



Aalborg Universitet

AALBORG UNIVERSITY  
DENMARK

**Decreased QOL and muscle strength are persistent 1 year after intramedullary nailing of a tibial shaft fracture**

*a prospective 1-year follow-up cohort study*

Larsen, Peter; Elsoe, Rasmus; Laessoe, Uffe; Graven-Nielsen, Thomas; Eriksen, Christian Berre; Rasmussen, Sten

*Published in:*  
Archives of Orthopaedic and Trauma Surgery

*DOI (link to publication from Publisher):*  
[10.1007/s00402-016-2537-2](https://doi.org/10.1007/s00402-016-2537-2)

*Publication date:*  
2016

*Document Version*  
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*

Larsen, P., Elsoe, R., Laessoe, U., Graven-Nielsen, T., Eriksen, C. B., & Rasmussen, S. (2016). Decreased QOL and muscle strength are persistent 1 year after intramedullary nailing of a tibial shaft fracture: a prospective 1-year follow-up cohort study. *Archives of Orthopaedic and Trauma Surgery*, 136(10), 1395-1402. <https://doi.org/10.1007/s00402-016-2537-2>

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- ? Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- ? You may not further distribute the material or use it for any profit-making activity or commercial gain
- ? You may freely distribute the URL identifying the publication in the public portal ?

**Take down policy**

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.

## Archives of Orthopaedic and Trauma Surgery

### 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 --Manuscript Draft--

<b>Manuscript Number:</b>	AOTS-D-16-00339R1
<b>Full Title:</b>	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
<b>Article Type:</b>	Original Article
<b>Section/Category:</b>	Trauma Surgery
<b>Keywords:</b>	intramedullary nailing, tibia shaft fracture, QOL, muscle strength
<b>Corresponding Author:</b>	Peter Larsen, Ph.D. Aalborg University Hospital, Denmark Aalborg, DENMARK
<b>Corresponding Author Secondary Information:</b>	
<b>Corresponding Author's Institution:</b>	Aalborg University Hospital, Denmark
<b>Corresponding Author's Secondary Institution:</b>	
<b>First Author:</b>	Peter Larsen, Ph.D.
<b>First Author Secondary Information:</b>	
<b>Order of Authors:</b>	Peter Larsen, Ph.D. Rasmus Elsoe, MD Uffe Laessoe, PT, Ph.D Thomas Graven-Nielsen, DMSc, Ph.D Christian Berre Eriksen, MD Sten Rasmussen, MD, Ph.D.
<b>Order of Authors Secondary Information:</b>	
<b>Funding Information:</b>	
<b>Abstract:</b>	<p><b>Introduction:</b> 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.</p> <p><b>Material and Methods:</b> 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.</p> <p><b>Results:</b> 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 (<math>P &lt; 0.001</math>). Twelve months postoperatively, increasing relative difference in muscle strength during knee extension show a fair correlation to worse QOL (<math>R = 0.541</math>, <math>P &lt; 0.001</math>).</p> <p><b>Conclusions:</b> 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 month compared with the injured leg.</p>

**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**

*Peter Larsen, MR, PhD<sup>1</sup>, Rasmus Elsoe, MD<sup>2</sup>, Uffe Laessoe, PT, PhD<sup>3,4</sup>, Thomas  
Graven-Nielsen, DMSc<sup>3</sup>, Christian Berre Eriksen, MD<sup>2</sup>, Sten Rasmussen, MD, PhD<sup>2,5</sup>*

<sup>1</sup> Department of Occupational Therapy and Physiotherapy, Aalborg University  
Hospital, Denmark.

<sup>2</sup> Department of Orthopaedic Surgery, Aalborg University Hospital, Denmark.

<sup>3</sup> Center for Neuroplasticity and Pain (CNAP), SMI, Department of Health Science  
and Technology, Faculty of Medicine, Aalborg University, Denmark.

<sup>4</sup> Physiotherapy Department, University College North Denmark, UCN, Denmark

<sup>5</sup> Department of Clinical Medicine, Faculty of Medicine, Aalborg University,  
Aalborg, Denmark

**Original paper for Archives of Orthopaedic and Trauma Surgery**

**Acknowledgement**

The Department of Orthopaedic surgery and the Department of Occupational and  
Physiotherapy Aalborg University Hospital, Denmark were acknowledged for proving  
unrestricted grants. Thomas Graven-Nielsen is a part of Center for Neuroplasticity  
and Pain (CNAP) which is supported by the Danish National Research Foundation  
(DNRF121).

The authors declare that they have no conflicts of interest to report. The authors did  
not receive benefits or grants in any form from a commercial part related directly or  
indirectly to the subject of this article.

Conflicts of Interest and Source of Funding: None

**Corresponding author:**

*Peter Larsen*

Department of Occupational Therapy and Physiotherapy,  
Aalborg University Hospital, Aalborg, Denmark

18-22 Hobrovej.

DK-9000 Aalborg.

E-mail: [peter.larsen@rn.dk](mailto:peter.larsen@rn.dk)

+45 99 32 31 05

+45 40 68 27 61 (mobile)

+45 99 32 31 09 (fax)

*Tibial Shaft Fracture QOL-muscle*

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

3

4

5

6

7

8        **Original paper for Archives of Orthopaedic and Trauma Surgery (AOTS)**

9

10

11

12

13

## ABSTRACT

14

**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.

15

16

**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.

17

18

19

20

21

**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 show a fair correlation to worse QOL ( $R=0.541$ ,  $P<0.001$ ).

22

23

24

25

26

27

28

29

30

**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 month compared with the injured leg.

31

32

33

34

**Keywords:** *intramedullary nailing, tibia shaft fracture, QOL, muscle strength*



35 **INTRODUCTION**

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

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

50 Several studies have reported decreased muscle strength following a tibial fracture  
51 [20,22-25]. To the authors knowledge no studies have described the association between the  
52 development in muscle strength postoperatively and the short-term patient-reported QOL and  
53 pain following a tibial shaft fracture. A recent study by Larsen et al. [26] reported a  
54 significant association between decreased muscle strength and worse patient-reported  
55 outcomes in patients following a femoral shaft fracture treated with intramedullary nailing.

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

60 following intramedullary nailing of a tibial shaft fracture.

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

66

## 67 **PATIENTS AND METHODS**

### 68 *Study design*

69 The study design was a prospective cohort follow-up study including all patients treated with  
70 intramedullary nailing after a tibial shaft fracture, between September 2012 and June 2014 at  
71 Aalborg University Hospital, Denmark. Patients below 18 years of age were excluded.

72 Patients with multi-trauma, bilateral fractures and patients with pathological fractures were  
73 excluded. Patients who were unable to fill out the questionnaires due to mental disabilities  
74 were excluded.

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

80         The primary outcome measurement of this study was the development in patient-  
81 reported QOL (Eq5d-5L index) from 6 weeks to 12 months after surgery. The secondary  
82 outcome measurements were the development in muscle strength (knee flexion and extension),  
83 30-seconds chair-to-stand test, knee pain and the Knee Injury and Osteoarthritis Outcome

84 Score (KOOS). Moreover, radiological evaluation regarding union and malalignment were  
85 obtained.

86 The Danish Data Protection Agency (J. nr. 2008-58-0028) and the local ethics  
87 committee (J.nr: N-201-200-11) approved the study, which was performed according to the  
88 principles of the Helsinki declaration. The reporting of the study complies with the  
89 Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement  
90 [27].

91

#### 92 *Patient reported measurements*

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

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

103

#### 104 *Assessments of objective measurements*

105 Isometric muscle strength was measured by a strap-mounted dynamometer attached to the  
106 wall (Mecmesin AFG2500, Mecmesin Ltd, West Sussex, UK). The strap-mounted isometric  
107 test was performed for knee flexion and knee extension for both legs. The patients were asked  
108 to perform an isometric maximal voluntary contraction (MVC) for 3 to 4 seconds. A pause of



109 30 seconds was maintained between the tests. All measurements were repeated twice, and the  
110 highest value was used for analysis. The test set-up was described and validated by Rathleff et  
111 al. [33].

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

116

#### 117 *Pain*

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

120

#### 121 *Radiological measurements*

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

126 The evaluation of bone union were defined as: *i*) visible callus formation on at least  
127 three of four sides, no visible fracture line and no pain from fracture at weight-bearing and  
128 following clinical examination (defined as: union), *ii*) visible callus formation on at least 1 of  
129 4 sides, with a visible fracture line (defined as: partial union), and *iii*) visible fracture lines  
130 and no visible callus formation (defined as: no union). The evaluation of union was performed  
131 in agreement with other studies evaluation union after tibial fractures [36].

132

#### 133 *Statistics*

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

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

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

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

148

## 149 **RESULTS**

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

155 Throughout the study period 5 patients were lost to follow-up. One patient was  
156 excluded between the 3 and the 6-month follow-up due to a tibial fracture of the opposite  
157 lower leg, and two patients refused to enter the study after the 3-month follow-up. One patient

158 died and one patient was diagnosed with a mental disability between the 6 and the 12-month  
159 follow-up.

160

161 *Patient reported outcome*

162 Twelve months postoperatively the mean Eq5d-5L index was 0.792 (95%CI: 0.747–0.837).  
163 The mean Eq5d-5L VAS was 84.6 (95%CI: 80.3–88.9). The mean Eq5d-5L index from the  
164 time of surgery to 12 months postoperatively compared to the age matched Danish reference  
165 norms [30], are presented in Figure 1. Throughout the 12 months postoperatively, patients  
166 reported worse QOL compared with the age matched established Danish reference population  
167 norms due to none overlapping 95%CI.

168 The mixed-model ANOVA of the Eq5d-5L indexes showed a substantial main effect  
169 for time (RM-MX\_ANOVA:  $F_{3,136}=25.3$ ,  $P<0.001$ ) showing an significant increase in the  
170 Eq5d-5L index between the 6-week and the 12-month time points. The post-hoc test showed  
171 an increase in the Eq5d-5L index between all the time points, apart from 6 to 12-months  
172 postoperatively ( $P<0.004$ ).

173 The KOOS score from the time of surgery to 12 months postoperatively is presented  
174 in Figure 2. At 12 months postoperatively the mean KOOS scores for the five subscales were:  
175 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–  
176 91.3), sports 57.2 (95%CI: 47.6–66.8) and QOL 63.4 (95%CI: 55.5–71.3). Compared with an  
177 established KOOS reference population [32], the study population showed statistically worse  
178 KOOS outcomes for two (QOL, Sport) of the five subgroups, due to none overlapping 95%CI.  
179 See Table 2.

180 A mixed-model ANOVA showed a significant main effect for time in all the five  
181 KOOS subscales (RM-MX\_ANOVA:  $F_{3,136}>2.9$ ,  $P<0.04$ ) showing a significant increase  
182 between the 6-week and the 12-month time points. The post-hoc test showed an increase in

183 the subscale Pain between the 6-week and the 6-months ( $P=0.006$ ) and 12-month ( $P=0.004$ ).  
184 For the subscale ADL and sport the post-hoc tests showed an increase between week 6 and  
185 the 3, 6 and 12-month ( $P<0.002$ ) and between 3 and 12-month ( $P=0.001$ ). The subscale QOL  
186 shows an increase between the 6-week and the 12-month ( $P=0.004$ ).

187

### 188 *Isometric muscle strength*

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

192 Non-injured leg: The mixed-model ANOVA showed a significant main effect for time  
193 in the non-injured leg for knee extension (RM-MX\_ANOVA:  $F_{3,136}=3.0$ ,  $P=0.03$ ) and knee  
194 flexion (RM-MX\_ANOVA:  $F_{3,136}=5.5$ ,  $P=0.004$ ) showing an increase in muscle strength  
195 between the 6-week and the 12-month time points. The post-hoc test showed a progressive  
196 increase in knee extension strength from 6 weeks to 6 months ( $P=0.03$ ) and knee flexion  
197 strength from 6 weeks to 12 months ( $P=0.01$ ).

198 Injured leg: The mixed-model ANOVA showed no significant main effect for time  
199 in the injured leg for knee extension and knee flexion (RM-MX\_ANOVA:  $F_{1,43}<2.7$ ,  $P>0.11$ )  
200 showing no significant increase in muscle strength between the 6- and the 12-month time  
201 points.

202 Injured vs. non-injured leg: The RM-ANOVA of the time points 6 and 12 months  
203 after surgery and muscle strength between the injured and non-injured leg showed a  
204 significant effect for difference between legs for knee extension (RM-MX\_ANOVA:  $F_{1,43}$   
205  $=49.0$ ,  $P<0.001$  and knee flexion (RM-MX\_ANOVA:  $F_{1,43}=39.6$ ,  $P<0.001$ ). The post-hoc  
206 test showed significant decreased muscle strength in the injured leg compared to the non-  
207 injured at both time points ( $P<0.001$ ).

208

209 *Functional performance outcome*

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

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

217

218 *Pain*

219 At the final examination, 12 months after surgery, the VAS score for the worst pain during  
220 the last 24 hours was reported with a range from 0 to 10 cm. Nineteen patients report a VAS  
221 of 0, 16 patients reported a VAS between 1 and 5, and 9 patients reported a VAS between 6  
222 and 10. The VAS score for resting pain was reported with a range from 0 to 5 cm. Eight  
223 patients reported a VAS between 1 and 5, and 36 reported a VAS score of 0. Throughout the  
224 12-month observational period the mean VAS score for the worst pain during the last 24  
225 hours was: 6 week=3.1(2.4SD), 3 month=3.6(2.7SD), 6 month=2.6(2.5SD) and 12  
226 month=2.4(2.9SD).

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

231

232 *Radiological measurements*



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

239

240 *Correlations between QOL, Pain and muscle strength (knee extension and knee flexion).*

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

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

249

## 250 **DISCUSSION**

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

255 In the 12-months observation period, the QOL (Eq5d-5L index) increased  
256 significantly with time. Twelve months postoperatively, patients had not recovered fully, and  
257 reported worse QOL compared to the age matched established Danish reference norms.

258 Moreover, the study showed a significant worse outcome in two of five KOOS subscales  
259 compared to the reference population at 12-months follow-up. These findings are supported  
260 by Skoog et al. [19] reporting that patients with tibial shaft fractures had not recovered fully  
261 to the pre-injury QOL neither 4 nor 12-months postoperatively, according to the SF-36  
262 questionnaire. Moreover, the present findings are supported by Tay et al. [38] reporting that  
263 patients with lower limb long bone shaft fractures presented with residual patient-reported  
264 physical disability during the first year after fracture.

265         Patients in the present study demonstrated significantly progressive increasing muscle  
266 strength in the contralateral leg from the time of surgery and onwards. The injured leg of the  
267 patients demonstrated decreased muscle strength compared to the non-injured leg for knee  
268 extension and knee flexion 6 and 12 months after surgery. Moreover, patients demonstrated  
269 significantly progressive increasing functional performance from the time of surgery and  
270 onwards. Several other studies have reported decreased muscle strength and function after  
271 tibial fractures [20,22-25]. Most studies are retrospective in design, including patients treated  
272 with various operative techniques, and no recent studies have compared the muscle strength to  
273 the patient-reported QOL. In a prospective study, Gaston et al. [24] reported that two weeks  
274 after a tibial fracture, the knee flexor and extensor muscles are reduced to about 40% of  
275 normal power, which rises to between 75% and 85% after one year. Moreover, Väistö et al.  
276 [22,25] reported, with a long-term (3.2 and 8.1 years) follow-up, a decreased muscle force for  
277 knee extension and flexion in the injured leg. Patients in the studies of Väistö et al. [22,25]  
278 with no knee pain reported almost a balanced muscle function between the two legs.  
279 Henriksen et al. [40] showed a significant inhibition of muscle strength for knee flexion and  
280 knee extension in healthy volunteers followed by experimental knee pain and that muscle  
281 strength was positively correlated to the pain intensity. The present study showing generally  
282 low level of pain and a weak correlations between increasing relative difference in muscle

283 strength and pain, 6 and 12 months after surgery.

284 This study evaluated the correlations between QOL and relative difference in muscle  
285 strength between the injured and non-injured leg following a tibial shaft fracture. The study  
286 showed a fair correlation between relative difference in muscle strength for knee extension  
287 and QOL 12 months after surgery, indicating that increasing relative difference in muscle  
288 strength was associated to worse QOL.

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

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

306

307 **CONCLUSION**

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

313

314

315 **REFERENCES**

- 316 1. Bone LB, Sucato D, Stegemann PM, Rohrbacher BJ (1997) Displaced isolated fractures of the tibial  
317 shaft treated with either a cast or intramedullary nailing. An outcome analysis of matched pairs of  
318 patients. *J Bone Joint Surg Am* 79:1336-1341
- 319 2. Hooper GJ, Keddell RG, Penny ID (1991) Conservative management or closed nailing for tibial  
320 shaft fractures. A randomised prospective trial. *J Bone Joint Surg Br* 73:83-85
- 321 3. Karladani AH, Granhed H, Edshage B, Jerre R, Styf J (2000) Displaced tibial shaft fractures: a  
322 prospective randomized study of closed intramedullary nailing versus cast treatment in 53 patients.  
323 *Acta Orthop Scand* 71:160-167
- 324 4. Larsen P, Elsoe R, Hansen SH, Graven-Nielsen T, Laessoe U, Rasmussen S (2015) Incidence and  
325 epidemiology of tibial shaft fractures. *Injury* 46(4):746-750
- 326 5. Court-Brown CM, Caesar B (2006) Epidemiology of adult fractures: A review. *Injury* 37:691-697
- 327 6. Babis GC, Benetos IS, Karachalios T, Soucacos PN (2007) Eight years' clinical experience with the  
328 Orthofix tibial nailing system in the treatment of tibial shaft fractures. *Injury* 38:227-234
- 329 7. Bhattacharyya T, Seng K, Nassif NA, Freedman I (2006) Knee pain after tibial nailing: the role of  
330 nail prominence. *Clin Orthop Relat Res* 449:303-307
- 331 8. Butcher JL, MacKenzie EJ, Cushing B, Jurkovich G, Morris J, Burgess A et al. (1996) Long-term  
332 outcomes after lower extremity trauma. *J Trauma* 41:4-9
- 333 9. Court-Brown CM (2004) Reamed intramedullary tibial nailing: an overview and analysis of 1106  
334 cases. *J Orthop Trauma* 18:96-101
- 335 10. Court-Brown CM, Gustilo T, Shaw AD (1997) Knee pain after intramedullary tibial nailing: its  
336 incidence, etiology, and outcome. *J Orthop Trauma* 11:103-105



- 337 11. Dogra AS, Ruiz AL, Marsh DR (2002) Late outcome of isolated tibial fractures treated by  
338 intramedullary nailing: the correlation between disease-specific and generic outcome measures. J  
339 Orthop Trauma 16:245-249
- 340 12. Ekeland A, Thoresen BO, Alho A, Strömsöe K, Follerås G, Haukebø A (1988) Interlocking  
341 intramedullary nailing in the treatment of tibial fractures. A report of 45 cases. Clin Orthop Relat Res  
342 (231):205-215
- 343 13. Holder-Powell HM, Rutherford OM (2000) Unilateral lower-limb musculoskeletal injury: its long-  
344 term effect on balance. Arch Phys Med Rehabil 81:265-268
- 345 14. Josten C, Marquass B, Schwarz C, Verheyden A (2010) Intramedullary nailing of proximal tibial  
346 fractures : Complications and risk factors. Unfallchirurg 113:21-28
- 347 15. Keating JF, Orfaly R, O'Brien PJ (1997) Knee pain after tibial nailing. J Orthop Trauma 11:10-13
- 348 16. Lefavre KA, Guy P, Chan H, Blachut PA (2008) Long-term follow-up of tibial shaft fractures  
349 treated with intramedullary nailing. J Orthop Trauma 22:525-529
- 350 17. Merchant TC, Dietz FR (1989) Long-term follow-up after fractures of the tibial and fibular shafts.  
351 J Bone Joint Surg Am 71:599-606
- 352 18. Ryan SP, Tornetta P 3rd, Dielwart C, Kaye-Krall E (2011) Knee pain correlates with union after  
353 tibial nailing. J Orthop Trauma 25:731-735
- 354 19. Skoog A, Soderqvist A, Tornkvist H, Ponzer S (2001) One-year outcome after tibial shaft  
355 fractures: results of a prospective fracture registry. J Orthop Trauma 15:210-215
- 356 20. Toivanen JA, Vaisto O, Kannus P, Latvala K, Honkonen SE, Järvinen MJ (2002) Anterior knee  
357 pain after intramedullary nailing of fractures of the tibial shaft. A prospective, randomized study  
358 comparing two different nail-insertion techniques. J Bone Joint Surg Am 84-A:580-585

- 359 21. Väistö O, Toivanen J, Kannus P, Järvinen M (2008) Anterior knee pain after intramedullary  
360 nailing of fractures of the tibial shaft: an eight-year follow-up of a prospective, randomized study  
361 comparing two different nail-insertion techniques. *J Trauma* 64:1511-1516
- 362 22. Väistö O, Toivanen J, Kannus P, Järvinen M (2007) Anterior knee pain and thigh muscle strength  
363 after intramedullary nailing of a tibial shaft fracture: an 8-year follow-up of 28 consecutive cases. *J*  
364 *Orthop Trauma* 21:165-171
- 365 23. Nyland J, Bealle DP, Kaufer H, Johnson DL (2001) Long-term quadriceps femoris functional  
366 deficits following intramedullary nailing of isolated tibial fractures. *Int Orthop* 24:342-346
- 367 24. Gaston P, Will E, McQueen MM, Elton RA, Court-Brown CM (2000) Analysis of muscle function  
368 in the lower limb after fracture of the diaphysis of the tibia in adults. *J Bone Joint Surg Br* 82:326-331
- 369 25. Väistö O, Toivanen J, Kannus P, Järvinen M (2004) Anterior knee pain and thigh muscle strength  
370 after intramedullary nailing of tibial shaft fractures: a report of 40 consecutive cases. *J Orthop Trauma*  
371 18:18-23
- 372 26. Larsen P, Elsoe R, Graven-Nielsen T, Laessoe U, Rasmussen S (2015) Decreased muscle strength  
373 is associated with impaired long-term functional outcome after intramedullary nailing of femoral shaft  
374 fracture. *Eur J Trauma Emerg Surg* 41(6):673-681
- 375 27. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2008) The  
376 Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:  
377 guidelines for reporting observational studies. *J Clin Epidemiol* 61:344-349
- 378 28. Eq-5d questionnaire. <http://www.euroqol.org/about-eq-5d/publications/user-guide.html>. ; Accessed  
379 May 2012
- 380 29. Wittrup-Jensen KU, Lauridsen J, Gudex C, Pedersen KM (2009) Generation of a Danish TTO  
381 value set for EQ-5D health states. *Scand J Public Health* 37:459-466

- 382 30. Sorensen J, Davidsen M, Gudex C, Pedersen KM, Brønnum-Hansen H (2009) Danish EQ-5D  
383 population norms. *Scand J Public Health* 37:467-474
- 384 31. KOOS questionnaire [KOOS web site]. Available at: <http://www.koos.nu>. Accessed May, 2012
- 385 32. Paradowski PT, Bergman S, Sunden-Lundius A, Lohmander LS, Roos EM (2006) Knee  
386 complaints vary with age and gender in the adult population. Population-based reference data for the  
387 Knee injury and Osteoarthritis Outcome Score (KOOS). *BMC Musculoskelet Disord* 7:38
- 388 33. Rathleff CR, Baird WN, Olesen JL, Roos EM, Rasmussen S, Rathleff MS (2013) Hip and knee  
389 strength is not affected in 12-16 year old adolescents with patellofemoral pain - a cross-sectional  
390 population-based study. *PLoS One* 8(11):e79153
- 391 34. Rikli RE, Jones CJ (1999) Development and validity of functional fitness test for community-  
392 residing older adults. *Journal of Aging and Physical Activity* 7:127-159
- 393 35. Marsh JL, Slongo TF, Agel J, Broderick JS, Creevey W, DeCoster TA, Prokuski L, Sirkin MS,  
394 Ziran B, Henly B, Audigé L (2007) Fracture and Dislocation Classification Compendium - 2007:  
395 Orthopaedic Trauma Association Classification, Database and Outcome Committee. *J Orthop Trauma*  
396 (10suppl)1-133
- 397 36. Templeton PA, Farrar MJ, Williams HR, Bruguera J, Smith RM (2000) Complications of tibial  
398 shaft soccer fractures. *Injury* 31:415-419
- 399 37. Walters SJ, Brazier JE (2005) Comparison of the minimally important difference for two health  
400 state utility measures: EQ-5D and SF-6D. *Qual Life Res* 14:1523-1532
- 401 38. Tay WH, de Steiger R, Richardson M, Gruen R, Balogh ZJ (2014) Health outcomes of delayed  
402 union and nonunion of femoral and tibial shaft fractures. *Injury* 45:1653-1658

- 403 39. Larsen P, Lund H, Laesoe U, Graven-Nielsen T, Rasmussen S (2014) Restrictions in Quality of  
404 Life after Intramedullary Nailing of Tibial Shaft Fracture: a retrospective follow-up study of 223  
405 cases. *J Orthop Trauma*. 28(9):507-512
- 406 40. Henriksen M, Rosager S, Aaboe J, Graven-Nielsen T, Bliddal H (2011) Experimental knee pain  
407 reduces muscle strength. *J Pain* 12:460-467
- 408 41. Appell HJ (1990) Muscular atrophy following immobilisation. A review. *Sports Med* 10:42-58
- 409 42. McNair PJ, Marshall RN, Maguire K (1996) Swelling of the knee joint: effects of exercise on  
410 quadriceps muscle strength. *Arch Phys Med Rehabil* 77:896-899
- 411

## 412 FIGURE LEGENDS AND TITLES

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

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

427

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

436

437 **Figure 3b:** Title: The development in muscle strength for knee flexion. Legends: The development in  
438 muscle strength for knee flexion (mean, 95%CI) at the time point 6 week, 3, 6 and 12 month  
439 postoperatively for the non-injured leg, and at time points 6 and 12 months for the injured leg.



440 The mixed-model ANOVA of the non-injured leg showed a significant increase in muscle strength  
441 between the 6-week and the 12-month time points ( $P=0.004$ ).

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

445

446 **Figure 3c:** Title: The development in functional performance. Legends: The development in functional  
447 performance (mean, 95%CI) at the time point 6 week, 3, 6 and 12 month postoperatively. A mixed-  
448 model ANOVA showed a significant main effect for time in 30-seconds chair-to-stand-test ( $P<0.001$ ).  
449 The post-hoc test showed a progressive increase in the number of standing between all the time  
450 points ( $*, P<0.001$ ).

451

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

453

454 **Table 2:** Title: Patient-reported outcomes 12 months after intramedullary nailing. Legends: \*  
455 Paradowski PT et al. BMC Musculoskeletal disord, 2006 [33]. \*\* Unpublished data. Ewa Roos  
456 personal communication, Nov 13, 2012. Paradowski et al. 2006.

457

458

459

460

Figure 1

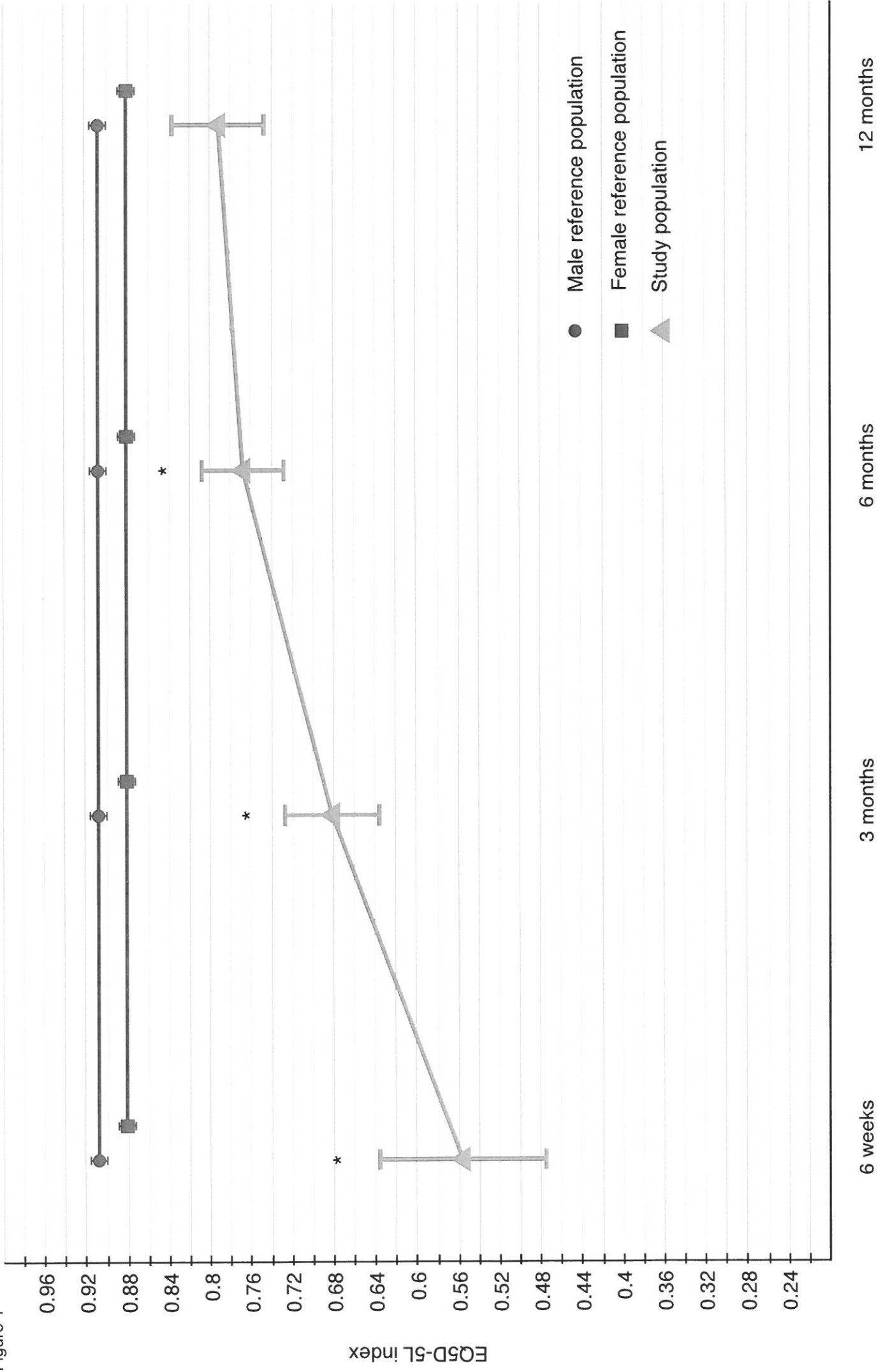


Figure 2

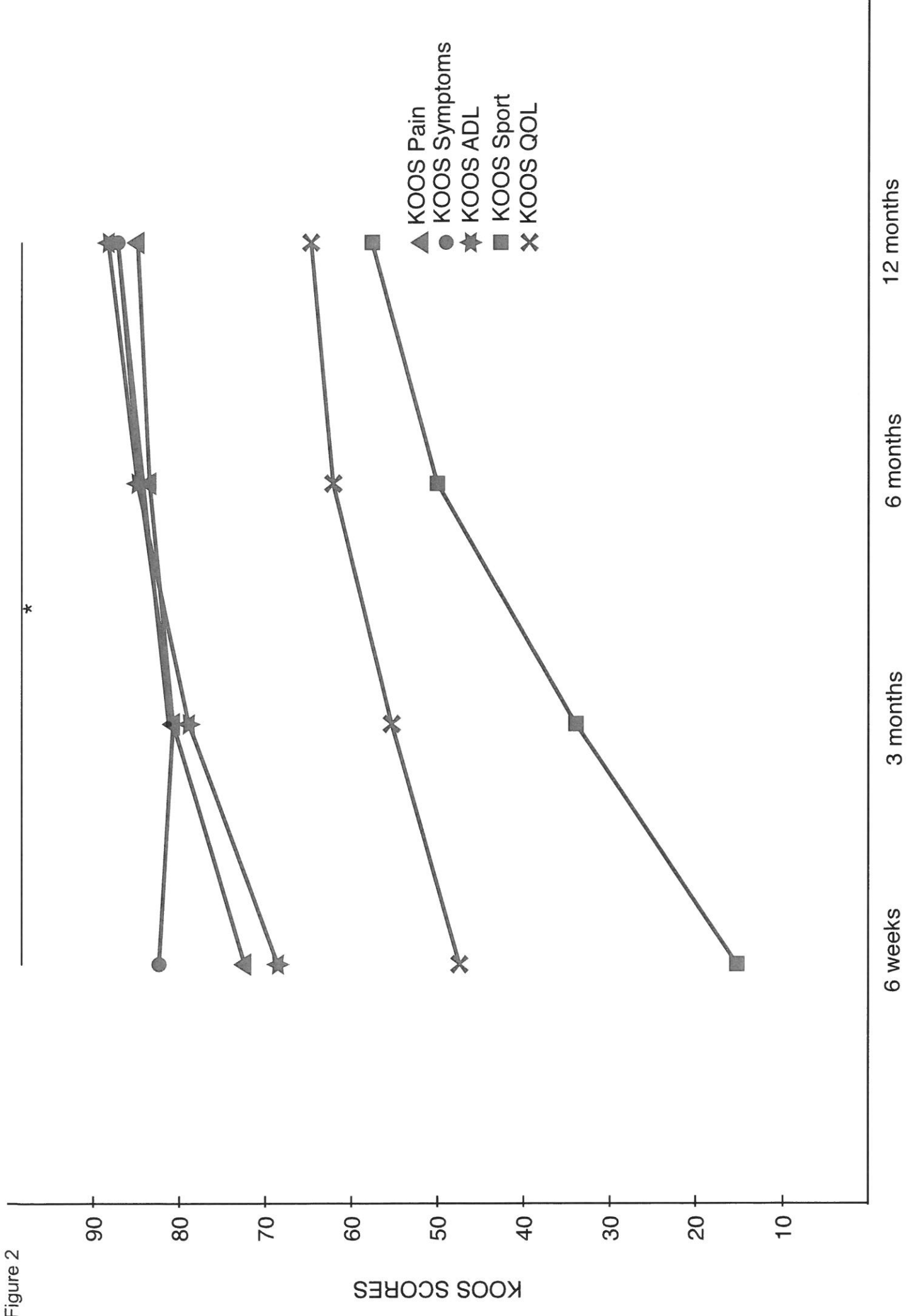
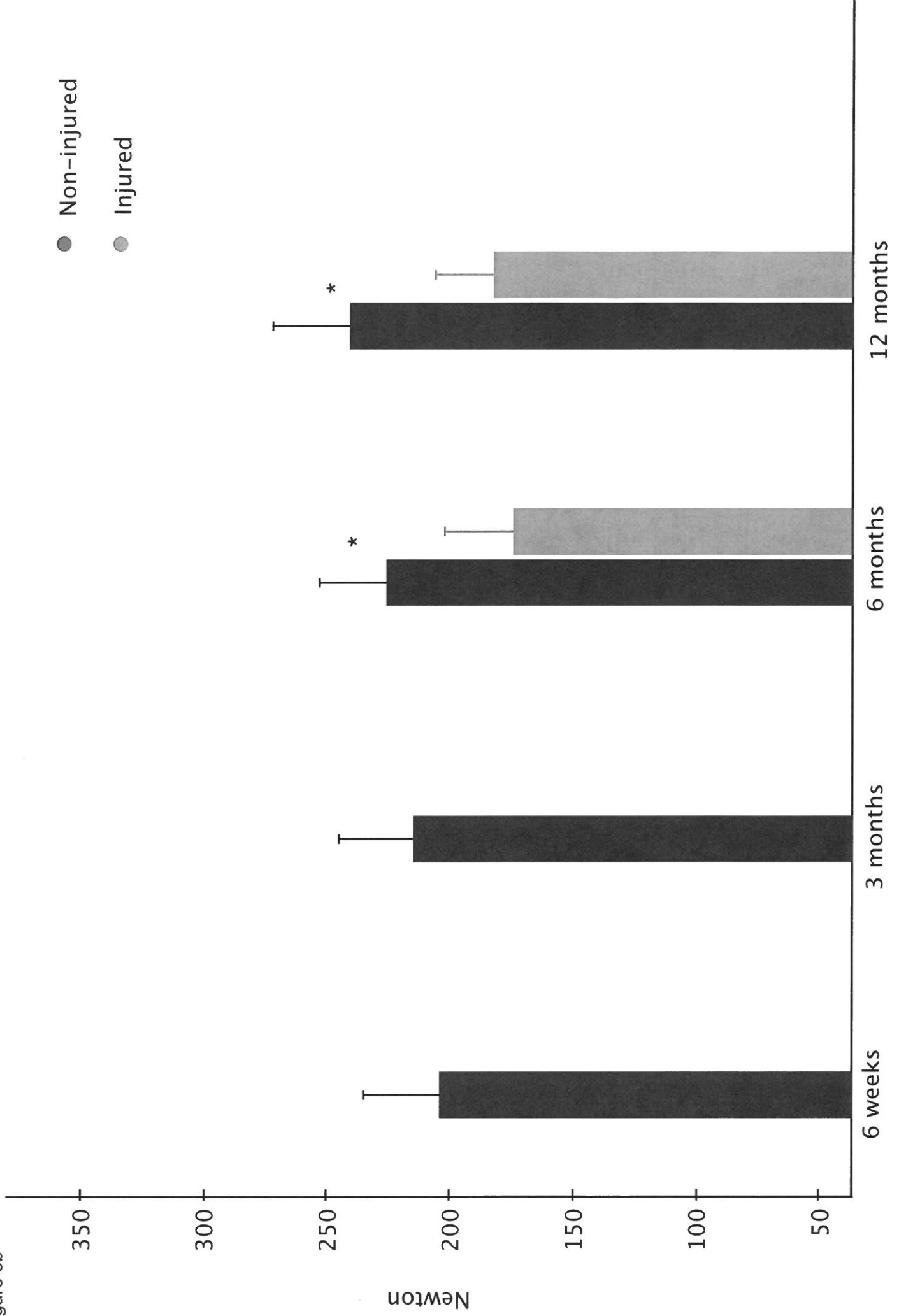


Figure 3b



● Non-injured

● Injured

Figure 3a

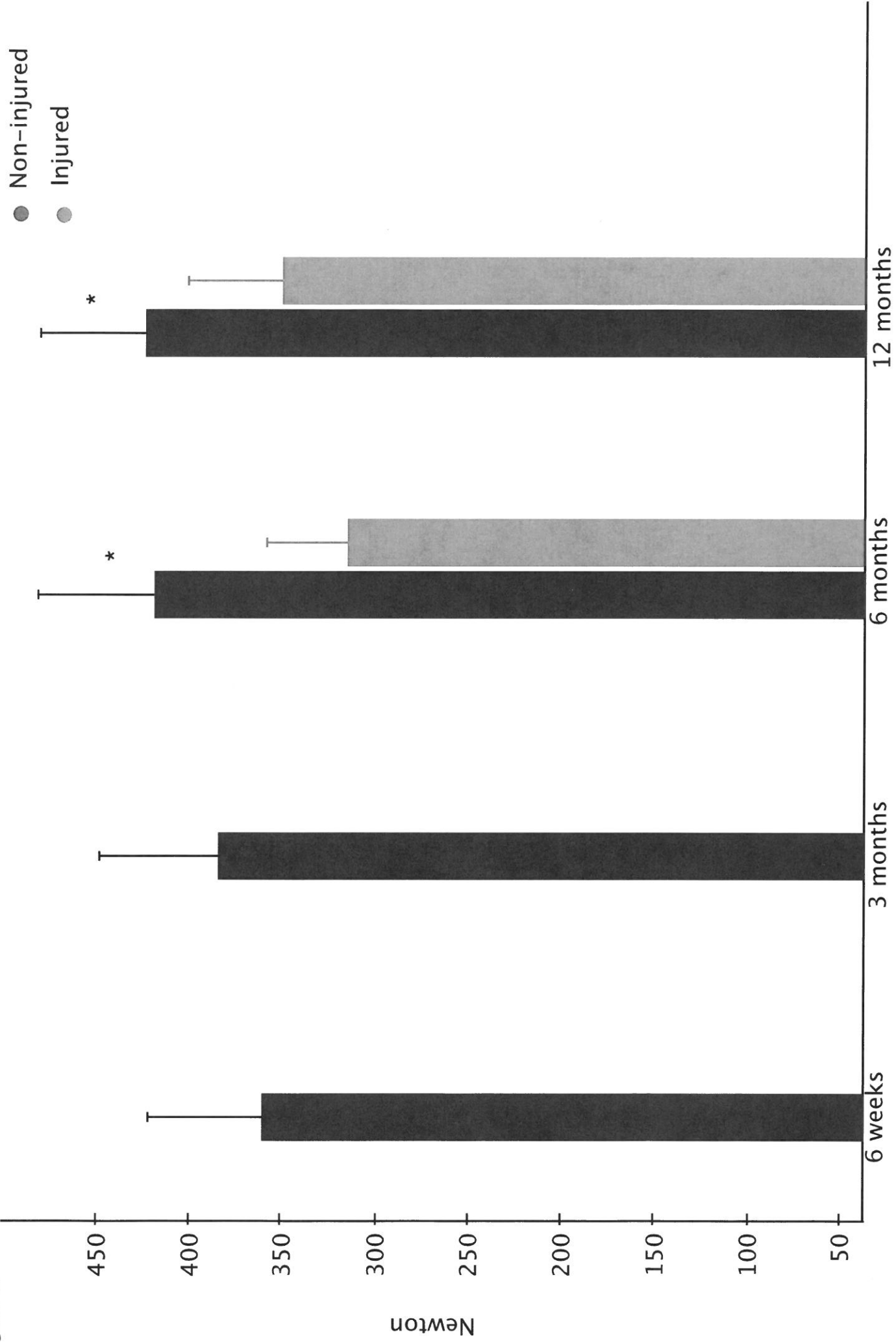
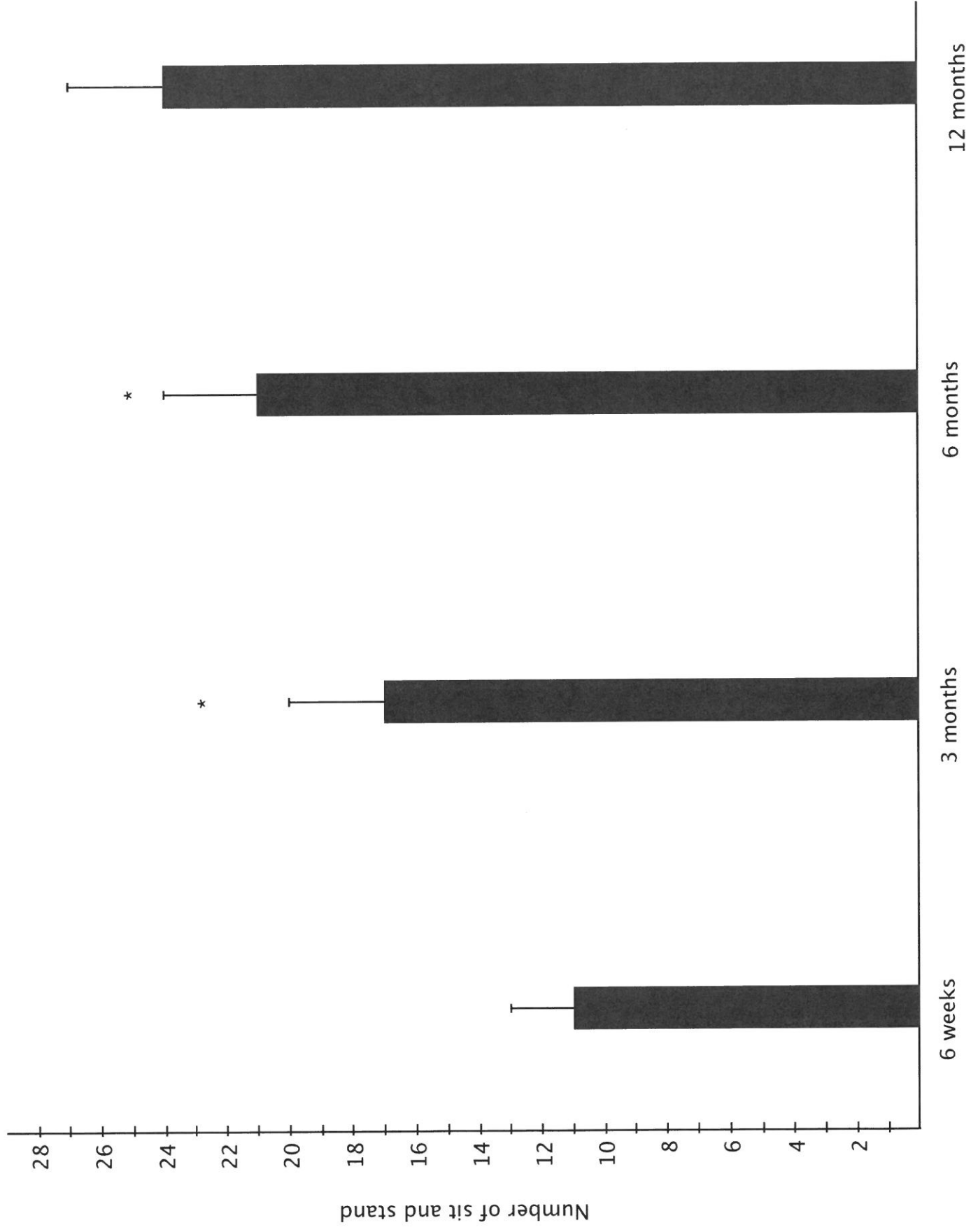




Figure 3c



**Table 1: Baseline characteristics of the 49 patients**

Age at time of fracture, mean (range)	43.1(18-79)
Gender, male/female	32/17
Height, mean (SD)	176.0 (11.2)
Weight, mean (SD)	77.7 (14.6)
BMI, mean (SD)	25.1 (3.7)
Smoker, yes/No	18/31
High/low-energy trauma	12/37
<b>Fracture classification AO-42-</b>	
A	30
B	14
C	5
Open/closed fracture	6/43
Fibula fracture, no/yes	5/44
<b>Additional treatment besides intramedullary nailing</b>	
Initial screw fixation of posterior aspect of the distal tibia	14
Matatarsfracture treated with Kirschner-wire	2
<b>Complications</b>	
Compartment syndrom	1
Broken screws	2

**Tabel 2: KOOS outcomes 12 months after intramedullary nailing of an tibial shaft fracture**

		KOOS				
		PAIN	ADL	SYMP	QOL	SPORT
Study population	Mean	84.5	86.4	86.9	63.4	57.2
	95% CI	79.5 – 89.5	81.5 – 91.3	82.7 – 91.1	55.5 – 71.3*	47.6 – 66.8*
Reference population **,**	95% CI	86.7 – 88.2	86.5 – 88.1	85.4 – 86.9	77.4 – 79.6	72.5 – 75.1