<td>23</td>
<td>–</td>
<td>16F, 7T</td>
<td>–</td>
<td>IM nail, plate fixation, osteotomy</td>
<td>Medical Outcomes Study Short Form, 36-Item Health Survey (SF-36)</td>
<td>236-740 (449) days post intervention 23/23</td>
<td>Improvement for united fractures at one year – scores poorer compared to American norms</td>
</tr>
<tr>
<td>Barker et al [92]</td>
<td>2004</td>
<td>Prospective case series</td>
<td>40</td>
<td>16-56 (33) 32M, 8F</td>
<td>9F, 31T</td>
<td>Failure of clinical union within 6 months and no progress on serial x-ray</td>
<td>Ilizarov</td>
<td>Toronto Extremity Salvage Score (TESS)</td>
<td>30 months post removal of frame –</td>
<td>Improvement from 6 to 12 months and 12 to 24 months</td>
</tr>
<tr>
<td>McKee et al [93]</td>
<td>1998</td>
<td>Prospective case series</td>
<td>25</td>
<td>18-72 (40) 12M, 10F</td>
<td>F, T</td>
<td>– (malunion included)</td>
<td>Ilizarov</td>
<td>Medical Outcomes Study Short Form, 36-Item Health Survey (SF-36), Nottingham Health Profile (NHP) Return to work</td>
<td>22-37 (29) months post intervention 22/25 (12 nonunion)</td>
<td>Improvement in SF-36 and NHP scores at 24 months; pre intervention SF-36 scores poorer compared to patients with other debilitating conditions</td>
</tr>
<tr>
<td>Bowen et al [95]</td>
<td>1996</td>
<td>Retrospective case series</td>
<td>15</td>
<td>17-69 (32) 13M, 2F</td>
<td>15T</td>
<td>As per May et al [94] and Cierny et al [96]</td>
<td>EF, IF, Ilizarov, BG, free muscle flap and STSG, amputation</td>
<td>Medical Outcomes Study Short Form, 36-Item Health Survey (SF-36), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)</td>
<td>1-6 (3) years post union or amputation 9/15</td>
<td>SF-36 scores for salvaged limbs at follow-up poorer than age-adjusted American norms</td>
</tr>
<tr>
<td>Toh et al [97]</td>
<td>1995</td>
<td>Case series</td>
<td>36</td>
<td>12-66 (33) 20M, 16F</td>
<td>37T</td>
<td>As per May et al [94]</td>
<td>EF, plate fixation, BG, local or free muscle flap, STSG</td>
<td>Nottingham Health Profile (NHP)</td>
<td>24-133 (61) months post intervention –</td>
<td>Scores reflected limb discomfort, lower energy, and problems with physical mobility and sleep</td>
</tr>
<tr>
<td>Lerner et al [3]</td>
<td>1993</td>
<td>Case series</td>
<td>50</td>
<td>18-79 (44) –</td>
<td>F, T</td>
<td>–</td>
<td>–</td>
<td>Arthritis Impact Measurement Scale (AIMS), Psychosocial Adjustment to Illness Scale (PAIS)</td>
<td>6.7 years post injury –</td>
<td>Presence of pain produced differences in AIMS and PAIS scores; no difference in AIMS overall scores between nonunion, osteomyelitis and below knee amputation</td>
</tr>
</tbody>
</table>

1 Range (mean), years; 2 M = male, F = female; 3 T = tibia, F = femur; 4 Ilizarov = Ilizarov frame, IM nail = intramedullary nail, EF = external fixation, IF = internal fixation, BG = bone graft, STSG = split thickness skin graft; 5 range (mean)
3.4. Discussion

There has been no review of published literature about the patient-reported outcomes of delayed union or nonunion of fractures in the lower limb. Given the paucity of existing data, a formal systematic review was not performed. To allow selection of some papers relevant to the research question, less rigorous criteria for methodological quality was necessary in the inclusion of articles for final assessment. The author was also the only reviewer and quantitative synthesis of the data was beyond the scope of this structured narrative review. It is possible that not all evidence regarding the health outcomes of delayed union or nonunion of femoral and tibial shaft fractures were gathered in this literature review. However, since all the major medical databases were searched, it is likely that a large percentage of relevant papers have been sourced.

This literature review supports the hypothesis that nonunion of femoral and tibial fractures is a cause for significant disability in patients that may be comparable to other chronic debilitating diseases [93] and post lower limb arthroplasty surgery [91, 93, 95]. Treatment of the nonunion by surgical intervention can reduce their disability [8, 91-93], but may not regain their premorbid function when compared to population peers [8, 95]. The majority of patients had well-established nonunion requiring specialised treatment, and were first assessed at greater than 12 months post injury. Four out of the seven studies utilised the more modern Medical Outcomes Study Short Form Health Survey as one of [91, 93, 95] or their main measurement tool [8]. Only one paper primarily examined the health outcomes of nonunion as a condition [3], while the remainder studies focused on the effect of their treatment on the functional status of patients with impaired fracture healing. There were no studies that compared the patient-reported outcomes of nonunion with normal union.

Several methodological limitations were identified in the current literature about the health outcomes of fracture nonunion in the lower limbs. All of the studies were case series with no control or comparison group. Case series are predisposed to selection bias and confounding variables [98, 99]. To properly establish the effect of nonunion on health status requires evaluation against the outcomes of comparable fractures with normal union. Despite one paper
including both patients with nonunion and malunion [93], each series was also
disadvantaged by a relatively small sample size. A study with a small sample size
has increased random sampling error and decreased power to differentiate a true
effect from no effect [98, 99].

In addition, three articles did not provide their definition of nonunion [3, 8, 93],
and more than one half of the papers did not describe the type of fractures that
were included [3, 92, 93, 95]. This is problematic when comparing their data
because of the variable definition of nonunion. For studies that include fractures
with articular involvement [8], results are potentially confounded as the
characteristics and outcomes of these injuries are not comparable to those of
extra-articular fractures [100-103].

Other common methodological weaknesses were the lack of details about the
sample population [3, 8] and follow-up rates [3, 92, 97], and poor descriptions of
the study’s inclusion and exclusion criteria [3, 8]. Sampling biases, such as poor
response rates and lack of non-respondent analysis, can contribute to systematic
error [98, 99]. Non-transparency of the method of inclusion and the
demographics of the study population may also mask selection bias [98, 99].
3.5. Conclusion

This structured literature review confirms the current lack of evidence regarding the effect on patient-reported outcomes of delayed union or nonunion of femoral and tibial shaft fractures in adult patients. In particular, there has been no study that has directly compared the health outcomes of patients with nonunion and normal union. It also highlights several methodological flaws in the existing literature. Future research should employ an appropriate study design with a control group, investigate similar types of fractures only, use a practical definition of delayed union and nonunion, and record a valid and reliable outcomes measurement.
SECTION THREE – THE STUDY

CHAPTER 4: OBJECTIVES

Primary Aims
1. To investigate the physical and mental health of patients with delayed union or nonunion of femoral and tibial shaft fractures at 6 and 12 months post injury.
2. To determine the return to work and pain status of patients with delayed union or nonunion of femoral and tibial shaft fractures at 6 and 12 months post injury.
3. To compare the aforementioned outcomes to patients with normal union.

Secondary Aims
1. To describe the patient demographics and injury profile of femoral and tibial shaft fractures treated at two level I adult trauma centres.
2. To compare these characteristics between patients with delayed union or nonunion and patients with normal union.
CHAPTER 5: PATIENTS AND METHODS

A retrospective analysis of prospective registry data, supplemented with patient medical record review, was conducted. Patients were selected from the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR) database with approval of the respective hospital ethics committees.

VOTOR includes all patients with orthopaedic injuries admitted to the two level I adult trauma centres in Victoria, Australia [104]. Participants were recruited into VOTOR using an opt-off method of consent, whereby all eligible patients are automatically registered upon admission and given the option to withdraw from the registry at any time [104]. Patients were enrolled in the registry from August 2003 to August 2004, and again from February 2005 to July 2006 [104]. The 5 months gap between the two sample collection periods was due to temporary funding issues with the registry.

Patients were shortlisted from the VOTOR database using the Abbreviated Injury Scale 1990 Revision [105] (AIS 90) and International Statistical Classification of Diseases and Related Health Problems Tenth Revision Australian Modification [106] (ICD-10-AM) codes listed in the Appendices. This list of injury codes was purposely kept inclusive to make sure that no potential patients were missed. The injury details recorded in the VOTOR database for each patient were then manually checked to identify relevant fractures for medical record review. All femoral and tibial fractures with a diagnosis description of fracture of the shaft or diaphysis, and a Müller AO classification of 32 and 42 were selected for study. In addition, all fractures with the AIS 90 codes 851814.3, 853420.2 and 853422.3 were included to ensure complete capture of all femoral and tibial shaft fractures.

Exclusion criteria included patients who sustained a pathological fracture or whose injury was managed by a non-orthopaedic team [104], fractures with joint involvement, and fractures in a subsequently amputated limb or in a patient deceased within 6 weeks post injury. Figure 4 illustrates the patient inclusion process.
Fracture healing was assessed by clinical and radiological evidence of union. The indication and timing for surgical intervention was determined by reviewing hospital medical records. Evidence of clinical union included the absence of tenderness at the fracture site and the ability to bear full weight on that limb without pain [107]. A fracture was deemed to have evidence of radiological union by the presence of adequate callus bridging the fracture site and disappearance of the fracture line [107, 108]. The earliest timing for surgery for delayed union was set at 6 weeks post fracture based on common local practice and included nail dynamisation. A fracture was considered to have progressed to nonunion if it required surgical intervention at greater than 6 months after injury, given that the...
majority of united fractures should have achieved the aforementioned clinical and radiological milestones. The outcome of a fracture was regarded as unknown if follow-up was for less than 12 weeks or if their clinical and radiological progress were unclear in the patient’s records.

Health, work and pain status were prospectively recorded at 6 and 12 months post injury as part of the VOTOR follow-up protocol [104]. The health status of patients was assessed using the SF-12, which has been tested for reliability [109-112] and validated for use within the Australian population [113] and in trauma patients [114]. Responses from the 12 questions in the self-reported survey are used to calculate a Physical Component Summary (PCS) and a Mental Component Summary (MCS) score, which correspond to the physical and mental health status of respondents, respectively [112, 115]. Each component is scored between 0 and 100, with higher scores indicating better health [112, 115] and a total greater than 50 representing no disability [116].

Patients were also asked whether they had returned to any form of work and whether they still had any pain from their injury [104]. Participants were interviewed by a trained research nurse [104]. Four contact attempts were made before a patient was considered lost to follow-up [104].

Patient demographics and injury details, including age, gender, fund source, mechanism of injury, open or closed fracture, and the Gustilo classification for open fractures, were retrieved from the VOTOR database. Hospital records were reviewed to determine other injuries and the cigarette smoking status of patients. To categorise other injuries, patients were identified as having sustained an isolated injury or multitrauma (other than ipsilateral extra-articular fractures of the fibula associated with fractures of the tibia, minor abrasions or lacerations, or loss of consciousness for less than 30 minutes without neurological sequelae) with and without head injury. Head injury was defined as having evidence of traumatic cerebral oedema, diffuse or focal brain injury, or intracranial haemorrhage.
In addition, the Charlson Comorbidity Index [117, 118] (CCI) was calculated for each patient using the ICD-10-AM diagnosis codes assigned for that admission. This was utilised as an aggregate measure of a patient’s general health.

The data was analysed using the statistical software package, Stata [119]. The p values for the categorical variables were calculated using Pearson’s chi-squared and Fisher’s exact two-tailed tests. The SF-12 PCS and MCS scores were analysed by linear regression modelling to calculate a correlation coefficient. The return to work and pain status results were analysed by logistic regression modelling to calculate a risk ratio. Multivariate analysis was employed to account for other variables.
CHAPTER 6: RESULTS

6.1. Fracture Outcomes
423 fractures had a known healing end point that was eligible for assessment of their patient-reported outcomes. From this sample, 285 fractures (67%) progressed to union and 138 fractures (33%) developed delayed union or nonunion. 119 fractures developed malunion or had an unknown outcome and were excluded from further analysis. The outcomes of the fractures selected for evaluation are summarised in Figure 5.

Figure 5: Flowchart of fracture outcome review

<table>
<thead>
<tr>
<th>Total fractures included for outcome review: <strong>542 fractures</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of hospital medical records</td>
</tr>
<tr>
<td>Excluded: <strong>119 fractures</strong></td>
</tr>
<tr>
<td>Malunion: 4 fractures</td>
</tr>
<tr>
<td>Unknown: 115 fractures</td>
</tr>
<tr>
<td>Total fractures included for outcome analysis: <strong>423 fractures</strong></td>
</tr>
<tr>
<td>Union: <strong>285 fractures</strong> (67%)</td>
</tr>
<tr>
<td>Delayed union or nonunion: <strong>138 fractures</strong> (33%)</td>
</tr>
</tbody>
</table>
6.2. Follow-up

The patient follow-up rates of each health outcome measured for the two study groups are shown in Table 2. The lowest response rate for the SF-12 was 72% for patients with delayed union or nonunion at 6 months following fracture. At least 65% of patients in both groups at 6 months post injury reported their work status. The lowest follow-up rate for pain status was 70% for patients with delayed union or nonunion at the 6 months interview.

Table 2: Follow-up rates (%) of health outcomes

<table>
<thead>
<tr>
<th>Health Outcome</th>
<th>Union</th>
<th>DU/NU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 285</td>
<td>n = 138</td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>76</td>
<td>72</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>76</td>
<td>72</td>
</tr>
<tr>
<td>RTW</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Pain</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>74</td>
<td>77</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>74</td>
<td>77</td>
</tr>
<tr>
<td>RTW</td>
<td>71</td>
<td>76</td>
</tr>
<tr>
<td>Pain</td>
<td>74</td>
<td>77</td>
</tr>
</tbody>
</table>

DU/NU = delayed union or nonunion  
PCS = Physical Component Summary  
MCS = Mental Component Summary  
RTW = return to work
6.3. Patient Demographics

The demographic distribution of patients in the union group compared to patients in the delayed union or nonunion group is shown in Table 3. The majority of fractures were sustained by male patients less than 65 years old. There was no significant difference in the age (p value 0.216) or gender (p value 0.148) allocation between patients in either study cohort.

Table 3: Patient demographics

<table>
<thead>
<tr>
<th></th>
<th>Union (%)</th>
<th>DU/NU (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>251 (88)</td>
<td>127 (92)</td>
<td>0.216</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>202 (71)</td>
<td>107 (78)</td>
<td>0.148</td>
</tr>
<tr>
<td>Fund source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compensable</td>
<td>205 (72)</td>
<td>115 (83)</td>
<td>0.010</td>
</tr>
<tr>
<td>Cigarette smoking¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>95 (41)</td>
<td>66 (53)</td>
<td>0.006</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, 2, 3 or 6</td>
<td>59 (21)</td>
<td>45 (33)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

¹Smoking status documented: Union n = 231, DU/NU n = 125

The larger proportion of injuries was compensable. This consisted of 72% of fractures in the union group compared to 83% of fractures that required surgical intervention for delayed union or nonunion (p value 0.010).

The smoking status of patients was documented for 356 fractures. 41% of patients in the union group were smokers compared to 53% of patients who progressed to delayed union or nonunion (p value 0.006).

The majority of fractures occurred in healthy patients. 21% of patients with union had one or more comorbidities compared to 33% of patients with delayed union or nonunion (p value 0.011).
6.4. Injury Profile

The injury profile for the two fracture healing outcome groups is shown in Table 4. Most fractures were the result of a road traffic accident. 73% of fractures with union were caused by a road vehicle injury compared to 86% of fractures with delayed union or nonunion (p value 0.007).

The larger proportion of injuries resulted from multitrauma. 46% and 15% of fractures that united were part of multitrauma with and without head injury, respectively. In comparison, 59% and 7% of fractures that required surgical intervention for delayed union or nonunion belonged to patients who sustained multitrauma with and without head injury, respectively (p value 0.015).

Table 4: Injury profile

<table>
<thead>
<tr>
<th></th>
<th>Union (%)</th>
<th>DU/NU (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Road traffic accident</td>
<td>208 (73)</td>
<td>119 (86)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Injury</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multitrauma without head injury</td>
<td>132 (46)</td>
<td>82 (59)</td>
<td>0.015</td>
</tr>
<tr>
<td>Multitrauma with head injury</td>
<td>43 (15)</td>
<td>10 (7)</td>
<td></td>
</tr>
<tr>
<td><strong>Wound</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open</td>
<td>85 (30)</td>
<td>60 (43)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Gustilo classification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>17 (27)</td>
<td>30 (63)</td>
<td>0.000</td>
</tr>
<tr>
<td><strong>Fixation method</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramedullary nail</td>
<td>244 (86)</td>
<td>121 (88)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

1Gustilo classification documented: Union n = 62, DU/NU n = 48

30% of fractures in the union cohort were open injuries compared to 43% of fractures with delayed union or nonunion (p value 0.006). The Gustilo classification was recorded for 110 out of 145 open fractures. 27% of fractures with normal union were grade III compared to 63% of fractures with delayed union or nonunion (p value 0.000). Most fractures in both outcome groups were fixed using an intramedullary nail.
6.5. SF-12 Physical and Mental Health

The SF-12 PCS and MCS median scores at 6 and 12 months post injury for patients with normal union and with delayed union or nonunion are shown in Table 5, together with their respective correlation coefficient values unadjusted and adjusted for other variables.

Table 5: Linear regression of effect of DU/NU on SF-12 median scores

<table>
<thead>
<tr>
<th></th>
<th>Union (IQR)</th>
<th>DU/NU (IQR)</th>
<th>Unadjusted coefficient (95% CI)</th>
<th>Adjusted¹ coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6² PCS</td>
<td>37 (16)</td>
<td>31 (10)</td>
<td>-6.67 (-9.40, -3.93)</td>
<td>-7.09 (-9.79, -4.39)</td>
</tr>
<tr>
<td>6 MCS</td>
<td>56 (15)</td>
<td>52 (24)</td>
<td>-4.60 (-8.26, -0.95)</td>
<td>-5.38 (-8.93, -1.83)</td>
</tr>
<tr>
<td>12³ PCS</td>
<td>44 (22)</td>
<td>32 (18)</td>
<td>-6.96 (-9.65, -4.26)</td>
<td>-7.33 (-9.89, -4.76)</td>
</tr>
<tr>
<td>12 MCS</td>
<td>56 (13)</td>
<td>51 (19)</td>
<td>-3.00 (-5.59, -0.41)</td>
<td>-3.25 (-5.78, -0.72)</td>
</tr>
</tbody>
</table>

IQR = interquartile range  
CI = confidence interval  
¹For age, gender and multiple injuries  
²6 months post injury  
³12 months post injury

The PCS median scores were less than 50 in both outcome groups at the two follow-up periods. There was a noticeable improvement in PCS scores from 6 to 12 months following injury in the union cohort. In contrast, the MCS median scores were greater than 50 at both follow-up interviews for the two study arms and did not significantly change from 6 to 12 months post fracture.

Patients in the union group scored higher in all categories compared to patients with delayed union or nonunion. These differences were significant (95% confidence) unadjusted and adjusted for age, gender and multiple injuries.
6.6. Return to Work and Pain

The return to work and pain status at 6 and 12 months post injury of patients with normal union compared to patients with delayed union or nonunion is shown in Table 6, together with their respective risk ratios unadjusted and adjusted for other variables. This analysis did not include 34 patients in the union group and 11 patients in the delayed union or nonunion group, who reported that they were not working prior to their fracture.

Table 6: Logistic regression of effect of DU/NU on return to work and pain

<table>
<thead>
<tr>
<th></th>
<th>Union (%)</th>
<th>DU/NU (%)</th>
<th>Unadjusted risk ratio (95% CI)</th>
<th>Adjusted risk ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 285</td>
<td>n = 138</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 RTW</td>
<td>97/186 (52)</td>
<td>40/90 (44)</td>
<td>0.85 (0.62, 1.09)</td>
<td>0.82 (0.59, 1.08)</td>
</tr>
<tr>
<td>6 Pain</td>
<td>146/215 (68)</td>
<td>71/96 (74)</td>
<td>1.09 (0.92, 1.22)</td>
<td>1.11 (0.94, 1.24)</td>
</tr>
<tr>
<td>12 RTW</td>
<td>145/202 (72)</td>
<td>62/105 (59)</td>
<td>0.82 (0.65, 0.98)</td>
<td>0.76 (0.57, 0.94)</td>
</tr>
<tr>
<td>12 Pain</td>
<td>114/212 (54)</td>
<td>76/106 (72)</td>
<td>1.33 (1.13, 1.50)</td>
<td>1.37 (1.16, 1.54)</td>
</tr>
</tbody>
</table>

1 For age, gender and multiple injuries

At 6 months post injury, 52% of patients in the union group had returned to work, which increased to 72% by 12 months. In comparison, 44% of subjects with delayed union or nonunion had resumed employment at 6 months. This improved to 59% at the final interview. The difference between the two groups at 12 months was significant (95% confidence) with a risk ratio of 0.82 and 0.76 for patients with delayed union or nonunion to return to work, unadjusted and adjusted for age, gender and multiple injuries, respectively.

Patients with union and with delayed union or nonunion continued to complain of pain in 68% and 74% of cases, respectively, at 6 months following fracture. At 12 months, 54% of patients with union had ongoing pain, while this was reported in 72% of patients with delayed union or nonunion. This difference was significant (95% confidence) at 12 months with a risk ratio of 1.33 and 1.37 for patients with delayed union or nonunion to complain of pain, unadjusted and adjusted for age, gender and multiple injuries, respectively.
Despite modern advances in intramedullary fixation and established treatment practices, the health outcomes of patients with lower limb long bone shaft fractures do not return to normal. Even patients who achieve union of their fracture can expect to have residual physical disability during the first year post injury. In addition, just over one half of individuals will have returned to some form of work at 6 months, and a similar proportion of patients will continue to have pain at 12 months. Not surprisingly, patients with delayed union or nonunion of their femoral and tibial shaft fractures fare even worse. They can expect greater physical impairment than if their fracture had healed without complication during their first year post injury. These patients are similarly more likely to remain unemployed and have pain at 12 months. This is of particular concern given that nearly one third of lower limb long bone shaft injuries treated at a tertiary trauma centre will develop delayed union or nonunion. This incidence is comparable to other Australian study cohorts [45, 65].

Reasons for the poorer health status of patients with delayed or nonunion are probably multifactorial. They include the direct debilitating effects from a painful ununited fracture, and the extra recovery required from multiple surgeries and extended rehabilitation. These patients are more likely to have sustained higher energy trauma and have other injuries or open wounds, which would further contribute to their poorer physical health. Frustration and personal loss may also arise from the disruption to the patient’s life while undergoing prolonged treatment and recuperation, which can adversely affect their relationships and career. This can be demoralising and difficult for the patient and their family to comprehend, especially when there may be a lay perception of their orthopaedic injury as simply a “broken bone” that is acute, “fixable” and without sequelae.

Interestingly, the SF-12 did not demonstrate any disability resulting from the mental health of patients with lower extremity long bone shaft fractures. These findings are consistent with a previous outcomes study of isolated tibial shaft fractures [120], and infer that the preliminary effects of these injuries during the recovery phase are primarily physical. Alternatively, the SF-12 may not have
been sensitive enough, despite the typical anecdotal experience of most surgeons that patients are also affected psychologically and socially by their traumatic injuries.

The patient and injury profile of our sample population was consistent with the literature. Patients who were smokers or had medical comorbidities were more likely to have fracture healing problems [1, 2]. High energy trauma, such as from road traffic accidents, open injuries and Gustilo grade III fractures, likewise recorded higher rates of delayed union and nonunion [1, 2]. In keeping with the abundant callus healing response commonly seen post brain injury [121], patients with associated head trauma showed the lowest rate of delayed union and nonunion.

Perhaps as a predictor for surgical intervention, patients whose treatment were compensable were also more likely to be reoperated on for their delayed union or nonunion. Potential explanations for this trend include easier access to surgery, since patients may be referred to private hospitals for their operation, and greater financial incentive for the surgeon to operate.

There are few trauma registries in the world that monitor patient-reported outcomes. Our study’s strength was the use of prospectively-collected data, which minimises bias from retrospective review and allows for follow-up at uniform time points. In addition, our sample data was obtained from the two major trauma centres in the state, which can be considered representative of the wider population and the accepted standard of care in Australia.

Our study’s main weakness was the retrospective identification of the healing outcomes of fractures by reviewing hospital medical records. Because of the lack of consensus in the assessment of fracture healing among surgeons [72] and to minimise the need for subjective interpretation of patients’ notes, surgical intervention was used as the major criterion for establishing a fracture with delayed union or nonunion. However, the decision making for surgery may have biased our analysis. For example, although the SPRINT trial showed no effect of dynamisation on union for tibial fractures [64], this was published after our study
recruitment and surgeons may have regularly dynamised the nail after 6 weeks post injury. The authors were blinded to all patient-reported outcomes during the patient inclusion and fracture outcome review process.

In our study, patients with delayed union and nonunion, femoral and tibial fractures, and isolated and multiple injuries were considered together. This limits this paper’s comparability with other data and can lead to bias from confounding factors. Patients with delayed union and nonunion were analysed collectively, since both conditions derive from the same disease process and only differ in temporal relation. Given their similar aetiology for fracture and function as the two weight bearing long bones in the lower limbs, the femur and tibia were also categorised together. To reduce confounding, comparison with a larger control group using multivariate analysis to adjust for other variables, including age, gender and multiple injuries, was employed.

Non-responder bias due to loss to follow-up is a further inevitable limitation of this study. The response rate of participants were maximised by a thorough follow-up protocol, which included multiple contact attempts via both telephone and post [104]. The follow-up rates for this project compared favourably to the overall rates for VOTOR and other prospective orthopaedic trauma registries [29, 114, 122].

It is essential that patients with lower extremity long bone shaft fractures are informed about the consequences of their injury, including delayed fracture healing and prolonged recovery. This will help patients to appreciate the severity and potential chronicity of their condition, and in turn motivate their compliance with therapy. The findings from this study may be used to educate patients’ expectations regarding their physical recovery and its practical implications like returning to work. This is particularly relevant given that the patients most likely to sustain femoral or tibial shaft fractures are working-age and previously healthy adults, and would also provide invaluable information to employers, insurers and other stakeholders.
At the same time, surgeons and physicians can utilise this prognostic data on patients’ functional outcomes as a basis for future research in treatment methods and rehabilitation programs. Surgeons should also be mindful to allow increased time for tibial shaft fractures to heal before intervening [64], as repeated surgeries may cause harm and paradoxically slow the patient’s recovery. In contrast, more aggressive surgical intervention may be necessary for patients at increased risk of nonunion. For example, open fractures sustained from high energy trauma with segmental bone loss may require early and staged bone grafting. Rehabilitation programmes should include vocation retraining and optimising pain management to assist patients to return to their premorbid function.

Future studies evaluating the patient-reported outcomes of delayed union or nonunion should ideally be carried out utilising a prospective study design, and be measured by both disease-specific and generic health questionnaires. However, acknowledging its limitations and using the current data available, separate subanalysis of patients with delayed union and nonunion, femoral and tibial shaft fractures, and isolated injuries and multitrauma should firstly be conducted to properly eliminate confounding from multiple variables. This would also improve the applicability of the data to more specific patient groups. To increase the power and generalisability of the study, patients enrolled by VOTOR at subsequent phases of data collection, including at sentinel hospitals, can be recruited.

Given its relatively common incidence, routine identification of patients with potential delayed union or nonunion as part of the VOTOR data collection protocol may be a practical consideration in the long term, in particular for tibial shaft fractures. For example, patients could be asked at their 6 and 12 months follow-up whether they had undergone any further surgery and if so have relevant details recorded. Furthermore, longer follow-up for such patients may be appropriate, since the sequelae of fracture nonunion remain considerable at one year post injury as highlighted by this thesis.

The VOTOR database is an extremely powerful resource, which could also be employed to formally investigate the predictors of delayed union and nonunion of
femoral and tibial shaft fractures. Knowledge about local population factors and practice methods could be useful to guide specific risk reduction strategies.
CHAPTER 8: CONCLUSION

The patients most likely to sustain femoral or tibial shaft fractures are working-age healthy adults. Up to one third of these fractures treated at a major trauma centre will develop delayed union or nonunion. Potential predictors of reoperation for impaired fracture healing include high energy or multitrauma without head injury, open fractures and a high Gustilo classification grade. Patient factors, such as smoking, having other comorbidities and being insured for treatment, are similarly associated with reoperation.

The patient-reported outcomes of lower limb long bone shaft fractures do not return to normal at one year. Even patients whose fractures unite in the expectant time frame will have residual physical disability. One in four patients will not have returned to work at 12 months post injury, and one in two will continue to have pain. Patients with delayed union or nonunion can expect poorer health outcomes. It is important to educate patients and their family about their injury so that they have realistic expectations. Their prognosis is also relevant for resource planning for employers and insurers.
SECTION FOUR – REFERENCES


55. Karladani AH, Granhed H, Kärrholm J, Styf J. The influence of fracture etiology and type on fracture healing: a review of 104 consecutive tibial


64. **Bhandari M, Guyatt GH, Tornetta III P, Schemitsch EH, Swiontkowski MF, Sanders D, Walter SD.** *Randomized trial of reamed and unreamed


83. **United States Food and Drug Administration.** Guidance document for the preparation of investigational device exemptions and pre-market approval


120. Dogra AS, Ruiz AL, Marsh DR. Late outcome of isolated tibial fractures treated by intramedullary nailing: the correlation between disease-specific


### A.1. AIS 90 codes used to search the VOTOR database

<table>
<thead>
<tr>
<th>Code</th>
<th>Injury Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>851800.3</td>
<td>Femur fracture not further specified as to site</td>
</tr>
<tr>
<td>851801.3</td>
<td>open/displaced/comminuted (any or combination)</td>
</tr>
<tr>
<td>851810.3</td>
<td>intertrochanteric</td>
</tr>
<tr>
<td>851814.3</td>
<td>Shaft</td>
</tr>
<tr>
<td>851818.3</td>
<td>subtrochanteric</td>
</tr>
<tr>
<td>851822.3</td>
<td>supracondylar</td>
</tr>
<tr>
<td>852002.2</td>
<td>Leg fracture not further specified</td>
</tr>
<tr>
<td>853499.1</td>
<td>Tibia not further specified</td>
</tr>
<tr>
<td>853404.2</td>
<td>fracture not further specified as to site</td>
</tr>
<tr>
<td>853405.3</td>
<td>open/displaced/comminuted (any or combination)</td>
</tr>
<tr>
<td>853420.2</td>
<td>Shaft</td>
</tr>
<tr>
<td>853422.3</td>
<td>open/displaced/comminuted (any or combination)</td>
</tr>
</tbody>
</table>
A.2. ICD-10-AM codes used to search the VOTOR database

<table>
<thead>
<tr>
<th>Code</th>
<th>Injury Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S72</td>
<td>fracture of femur</td>
</tr>
<tr>
<td>S72.1</td>
<td>pertrochanteric fracture</td>
</tr>
<tr>
<td>S72.10</td>
<td>fracture of trochanteric section of femur, unspecified</td>
</tr>
<tr>
<td>S72.11</td>
<td>fracture of intertrochanteric section of femur</td>
</tr>
<tr>
<td>S72.2</td>
<td>subtrochanteric fracture</td>
</tr>
<tr>
<td>S72.3</td>
<td>fracture of shaft of femur</td>
</tr>
<tr>
<td>S72.4</td>
<td>fracture of lower end of femur</td>
</tr>
<tr>
<td>S72.40</td>
<td>fracture of lower end of femur, part unspecified</td>
</tr>
<tr>
<td>S72.43</td>
<td>supracondylar fracture of femur</td>
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<tr>
<td>S72.44</td>
<td>intercondylar fracture of femur</td>
</tr>
<tr>
<td>S72.7</td>
<td>multiple fractures of femur</td>
</tr>
<tr>
<td>S72.8</td>
<td>fractures of other parts of femur</td>
</tr>
<tr>
<td>S72.9</td>
<td>fracture of femur, part unspecified</td>
</tr>
<tr>
<td>S82</td>
<td>fracture of lower leg, including ankle</td>
</tr>
<tr>
<td>S82.1</td>
<td>fracture of upper end of tibia</td>
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<tr>
<td>S82.11</td>
<td>fracture of upper end of tibia with fracture of fibula (any part)</td>
</tr>
<tr>
<td>S82.18</td>
<td>other fracture of upper end of tibia</td>
</tr>
<tr>
<td>S82.2</td>
<td>fracture of shaft of tibia</td>
</tr>
<tr>
<td>S82.21</td>
<td>fracture of shaft of tibia with fracture of fibula (any part)</td>
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<tr>
<td>S82.28</td>
<td>other fracture of shaft of tibia</td>
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<tr>
<td>S82.3</td>
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<td>fracture of lower end of tibia with fracture of fibula (any part)</td>
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<td>S82.38</td>
<td>other fracture of lower end of tibia</td>
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<td>S82.7</td>
<td>multiple fractures of lower leg</td>
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<td>S82.8</td>
<td>fractures of other parts of lower leg</td>
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<td>S82.88</td>
<td>fracture of other parts of lower leg</td>
</tr>
<tr>
<td>S82.9</td>
<td>fracture of lower leg, part unspecified</td>
</tr>
</tbody>
</table>
Author/s: TAY, WEI-HAN

Title: Health outcomes of delayed union and nonunion of femoral and tibial shaft fractures

Date: 2015

Persistent Link: http://hdl.handle.net/11343/55300

File Description: Health outcomes of delayed union and nonunion of femoral and tibial shaft fractures