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Decreased QOL and muscle strength are persistent one year after intramedullary nailing of a tibial shaft fracture - a prospective one-year follow-up cohort study

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Introduction: To evaluate the development in patient-reported quality of life (QOL) and muscle strength in the period from surgery to 12 months postoperatively after intramedullary nailing of a tibial shaft fracture.

Material and Methods: The design was a prospective, follow-up cohort study. QOL was measured with the questionnaire EQ5D-5L and compared to norm data from a reference population. Recordings of pain and contralateral muscle strength (isometric maximal voluntary contraction (MVC) for knee flexion and extension were collected at 6 weeks, 3, 6, and 12 months postoperatively. Ipsilateral MVCs were recorded at 6 and 12 months.

Results: Forty-nine patients were included. The mean age at the time of fracture was 43.1 years (18 to 79 years). Twelve months postoperatively, the mean EQ5D-5L index was 0.792 (95% CI: 0.747-0.837). Throughout the 12 months postoperatively, patients reported worse QOL compared to the reference population. Six and twelve months after surgery patients demonstrated decreased muscle strength in the injured leg compared to the non-injured leg for knee extension and flexion (P<0.001). Twelve months postoperatively, increasing relative difference in muscle strength during knee extension showed a fair correlation to worse QOL (R=0.541, P<0.001).

Conclusions: Throughout the 12 months postoperatively, patients reported worse QOL compared to the reference population. Muscle strength in the non-injured leg improved over time and was higher after 6 and 12 months compared with the injured leg.
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Keywords: intramedullary nailing, tibia shaft fracture, QOL, muscle strength
INTRODUCTION

During the last decades, intramedullary nailing has been the standard treatment method in the treatment of tibia shaft fractures [1-3]. A recent study reported the incidence of tibial shaft fractures to be 16.9/100,000/year [4] representing around 40% of all long-bone fractures in adults [5].

Several studies report the functional and radiological long-term outcome after intramedullary nailing of tibial shaft fractures. Knee and ankle pain, joint stiffness, degenerative joint disease, rotational malalignment, complications due to soft tissue injury, muscle weakness, and limitations in activity of daily living and quality of life (QOL) are commonly reported [6-22]. A study by Skoog et al. [19] reports that patients with tibial shaft fractures had not recovered to their pre-injury QOL, neither at four nor at twelve months postoperatively. However, there is a lack of prospective studies evaluating the development in short-term outcomes from the time of surgery and onwards. This information is especially important for clinicians when advising patients on development in QOL and muscle strength following a fracture of the tibia.

Several studies have reported decreased muscle strength following a tibial fracture [20,22-25]. To the authors knowledge no studies have described the association between the development in muscle strength postoperatively and the short-term patient-reported QOL and pain following a tibial shaft fracture. A recent study by Larsen et al. [26] reported a significant association between decreased muscle strength and worse patient-reported outcomes in patients following a femoral shaft fracture treated with intramedullary nailing.

The objective of the present study was to evaluate the development in patient-reported QOL and muscle strength in a period from surgery to 12 months postoperatively after intramedullary nailing of a tibial shaft fracture. The explorative aim was to report the association between muscle strength, pain and QOL at 6 and 12 months postoperatively.
following intramedullary nailing of a tibial shaft fracture.

The primary hypothesis was that patients would report worse patient-reported QOL compared to an established reference-population in a period from 6 weeks to 12 months postoperatively. Moreover, the hypothesis was that patients would show impaired muscle strength in the injured leg compared to the non-injured leg in a period from 6 weeks to 12 months postoperatively.

PATIENTS AND METHODS

Study design

The study design was a prospective cohort follow-up study including all patients treated with intramedullary nailing after a tibial shaft fracture, between September 2012 and June 2014 at Aalborg University Hospital, Denmark. Patients below 18 years of age were excluded. Patients with multi-trauma, bilateral fractures and patients with pathological fractures were excluded. Patients who were unable to fill out the questionnaires due to mental disabilities were excluded.

Basic characteristics regarding age, gender, body mass index (BMI), trauma mechanism, type of trauma, fracture classification were obtained at the time of admission to hospital where participants also gave written informed consent. Complications were reported throughout the study. All patients were systematically examined at the outpatient clinic at 6 weeks, and at 3, 6 and 12 months postoperatively.

The primary outcome measurement of this study was the development in patient-reported QOL (Eq5d-5L index) from 6 weeks to 12 months after surgery. The secondary outcome measurements were the development in muscle strength (knee flexion and extension), 30-seconds chair-to-stand test, knee pain and the Knee Injury and Osteoarthritis Outcome
Score (KOOS). Moreover, radiological evaluation regarding union and malignment were obtained.

The Danish Data Protection Agency (J. nr. 2008-58-0028) and the local ethics committee (J.nr: N-201-200-11) approved the study, which was performed according to the principles of the Helsinki declaration. The reporting of the study complies with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement [27].

Patient reported measurements

Eq5D-5L is a standardized and validated instrument to assess health outcome [28]. It consists of five dimensions: Mobility, self-care, usual activities, pain/discomfort and anxiety/depression, and a self-rated health scale on a 20 cm vertical, visual analogue scale with endpoints labelled ‘the best health you can imagine’ and ‘the worst health you can imagine’. An Eq5D-5L index at 1.0 indicated full health, and -0.59 denoted death. Eq5d reference data form a general population-based sample in Denmark is available [30].

The Knee Injury and Osteoarthritis Outcome Score (KOOS) [31] is a standardized and validated instrument to evaluate knee and associated problems. The questionnaire includes 5 subscales. A total score of 100 indicates no symptoms, and 0 indicates major symptoms. KOOS reference data [32] from a general population-based sample in southern Sweden is available.

Assessments of objective measurements

Isometric muscle strength was measured by a strap-mounted dynamometer attached to the wall (Mecmesin AFG2500, Mecmesin Ltd, West Sussex, UK). The strap-mounted isometric test was performed for knee flexion and knee extension for both legs. The patients were asked to perform an isometric maximal voluntary contraction (MVC) for 3 to 4 seconds. A pause of
30 seconds was maintained between the tests. All measurements were repeated twice, and the highest value was used for analysis. The test set-up was described and validated by Rathleff et al. [33].

Functional performance was assessed by the 30-seconds chair-to-stand test. The patients were asked to rise and sit as many times as possible in a period of 30 seconds from a standard height (43 cm) chair without armrests. The number of times they stood up was the outcome measure [34].

Pain

The pain intensity was measured on a 10 cm visual analogue scale (VAS) with endpoints “no pain” and “maximal pain” for the worst pain during the last 24 hours and resting pain.

Radiological measurements

Fracture classification was performed according to the AO classification [35] and was conducted on preoperatively obtained X-rays. Postoperatively, X-rays of the fractured lower leg were obtained and used to evaluate the bone healing and alignment. The radiological assessments were made on AP and side X-rays.

The evaluation of bone union were defined as: i) visible callus formation on at least three of four sides, no visible fracture line and no pain from fracture at weight-bearing and following clinical examination (defined as: union), ii) visible callus formation on at least 1 of 4 sides, with a visible fracture line (defined as: partial union), and iii) visible fracture lines and no visible callus formation (defined as: no union). The evaluation of union was performed in agreement with other studies evaluation union after tibial fractures [36].

Statistics
Continuous data were expressed with mean and standard deviations (SD). The Eq5d and KOOS were expressed with mean and 95% confidence intervals (95%CI). The assumption of normal distribution variables was checked visually by QQ-plots. Categorical data were expressed as frequencies.

A two-way mixed repeated measures analysis of variance (ANOVA) was used to analyze the development in Eq5d-5L index, KOOS, MVC, chair-to-stand test and pain between the time points 6 weeks, and 3, 6 and 12 months postoperatively. If significant ANOVA factors or interactions were found, multiple pairwise analyses with post hoc-test (Bonferroni) corrections were used.

At 6 and 12 months postoperatively a Spearman’s rank test was used for analysis of the correlation between QOL, VAS pain and relative difference in muscle strength between the injured and non-injured leg.

A P-value of < 0.05 was considered significant. The statistical analysis was performed by SPSS (version 22).

RESULTS

A total of 50 patients were treated for a tibial shaft fracture with intramedullary nailing during the study period. One patient was initially excluded due to a pathological fracture. Thus, the study population consists of 17 females and 32 males. The mean age at the time of the fracture was 43.1 years, ranging from 18 to 79 years. The baseline characteristics of all patients are presented in Table 1.

Throughout the study period 5 patients were lost to follow-up. One patient was excluded between the 3 and the 6-month follow-up due to a tibial fracture of the opposite lower leg, and two patients refused to enter the study after the 3-month follow-up. One patient
died and one patient was diagnosed with a mental disability between the 6 and the 12-month follow-up.

Patient reported outcome

Twelve months postoperatively the mean EQ5d-5L index was 0.792 (95% CI: 0.747–0.837). The mean EQ5d-5L VAS was 84.6 (95% CI: 80.3–88.9). The mean EQ5d-5L index from the time of surgery to 12 months postoperatively compared to the age matched Danish reference norms [30], are presented in Figure 1. Throughout the 12 months postoperatively, patients reported worse QOL compared with the age matched established Danish reference population norms due to none overlapping 95% CI.

The mixed-model ANOVA of the EQ5d-5L indexes showed a substantial main effect for time (RM-MX_ANOVA: $F_{3,136} = 25.3$, $P < 0.001$) showing a significant increase in the EQ5d-5L index between the 6-week and the 12-month time points. The post-hoc test showed an increase in the EQ5d-5L index between all the time points, apart from 6 to 12-months postoperatively ($P < 0.004$).

The KOOS score from the time of surgery to 12 months postoperatively is presented in Figure 2. At 12 months postoperatively the mean KOOS scores for the five subscales were: Pain 84.5 (95% CI: 79.5–89.5), symptoms 86.9 (95% CI: 82.7–91.1), ADL 86.4 (95% CI: 81.5–91.3), sports 57.2 (95% CI: 47.6–66.8) and QOL 63.4 (95% CI: 55.5–71.3). Compared with an established KOOS reference population [32], the study population showed statistically worse KOOS outcomes for two (QOL, Sport) of the five subgroups, due to none overlapping 95% CI.

See Table 2.

A mixed-model ANOVA showed a significant main effect for time in all the five KOOS subscales (RM-MX_ANOVA: $F_{3,136} > 2.9$, $P < 0.04$) showing a significant increase between the 6-week and the 12-month time points. The post-hoc test showed an increase in
the subscale Pain between the 6-week and the 6-months (P=0.006) and 12-month (P=0.004).

For the subscale ADL and sport the post-hoc tests showed an increase between week 6 and 
the 3, 6 and 12-month (P<0.002) and between 3 and 12-month (P=0.001). The subscale QOL 
shows an increase between the 6-week and the 12-month (P=0.004).

Isometric muscle strength

The development in muscle strength from surgery to final follow up at 12 months 
postoperatively divided into injured and non-injured legs are presented in Figure 3a (knee-
extension strength) and 3b (knee-flexion strength).

Non-injured leg: The mixed-model ANOVA showed a significant main effect for time 
in the non-injured leg for knee extension (RM-MX_ANOVA: F3,136 =3.0, P=0.03) and knee 
flexion (RM-MX_ANOVA: F3,136 =5.5, P=0.004) showing an increase in muscle strength 
between the 6-week and the 12-month time points. The post-hoc test showed a progressive 
increase in knee extension strength from 6 weeks to 6 months (P=0.03) and knee flexion 
strength from 6 weeks to 12 months (P=0.01).

Injured leg: The mixed-model ANOVA showed no significant main effect for time 
in the injured leg for knee extension and knee flexion (RM-MX_ANOVA: F1,43 <2.7, P>0.11) 
showing no significant increase in muscle strength between the 6- and the 12-month time 
points.

Injured vs. non-injured leg: The RM-ANOVA of the time points 6 and 12 months 
after surgery and muscle strength between the injured and non-injured leg showed a 
significant effect for difference between legs for knee extension (RM-MX_ANOVA: F1,43 
=49.0, P<0.001 and knee flexion (RM-MX_ANOVA: F1,43 =39.6, P<0.001). The post-hoc 
test showed significant decreased muscle strength in the injured leg compared to the non-
injured at both time points (P<0.001).
**Functional performance outcome**

Twelve months after surgery, the mean number of standings for the 30-second chair-to-stand test was 23.9 (9.7SD). The development in the 30-second chair-to-stand test from surgery to the final follow up at 12-months postoperatively is presented in Figure 3c.

A mixed-model ANOVA showed a significant main effect for time in 30-seconds chair-to-stand-test (RM-MX_ANOVA: $F_{3,136}=101.2$, $P<0.001$) showing a significant increase between the 6-week and the 12-month time points. The post-hoc test showed a progressive increase in the number of standing between all the time points ($P<0.001$).

**Pain**

At the final examination, 12 months after surgery, the VAS score for the worst pain during the last 24 hours was reported with a range from 0 to 10 cm. Nineteen patients report a VAS of 0, 16 patients reported a VAS between 1 and 5, and 9 patients reported a VAS between 6 and 10. The VAS score for resting pain was reported with a range from 0 to 5 cm. Eight patients reported a VAS between 1 and 5, and 36 reported a VAS score of 0. Throughout the 12-month observational period the mean VAS score for the worst pain during the last 24 hours was: 6 week=3.1(2.4SD), 3 month=3.6(2.7SD), 6 month=2.6(2.5SD) and 12 month=2.4(2.9SD).

The mixed-model ANOVA showed a significant main effect for time and worst pain during the last 24 hours (RM-MX_ANOVA: $F_{3,136}=4.5$, $P=0.005$) showing a significant increase between the 6-week and the 12-month time points. The post-hoc test showed a progressive decrease in VAS scores between the time points 3- and 12-month ($P=0.04$).

**Radiological measurements**
All fractures united during the 12-month study period (N=44, completed the final radiological
examination). At the 3-month follow-up, 3 fractures presented with union, 39 with partial
union and 7 fractures with no union. Six months postoperatively, 36 patients presented with
union and 10 with partial union. Twelve months after surgery, two patients were out of
alignment, representing a varus deformity of 7° and 9° respectively. No patients presented
with flexion, extension or valgus deformity >5°.

Correlations between QOL, Pain and muscle strength (knee extension and knee flexion).
The relationship between individual VAS scores (worst pain during the last 24 hours)
and the relative difference in muscle strength between legs at 6- and 12- months
postoperatively showed weak correlations for both knee extension and knee flexion
(Spearman’s rank test: $R > 0.386, P < 0.01$).

The relationship between QOL (Eq5d-5L) and the relative difference in muscle
strength between legs at 6 and 12 months postoperatively showed no significant correlations
at 6 months but a fair correlation for knee extension at 12 months postoperatively
(Spearman’s rank test: $R = 0.541, P < 0.001$).

DISCUSSION
To our knowledge this is the first study to systematically report the short-term development in
patient-reported QOL, knee function and the maximum isometric voluntary contraction
strength in a period from the time of fracture to 12 months after surgery in a non-selected
group of patients with isolated tibial shaft fractures, all treated with intramedullary nailing.

In the 12-months observation period, the QOL (Eq5d-5L index) increased
significantly with time. Twelve months postoperatively, patients had not recovered fully, and
reported worse QOL compared to the age matched established Danish reference norms.
Moreover, the study showed a significant worse outcome in two of five KOOS subscales compared to the reference population at 12-months follow-up. These findings are supported by Skoog et al. [19] reporting that patients with tibial shaft fractures had not recovered fully to the pre-injury QOL neither 4 nor 12-months postoperatively, according to the SF-36 questionnaire. Moreover, the present findings are supported by Tay et al. [38] reporting that patients with lower limb long bone shaft fractures presented with residual patient-reported physical disability during the first year after fracture.

Patients in the present study demonstrated significantly progressive increasing muscle strength in the contralateral leg from the time of surgery and onwards. The injured leg of the patients demonstrated decreased muscle strength compared to the non-injured leg for knee extension and knee flexion 6 and 12 months after surgery. Moreover, patients demonstrated significantly progressive increasing functional performance from the time of surgery and onwards. Several other studies have reported decreased muscle strength and function after tibial fractures [20,22-25]. Most studies are retrospective in design, including patients treated with various operative techniques, and no recent studies have compared the muscle strength to the patient-reported QOL. In a prospective study, Gaston et al. [24] reported that two weeks after a tibial fracture, the knee flexor and extensor muscles are reduced to about 40% of normal power, which rises to between 75% and 85% after one year. Moreover, Väistö et al. [22,25] reported, with a long-term (3.2 and 8.1 years) follow-up, a decreased muscle force for knee extension and flexion in the injured leg. Patients in the studies of Väistö et al. [22,25] with no knee pain reported almost a balanced muscle function between the two legs.

Henriksen et al. [40] showed a significant inhibition of muscle strength for knee flexion and knee extension in healthy volunteers followed by experimental knee pain and that muscle strength was positively correlated to the pain intensity. The present study showing generally low level of pain and a weak correlations between increasing relative difference in muscle
This study evaluated the correlations between QOL and relative difference in muscle strength between the injured and non-injured leg following a tibial shaft fracture. The study showed a fair correlation between relative difference in muscle strength for knee extension and QOL 12 months after surgery, indicating that increasing relative difference in muscle strength was associated to worse QOL.

Findings from the present study indicate that it takes considerable time to regain muscle function and balanced muscle strength after a fracture of the tibial shaft. Focus on muscle function in physiotherapy and postoperative rehabilitation may be important. Intervention studies are needed to investigate whether rehabilitation, including muscle strength training, can improve QOL after intramedullary nailing of isolated tibial shaft fractures.

The main limitations of this study are the observational design, implying that no conclusions regarding causality can be drawn. However, the study provided novel findings and useful, clinically relevant hypothesis generating information, relevant for future clinical trials. The present study uses several different measures and analysis to capture different aspects of the outcome following a tibial shaft fracture. The high number of analysis may increase the risk of Type 1 errors. The strength of this study is the existence of the KOOS and Eq5d-5L reference populations. Reference populations offer a unique opportunity to evaluate the outcomes of patients compared to the general population. Finally, a strength of the study is the information included of the associations between QOL, pain and muscle strength, which is novel. A further limitation is the inability of the study to perform multiple analysis, due to the number of included patients in the study.

CONCLUSION
Throughout the 12 months postoperatively, patients reported worse QOL compared to the age matched Danish reference population. Muscle strength in the non-injured leg improved over time and was higher after 6 and 12 month compared with the injured leg. The findings indicate that focus on muscle function in postoperative rehabilitation may be important following a fracture of the tibial shaft.
REFERENCES


FIGURE LEGENDS AND TITLES

Figure 1: Title: The development in Eq5d-5L index. Legends: The development in Eq5d-5L index (mean, 95%Cİ) at the time points 6 week, 3, 6 and 12 month postoperatively compared with age matched reference population. Reference population norms (mean, 95%Cİ). The mixed-model ANOVA of the Eq5d-5L indexes showed a substantial main effect for time (P<0.001) showing an significant increase in the Eq5d-5L index between the 6-week and the 12-month time points. The post-hoc test showed an increase in the Eq5d-5L index between all the time points, apart from 6 to 12-months postoperatively (*,P<0.004).

Figure 2: Title: The development in KOOS subscales. Legends: The development in KOOS subscales (mean) at the time point 6 week, 3, 6 and 12 month postoperatively. A mixed-model ANOVA showed a significant main effect for time in all the 5 KOOS subscales (*, P<0.04). The post-hoc test showed a significant increase in the subscale Pain between the 6-week and the 6-months (P=0.006) and 12-month (P=0.004). For the subscale ADL and sport the post-hoc tests showed an increase between week 6 and the 3, 6 and 12-month (P<0.002) and between 3 and 12-month (P=0.001). The subscale QOL shows an increase between the 6-week and the 12 months (P=0.004).

Figure 3a: Title: The development in muscle strength for knee extension. Legends: The development in muscle strength for knee extension (mean, 95%Cİ) at the time point 6 week, 3, 6 and 12 month postoperatively for the non-injured leg, and at time points 6 and 12 months for the injured leg. The mixed-model ANOVA of the non-injured leg showed a significant increase in muscle strength between the 6-week and the 12-month time points (P=0.03). The RM-ANOVA of the time points 6 and 12 months after surgery and muscle strength between injured and non-injured leg showed a significant decreased muscle strength in the injured leg compared to the non-injured at both time points (*,P<0.001).

Figure 3b: Title: The development in muscle strength for knee flexion. Legends: The development in muscle strength for knee flexion (mean, 95%Cİ) at the time point 6 week, 3, 6 and 12 month postoperatively for the non-injured leg, and at time points 6 and 12 months for the injured leg.
The mixed-model ANOVA of the non-injured leg showed a significant increase in muscle strength between the 6-week and the 12-month time points (P=0.004).

The RM-ANOVA of the time points 6 and 12 months after surgery and muscle strength between injured and non-injured leg showed a significant decreased muscle strength in the injured leg compared to the non-injured at both time points (*,P<0.001).

**Figure 3c:** Title: The development in functional performance. Legends: The development in functional performance (mean, 95%CI) at the time point 6 week, 3, 6 and 12 month postoperatively. A mixed-model ANOVA showed a significant main effect for time in 30-seconds chair-to-stand-test (P<0.001).

The post-hoc test showed a progressive increase in the number of standing between all the time points (*, P<0.001).

**Table 1:** Title: The baseline characteristics of all patients. No legends.

**Table 2:** Title: Patient-reported outcomes 12 months after intramedullary nailing. Legends: *

Figure 2

KOOS Scores vs. Time:
- KOOS Pain
- KOOS Symptoms
- KOOS ADL
- KOOS Sport
- KOOS QOL

Time Points:
- 6 weeks
- 3 months
- 6 months
- 12 months
Figure 3a

- Non-injured
- Injured

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<td>*</td>
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<tr>
<td>12 months</td>
<td>*</td>
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<td>Table 1: Baseline characteristics of the 49 patients</td>
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<td>Age at time of fracture, mean (range) 43.1 (18-79)</td>
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<td>Gender, male/female 32/17</td>
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<td>Height, mean (SD) 176.0 (11.2)</td>
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<td>High/low-energy trauma 12/37</td>
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**Fracture classification AO-42-**

- A 30
- B 14
- C 5
- Open/closed fracture 6/43
- Fibula fracture, no/yes 5/44

**Additional treatment besides intramedullary nailing**

- Initial screw fixation of posterior aspect of the distal tibia 14
- Metatarsal fracture treated with Kirschner-wire 2

**Complications**

- Compartment syndrom 1
- Broken screws 2
<table>
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<th>Study population</th>
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<tr>
<td></td>
<td>Mean</td>
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<td>Reference population</td>
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Tabel 2: KOOS outcomes 12 months after intramedullary nailing of an tibial shaft fracture