PREDICTORS OF PHYSICAL FUNCTIONING FOLLOWING INTRAMEDULLARY NAILING OF TIBIAL SHAFT FRACTURES

PREDICTORS OF PHYSICAL FUNCTIONING FOLLOWING INTRAMEDULLARY NAILING OF TIBIAL SHAFT FRACTURES

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ABSTRACT

Tibia fractures are common injuries that have overwhelming consequences on patients in terms of pain and function. Tibia fracture fixation can deliver excellent outcomes; however, the physical function of this patient population could vary. The purpose of my thesis was to explore modifiable and non-modifiable factors that influence the physical health-related quality of life in this patient population, thus, allowing patients and surgeon tailor management accordingly.

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DECLARATION OF ACADEMIC ACHIEVEMENT

I, Fawaz Findakli, hereby declare that I was significantly involved in the design, analysis, interpretation of data, and drafting manuscripts of the enclosed thesis, titled Predictors of Physical Functioning Following Intramedullary Nailing of Tibial Shaft Fractures. I have completed this thesis under the supervision of Dr. Mohit Bhandari.

My co-authors also made important contributions to this thesis and have been acknowledged and listed.

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Predictors of Physical Functioning Following Intramedullary Nailing of Tibial Shaft Fractures

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ABSTRACT

Background: Tibial fractures are associated with prolonged recovery. The aim of this study was to identify predictors of long-term physical functioning after tibial shaft fracture.

Methods: We used data from the Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST) to determine, in patients with unilateral, open or closed tibial shaft fracture, the association between baseline factors and physical functioning at 1-year. All fractures were fixed using intramedullary nails. Physical functioning was measured using the 100-point Short Form-36 (SF-36) Physical Component Summary (PCS) score; higher is better; minimally important difference is 2 to 5 points.

Results: There were 299 tibial fracture patients with complete data available for analysis. In an adjusted analysis, the factors associated with lower physical functioning at 1-year were: (1) current smokers (mean difference [MD] -2.55, 95% confidence interval [95%CI] -4.63 to -0.46, p=0.017), (2) body mass index >30 kg/m² (MD -2.57, 95% CI -4.86, -0.27, p = 0.029), and (3) patients who were receiving disability benefits or involved in litigation, or planned to be (MD -2.65, 95% CI -4.58 to -0.72, p = 0.007). Patients who were employed at the time of their fracture reported significantly higher physical functioning at 1-year (MD 4.56, 95% CI 2.32 to 6.80, p= <0.001) and those who were allowed to partial or full weight-bear post-operatively (MD 1.98, 95% CI 0.13 to 3.82, p=0.036). Neither age, sex, fracture severity or receipt of physical therapy were associated with long-term physical functioning.

Conclusions: Among patients undergoing surgical repair of tibial fractures, partial or full weight-bearing post-operatively and employment at the time of injury predict better long-term functioning, whereas smoking, obesity, and receipt of disability benefits or involvement in litigation (or plans to be) predict worse long-term functioning.

BACKGROUND

Forty percent of adult long bone fractures involve the tibia [1], with an estimated incidence of 17/100,000/year in the developed world [2, 3]. The incidence of tibial fractures is expected to rise in countries with developing economies due to the growth in loosely-regulated and unsafe public transport [4]. Patients undergoing tibia fracture fixation may experience adverse events, such as prolonged knee pain [5, 6], muscle weakness [7], reoperation [8], and angular malalignment [9]. Moreover, a number of studies have reported variable outcomes regarding health-related quality of life (HRQL) following tibial fractures [10-12].

For example, a cross-sectional study of 49 tibial fracture patients, one-year after injury, found significant limitations in activities and restrictions in quality of life when compared to a reference population [Larsen, 2016]. Another investigation of 1319 tibial fracture patients found that functional outcomes at one year, as measured by the short-form 36 (SF-36) physical component summary (PCS) score, were significantly below pre-injury scores in patients with reamed (42.8 vs. 52.4, 95% CI of the difference -10.8 to -8.4, $P < 0.001$) and unreamed tibias (43.7 vs. 52.9, 95% CI, –10.5 to -7.9, $P < 0.001$) [13]. The identification of prognostic factors associated with long-term physical function could help inform optimal treatment after fracture. We aimed to identify baseline, surgical, and treatment characteristics associated with long-term physical function after tibial fracture repair.

METHODS

Study Design

This study utilized data from the Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST) [14]. A randomized, blinded, sham controlled clinical trial of 501 participants who were allocated centrally to self-administer daily low intensity pulsed ultrasound

(LIPUS) or a sham device, and were followed for one year. The primary outcomes were time to radiographic healing and short form-36 (SF-36) physical component summary (PCS) scores. A blinded interim analysis showed no differences in SF-36 PCS scores and time to radiographic healing between treatment groups, and the study sponsor terminated the study early due to futility. The TRUST trial protocol was approved by the McMaster University research ethics board (REB#08-171) and local boards at 42 participating trauma centers in Canada and United States. This trial was registered at www.clinicaltrials.gov with the identifier: NCT00667849.

Skeletally mature patients with an open (Gustilo type I – III B) or closed (Tscherene grade 0-3) tibial fracture amenable to intramedullary nail fixation were eligible for enrollment in the TRUST trial. The exclusion criteria were: 1) pilon fractures, 2) tibial shaft fractures extending into the knee or ankle joint and requiring reduction, 3) pathologic fractures, 4) bilateral tibial fractures, 5) segmental fractures, 6) spiral fractures >7.5 cm in length, 7) concomitant injuries that were likely to impair function for at least as long as the patients tibial fracture, 8) tibial fractures that showed less than 25% cortical contact and >1 cm gap after intramedullary nail fixation, 9) likely problems with maintaining follow-up, 10) patients with cognitive impairment or language difficulties, 11) women who were pregnant or nursing or planned to become pregnant during their enrollment period, 12) patients with osteobiologics or implants at the site of their tibial fracture or with active implanted devices such as cardiac pacemakers.

Measuring Physical Functioning

We measured physical function via SF-36 PCS scores at 1-year post-surgery. The SF-36 is a widely accepted, well-validated [15, 16] instrument which measures quality of life across eight domains, including: physical functioning; role limitations due to physical health; role limitations due to emotional problems; energy/fatigue; emotional well-being; social functioning; pain; general health. These scores can be aggregated into physical and mental summary scores. SF-36 PCS scores range from 0 (worst possible function) to 100 (best possible function). The minimal important difference (MID) for PCS scores in an orthopedic population have been estimated to range from 2-5 points [16-18].

Selection of Prognostic Factors

We identified 10 factors potentially associated with PCS scores at 1-year from data collected as part of the TRUST trial, based on biological and clinical rationale and reference to previous literature [35-37, 40]: (1) age, by decade as a continuous variable; (2) gender [male vs. female]; (3) current smoker [yes vs. no]; (4) employment status [employed at time of injury vs. not]; (5) body mass index (BMI) [18-25 kg/m² vs. 25-30 kg/m² vs. > 30 kg/m²]; (6) fracture type [open vs. closed]; (7) post-operative weight bearing status [non-weight-bearing vs. partial or full weight bearing]; (8) receiving disability benefits or lawyer/litigation involvement [yes or likely I will vs. no or its possible I will]; (9) receipt of physiotherapy by 6 weeks [yes vs. no]. We also adjusted for interventions administered in the TRUST study: LIPUS and sham therapy [14].

Statistical Analysis

We reported the mean and standard deviation of continuous variables, and the frequency of occurrences and percentages for categorical variables. We constructed a linear regression model to explore the association between our independent factors and SF-36 PCS scores at 1-year post-surgery. All participants with incomplete data were excluded from the analysis, and all potential prognostic factors were entered simultaneously into the model. We calculated that we would require at least 100 patients with complete data in order to avoid over-fitting our regression model (10 respondents for each level of independent variable considered) [19]. We excluded independent variables with fewer than 50 observations, unless we were able to collapse them with other related variables to exceed this threshold.

We tested for multicollinearity between included variables using the Variance Inflation Factor (VIF) statistic, and excluded variables with a VIF $\geq$5. We reported mean differences (MDs) with associated 95% confidence intervals (CIs) and p-values for all predictors. Overall goodness-of-fit of the model was assessed using the R^2 value. This value reflects the amount of variance in the dependent variable that is explained by the predictors in the model. In addition, F-test was performed and overall significance of the model was determined. All analyses were performed using IBM SPSS Statistics for Macintosh, version 25 (IBM Corp., Armonk, N.Y., USA) using 2-tailed tests with a significance level of alpha=0.05.

RESULTS

Of 501 eligible patients enrolled in TRUST, 73 patients were followed up for fewer than 12 months as a result of the industry sponsor's decision to stop the study early. Of the remaining 428 patients, 299 (69.9%) provided complete baseline data and completed the SF-36 questionnaire at 1-year follow-up, and were included in our analysis. Study patients were in their 30s and 40s (mean [SD], 39.4 [13.9]) and predominantly male (65.6%; 196 of 299). The incidence of current smokers was 29.1% (87 of 299) with a 4.7% rate of diabetes (14 of 299). The majority of included patients were employed (75.9%, 227 of 299). One in five tibial fractures were open (20.4%, 61 of 299), of which, 13 patients suffered Gustilo-Anderson types IIIA and IIIB. Baseline characteristics were similar between patients eligible for our study and all patients enrolled in the TRUST trial. (**Table 1**)

In our adjusted model, partial or full weight-bearing post-operatively (MD 1.98, 95% CI 0.13 to 3.82) and employment at the time of injury (MD 4.56, 95% CI 2.32 to 6.80) were associated with greater physical functioning at 1-year follow-up. Three factors were associated with lower SF-36 PCS scores at 1-year: (1) current smoker (MD -2.53, 95% CI -4.62 to -0.44); (2) obesity (MD for BMI >30 kg/m² -2.42, 95% CI -4.75, -0.10); and (3) receiving, or very likely to receive, disability benefits or engage in litigation (MD -2.69, 95% CI -4.62 to -0.75) (**Table 2**). Standardized residual plots showed no violation of model assumptions. The variance inflation factor was less than 5 for each independent variable, suggesting no issues with multicollinearity. Our model explained approximately 15% of the variation (adjusted $R^2 = 0.152$) in SF-36 PCS scores at 1-year postsurgical fixation. The F-test showed that the model is significant $p<0.001$ at 11 and 286 degrees of freedom (the total number of independent values estimated), thus, our model provides a better fit than the intercept-only model.

DISCUSSION

We found that current smokers, obese patients (BMI >30 kg/m²), and receiving disability benefit or being involved with a lawyer (or plans to be) were associated with lower physical function one year after surgical fixation of tibial fractures. Being employed at the time of injury and partial or full weight-bearing post-operatively were significantly associated with higher physical function at 1-year. Fracture severity (open vs. closed), age, sex or receipt of physical therapy was not associated with long-term physical functioning.

Our participants' characteristics are comparable to those of other studies on patients with tibial shaft fractures in terms of age, gender distribution, and smoking status [20, 9]. Our findings are consistent with other studies that have found smoking negatively impacts outcomes of orthopedic patients due to impaired wound healing [21], higher rates of surgical site and deep wound infection [22], and increased risk of nonunion [23]. Moreover, smoking is associated with lower HRQL in other disease groups [24, 25] and in the general population [26, 27].

In the absence of comorbidities, patients with higher BMI do not seem to have higher postoperative complication rates when compared to those with normal weight [28]. However, similar to previous studies [29-31], we also found that obesity is associated with lower physical functioning after surgery, suggesting that BMI is a modifiable factor that surgeons could emphasize its importance to patients at risk.

Our finding that receipt of disability benefits or involvement in litigation, or plans to do so, were associated with worse long-term function is consistent with a systematic review on this topic [32]. Specifically, a meta-analysis of 129 studies revealed that the odds of an unsatisfactory outcome in surgical patients receiving disability benefits or engaged in litigation was 3.79 times greater (95% CI 3.28 to 4.37) versus similar patients not in receipt of disability benefits or pursuing litigation. We also found that being employed was associated with higher 1-year SF-36 PCS scores. Reasons for this are not clear; however, many TRUST patients were recruited from US trauma centers and most US workers have access to health care insurance through their employer [33]. Most personal bankruptcies in the US are the result of medical expenses [34], and fear of losing health insurance is likely a powerful incentive to pursue recovery and return to work.

In keeping with our findings, neither age nor gender has shown an association with long-term functional outcomes in previous studies of tibial fracture patients [35 - 37]. Our finding that fracture severity is not associated with functional recovery is not consistent with prior studies, which have found worse function at 1-year with open vs. closed fractures [35, 36]. Our results showed a near-significant trend in this direction, and lack of significant may be due to the limited number of patients with open fractures available for analysis (n=61). A study by Houben *et al*. concluded that delayed weight bearing increases the risk of impaired healing in patients with tibial shaft fractures [38]. Similarly, we found that participants who were advised to fully or partially weight-bear post operatively reported higher one-year physical function than those who did not.

Our study has a number of strengths. First, our study patients were part of a randomized controlled trial in which the surgical procedure and postoperative care were standardized, which limits the impact that these variables may have had on functional outcomes. Second, recruiting from multiple trauma centers increases the generalizability of our findings to North American tibial fracture patients. Third, we used a well-validated instrument (the SF-36) to assess physical functioning [16, 18, 39]. Fourth, adjustment of our regression model for clinically relevant patient and injury characteristics strengthens inferences from our results.

There are limitations to our study. Although our study cohort was similar to the full TRUST population, our findings are restricted to 70% of enrolled patients. Moreover, the results of this analysis are limited to the variables that were collected as part of the TRUST trial, and do not include all potential prognostics factors (e.g. anxiety). Furthermore, the generalizability of our findings to tibial fracture patients outside of North America is uncertain.

In summary, the current study found that employment at the time of injury predicts better long-term functioning, whereas smoking, obesity, and receipt of disability benefits or involvement in litigation (or plans to be) predict worse long-term functioning. Surgeons should be aware of the effect of these factors on recovery when managing tibial fractures and inform patients about their impact on postoperative outcomes. Future research should explore strategies to improve functional recovery among high-risk patients.

Table 1: Patient Characteristics

Characteristics	Current Cohort (N=299)	All TRUST Patients (N=501)
	Incidence of Predictors n (%)*	
Baseline Patient Characteristics		
Age, *mean (SD)*	39.4 (13.9)	38.1 (13.9)
Male	196 (65.6)	345 (68.9)
Current smoker	87 (29.1)	165 (32.9)
Diabetic	14 (4.7)	30 (6.0)
Employed	227 (75.9)	368 (74.0)
Body Mass Index		
18 – 25 kg/m²	112 (37.5)	197 (39.3)
25-30 kg/m²	106 (35.5)	170 (33.9)
>30 kg/m²	81 (27.1)	129 (25.7)
Fracture Characteristics		
Open fracture	61 (20.4)	114 (22.8)
AO classification		
Class A	201 (67.2)	337 (67.3)
Class B	90 (30.1)	148 (29.5)
Class C	8 (2.7)	15 (3.2)
Gustilo-Ansderson classification		
Type I	34 (11.4)	51 (10.2)
Type II	14 (4.7)	34 (6.7)
Types IIIA & IIIB	13 (4.3)	29 (5.8)
Tscherne Classification		
0	77 (25.8)	126 (25.1)
1	138 (46.2)	220 (43.8)
2	22 (7.4)	37 (7.4)
3	2 (0.7)	5 (1.0)
Treatment Characteristics		
Randomization group:		
LIPUS	152 (50.8)	250 (49.9)
Sham	147 (49.2)	251 (50.1)
Post-operative weight bearing status:		
Non-weight-bearing	141 (47.2)	220 (43.9)
Partial or full weight-bearing	158 (52.8)	281 (56.1)
Receiving physiotherapy at 6 weeks	88 (29.4)	141 (29.5)
Benefits		
Receiving disability benefit or lawyer/litigation involvement:		
No or it is possible I will	185 (61.9)	299 (62.6)
Yes or likely I will	114 (38.1)	175 (36.6)

LIPUS: Low Intensity Pulsed Ultrasound
* = unless otherwise specified

Table 2: Multivariable linear regression with PCS scores as the dependent variable

Independent Variable	Unadjusted mean difference (95% CI)	P-value	Adjusted mean difference (95% CI)	*P*-value
Baseline Patient Characteristics				
Age (per 10-year increase)	-0.05 (-0.12, 0.18)	0.145	-0.37 (-1.05, 0.09)	0.285
Sex				
Female	Reference category		Reference category	
Male	-0.71 (02.71, 1.23)	0.487	-0.42 (-2.44, 1.60)	0.681
Smoking status				
Non-smoker or prior smoker	Reference category		Reference category	
Current smoker	-2.86 (-4.93, -0.80)	0.007	-2.55 (-4.63, -0.46)	0.017
Employment status				
Unemployed	Reference category		Reference category	
Employed	4.36 (2.19, 6.53)	<0.001	4.56 (2.32, 6.80)	< 0.001
Body Mass Index				
18 – 25 kg/m²	Reference category		Reference category	
25-30 kg/m²	-1.33 (-3.55, 0.897)	0.241	-1.78 (-3.94, 0.37)	0.105
>30 kg/m²	-1.78 (-4.17, 0.61)	0.144	-2.57 (-4.86, -0.27)	0.029
Fracture Characteristics				
Fracture type				
Open fracture	Reference group		Reference category	
Closed fracture	2.21 (-0.14, 4.57)	0.065	2.08 (-0.23, 4.38)	0.078
Treatment Characteristics				
Randomization group:				
Sham	Reference category		Reference category	
LIPUS	1.55 (-0.34, 3.45)	0.107	1.22 (-0.58, 3.02)	0.182
Post-operative weight bearing status:				
Non-weight-bearing	Reference category		Reference category	
Partial or full weight-bearing	1.67 (-0.23, 3.56)	0.084	1.98 (0.13, 3.82)	0.036
Receiving physiotherapy at 6 weeks	-1.28 (-3.37, 0.80)	0.227	-1.23 (-3.21, 0.75)	0.249
Benefits				
Receiving disability benefit or lawyer/litigation involvement:				
No or it is possible I will	Reference category		Reference category	
Yes or likely I will	-2.25 (-4.18, -0.31)	0.023	-2.65 (-4.58, -0.72)	0.007

LIPUS: Low Intensity Pulsed Ultrasound

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