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Original Article

Mid-femoral and mid-tibial muscle cross-sectional area as predictors of tibial bone strength in middle-aged and older men

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Abstract

While it is widely acknowledged that bones adapt to the site-specific prevalent loading environment, reasonable ways to estimate skeletal loads are not necessarily available. For long bone shafts, muscles acting to bend the bone may provide a more appropriate surrogate of the loading than muscles expected to cause compressive loads. Thus, the aim of this study was to investigate whether mid-thigh muscle cross-sectional area (CSA) was a better predictor of tibial mid-shaft bone strength than mid-tibia muscle CSA in middle aged and older men. 181 Caucasian men aged 50–79 years (mean±SD; 61±7 years) participated in this study. Mid-femoral and mid-tibial bone traits cortical area , density weighted polar moment of area and muscle CSA [cm^2] were assessed with computed tomography. Tibial bone traits were positively associated with both the mid-femur (r=0.44 to 0.46, P<0.001) and the mid-tibia muscle CSA (r=0.35 to 0.37, P<0.001). Multivariate regression analysis, adjusting for age, weight, physical activity and femoral length, indicated that mid-femur muscle CSA predicted tibial mid-shaft bone strength indices better than mid-tibia muscle CSA. In conclusion, the association between a given skeletal site and functionally adjacent muscles may provide a meaningful probe of the site-specific effect of loading on bone.

Keywords: Muscle Cross-Sectional, Bone Strength, QCT, Older Men, Muscle-Bone Interaction

Introduction

Muscles and bones are inextricably linked and it is widely reported that bones adapt their mass, structure and strength to increased loads through forceful muscle contractions that result in increased stress and strain on bones[1-3]. This biomechanical link between muscle and bone supports the concept of the functional 'muscle-bone' unit[4], which predicts that any changes in muscle mass, size and strength should affect bone mass, structure and strength predictably and correspondingly[5].

Skeletal loading can be directly measured *in vivo*, e.g. with strain gauges[6] or with instrumented implants[7] but due to the invasive nature of direct measurements, indirect estimates are used more often. There are several indirect ways to estimate the loads imposed on bones, of which two approaches have been widely utilized. In the first approach, the loads have been estimated with performance (strength) measured by dynamometry[8]. In the other approach, muscle mass or muscle cross-sectional area has been quantified as a surrogate of the forces acting on bone[9]. When using muscle mass or size as a predictor of the loads imposed on bones, one might expect a stronger relationship with muscle(s) which act to bend long bones rather than those which run parallel to bones at skeletal sites subjected to bending (refer to Appendix for a simple numerical example)[10]. For example, the knee extensors are likely to be more strongly related to proximal and mid tibial bone strength than the foot extensors. There is a sound rationale to support this hypothesis. The tibia as a whole is subject to both bending and compressive loads caused by muscles and ground reaction forces[11,12]. Furthermore, modeling studies have indicated that

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in gait (arguably a typical loading scenario for the tibia), internal moments causing bending seem to be greater at proximal than at distal regions of the tibia; the distal regions undergoing predominantly compressive forces[13]. Lastly, the shape of the tibia is more circular and has less bone mineral content at the distal compared to proximal regions with the geometry apparently adapted to resist antero-posterior bending loads at the proximal end[14]. However, few studies have assessed whether thigh musculature, which may be expected to cause more bending moments than shank musculature, is also more closely associated with tibial shaft bone traits than shank musculature. Therefore, the aim of this study was to investigate whether mid-thigh muscle cross-sectional area was a better predictor of tibial mid-shaft bone strength and geometry than mid-tibia muscle cross-sectional area in middle aged and older men.

Characteristics	Mean (SD)
Age, years	61.0 (7.5)
Height, cm	174 (6)
Weight, kg	83.9 (11.0)
BMI, kg/m²	27.6 (3.4)
Physical activity, hr/week	3.6 (3.9)
Bone Measures	
Mid-Femur	
Femoral length, cm	47.3 (3.3)
I_{polar}, mg/cm	8015 (1669)
Cortical area, mm²	505 (49)
Mid-Tibia	
Tibia length, cm	38.2 (21.8)
I_{polar}, mg/cm	5146 (1147)
Cortical area, mm²	380 (43)
Muscle CSA	
Mid femur CSA, cm²	148 (19)
Mid tibia CSA, cm²	56 (9)

I_{polar} = Density weighted polar cross-sectional moment of inertia; CoA =cortical cross-sectional area; Muscle CSA= muscle cross-sectional area.

Table 1. Descriptive characteristics of the participants and bone and muscle indices at the mid-femur and mid tibia of the study group of middle-aged and older men (n=181).

Methods

Participants

The participants in this study were recruited for a randomized controlled trial designed to examine the effects of exercise and calcium-vitamin D on bone and muscle health and function in older men[15-17]. Thus, this study represents a secondary analysis using the baseline measurements from this intervention trial which included computed tomography measures of both tibial and femoral bone and muscle. Briefly, 181 Caucasian men aged 50-79 years were recruited from within the local community in Geelong and the surrounding areas in Victoria, Australia. Participants were excluded if they had taken calcium and/or vitamin D supplements, had participated in resistance training in the past 12 months or in weight bearing impact exercise for >30 minutes for 3 times per week in the preceding 6 months, had a body mass index (BMI) >35 kg/m^2, had a history of osteoporotic fracture or any medical condition or used medication known to affect bone metabolism, were lactose intolerant, consumed >4 standard alcoholic drinks per day, were current smokers, or had any chronic condition that might limit their ability to be involved in the intervention. Only men with normal to below average areal bone mineral density (total hip or femoral neck T-score between +0.4 and -2.4 SD) were included in the study. The study was approved by the Deakin University Human Ethics Committee and Barwon Health Research and Ethics Advisory Committee, and written consent was obtained from all participants.

Anthropometry

Standing height was assessed using a Holtain wall stadiometer (Crymych, Dyfed) to the nearest 0.1 cm. Body weight was measured using an A&D UC-321 electronic scale to the nearest 0.1 kg. Body mass index (BMI) was calculated as body weight (kg) divided by height (m) squared (kg/m^2).

CT assessment and analysis of bone and soft tissue

As previously reported[17], computed tomography was performed at the mid-femur and at the mid-tibia of the left leg (QCT; Philips Mx8000 Quad CT scanner, Philips Medical Systems). The scan parameters were 120 kVp, 85 mAs, and 2.5-mm slice thickness. Fluid dipotassium hydrogen phosphate (K_2HPO_4) bone equivalent calibration phantoms containing differing concentrations of K_2HPO_4 (50, 100, 150, 250 mg/cm^3) were scanned simultaneously with all participants. A series of four, 2.5-mm slices were taken at the midpoint of each segment, with the middle two slices analyzed and averaged. All cross-sectional QCT images were analyzed using the Geanie software program (BonAlyse Oy, Jyvaskyla, Finland). Mid-femur and mid-tibia cortical area (CoA, cm^2) and the density weighted polar moment of area (I_{polar}, mg/cm) were assessed using the Geanie 2.1 software program (BonAlyse Oy, Jyvaskyla, Finland) using a threshold of 600 mg/cm^3 [17,18]. We have previously reported that the short-term CV for two consecutive measurements in our laboratory was 0.14 to 0.69%[18]. Muscle cross-sectional area (CSA) was obtained by measuring the area defined within an attenuation range from 0 to 200 HU excluding the bone and marrow from both the tibial and femoral scan. We have previously reported that the short-term CV for two consecutive measurements in our laboratory was 0.40%[16].

Physical activity

As reported previously[17], leisure time and habitual physical activity (hours of weight bearing exercise per week, h/week) were assessed using the CHAMPS Physical Activity Questionnaire[19].

Statistical analysis

Unless otherwise noted, all results are reported as means and standard deviations (SD). Pearson correlation coefficients

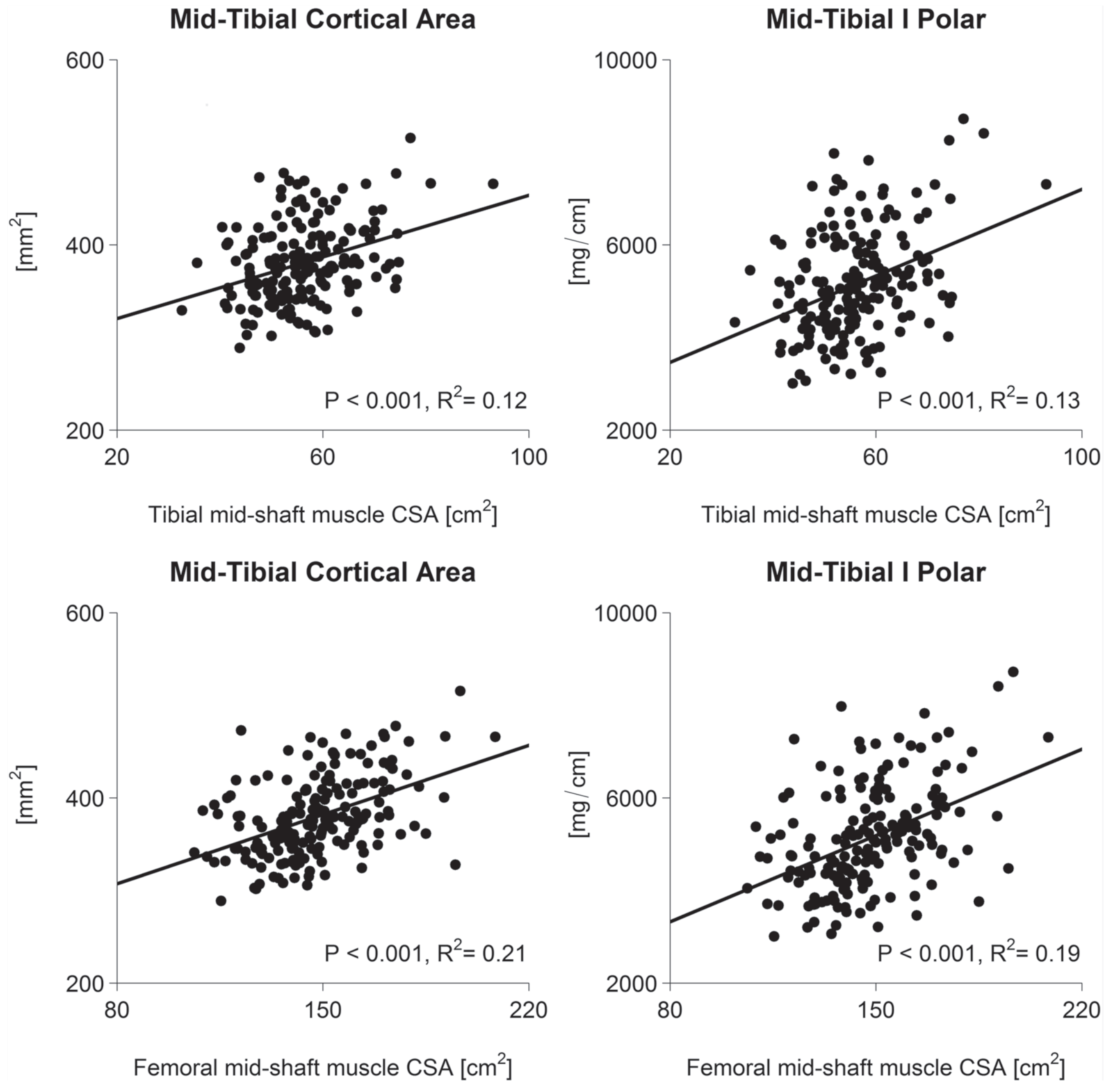

Figure 1. Associations between tibial mid-shaft bone strength indices (I_{polar}=density weighted polar cross-sectional moment of inertia, CoA=cortical area) and femoral and tibial mid-shaft muscle cross-sectional area (CSA) in 181 healthy middle-aged and older men.

were used to assess the association between tibial mid-shaft I_{polar} and CoA and mid-tibia and mid-femur muscle CSA. Forced entry stepwise regression analysis was performed using tibial bone strength indices (I_{polar} and CoA) as the dependent variable with age, weight, physical activity, femoral length and muscle CSA included as predictors in different models. Overall, five forced entry stepwise regression models were built, with the first step (base model) including age, weight, physical activity and femoral length. Thereafter, mid-femur and mid-tibia muscle CSA were added to the base regression model in different combination: 1) base model plus mid-tibia muscle CSA; 2) base model plus mid-femur muscle CSA; 3) base model plus mid-tibia and mid-femur CSA; 4) base model plus mid tibia muscle CSA entered first followed by mid-femur muscle CSA, and 5) base model plus mid-femur muscle CSA entered first followed by mid-tibia muscle CSA. Regression analyses were run on Z-transformed data to produce β-coefficients comparable between variables and between models. Statistical analyses were conducted with SPSS 17.0.1 (SPSS Inc.) software and the significance level was set at $P \leq 0.05$.

Results

The descriptive characteristics of the 181 men included in this study are shown in Table 1. Briefly, the men were aged 50 to 79 years (mean±SD; 61.0±7.5 years) with a mean BMI of 27.6±3.4 kg/m^2; 57% of the men were classified as overweight (BMI 25-29.9 kg/m^2) and 22% were obese (BMI>30 kg/m^2). On average, the men engaged in 3.6±3.9 hours of weight-bearing physical activity each week.

Table 1 shows bone strength indices and mid-femur and mid-tibia muscle CSA for all men. Tibial mid-shaft bone

	Model 1 Mid-tibia muscle CSA				Model 2 Mid-femur muscle CSA				Model 3 Both			
	I_{polar} [mm³]		Cortical Area [mm²]		I_{polar} [mm³]		Cortical Area [mm²]		I_{polar} [mm³]		Cortical Area [mm²]	
	β	*P-value*	β	*P-value*	β	*P-value*	β	*P-value*	β	*P-value*	β	*P-value*
Age, years	0.05	0.45	-0.01	0.89	0.11	0.07	0.07	0.28	0.12	0.06	0.07	0.26
Weight, kg	**0.21**	**<0.01**	**0.17**	**<0.05**	0.13	0.07	0.07	0.37	0.10	0.15	0.05	0.53
Tibial length, mm	**0.42**	**<0.001**	**0.33**	**<0.001**	**0.42**	**<0.001**	**0.33**	**<0.001**	**0.43**	**<0.001**	**0.34**	**<0.001**
Physical activity, h/week	0.09	0.13	**0.14**	**<0.05**	0.06	0.30	0.12	0.06	0.07	0.23	**0.12**	**<0.05**
Model R^2	***0.35***	***<0.001***	***0.25***	***<0.001***	***0.34***	***<0.001***	***0.24***	***<0.001***	***0.34***	***<0.001***	***0.24***	***<0.001***
Mid-tibia muscle CSA, mm²	**0.24**	**<0.001**	**0.24**	**<0.01**	-	-	-	-	0.11	0.13	0.09	0.27
Mid-femur muscle CSA, mm²	-	-	-	-	**0.38**	**<0.001**	**0.43**	**<0.001**	**0.34**	**<0.001**	**0.39**	**<0.001**
Change in model R^2	***0.05***	***<0.001***	***0.04***	***<0.01***	***0.09***	***<0.001***	***0.11***	***<0.001***	***0.10***	***<0.001***	***0.12***	***<0.001***

Beta (b) coefficients represent Z-transformed unstandardized coefficients in the full model including muscle CSA.
Forced entry stepwise regression analysis was performed using tibial bone strength indices (I_{polar} and CoA) as the dependent variable with age, weight, physical activity, femoral length and muscle CSA included as predictors in different models. The first step (base model) included age, weight, physical activity and femoral length. The second step was adding: mid-tibia muscle CSA in model 1, mid-femur muscle CSA in model 2 and mid-tibia and mid-femur CSA in model 3.

Table 2. Regression models predicting tibial midshaft bone traits in data from 181 middle-aged and older men.

strength indices were positively associated with both mid-femur muscle CSA (r=0.44 to 0.46, P<0.001) and mid-tibia muscle CSA (r=0.35 to 0.37, P<0.001) (Figure 1). In addition, femoral mid-shaft bone strength indices were also positively associated with mid-femur (r=0.45 to 0.49, P<0.001) and mid-tibia muscle CSA (r=0.31 to 0.37, P<0.001).

Multivariate linear regression analysis with only age, bone length, weight and physical activity included in the model revealed that these variables explained 25% and 35% of the variation in mid-tibial cortical area and I_{polar}, respectively (Table 2). When either mid-tibia muscle CSA, mid-femur muscle CSA or both were added to the models (regression models 1 to 3), we found that mid-femur muscle CSA predicted tibial mid-shaft bone strength indices rather than mid-tibia muscle CSA (Table 2). Including mid-femur muscle CSA to the regression model after mid-tibia muscle CSA (regression model 4) added an additional 6.0% and 7.8% (P<0.001) to the predictive power of the model for cortical area and I_{polar}, respectively. In contrast, including mid-tibia muscle CSA to the model after mid-femur muscle CSA (regression model 5) did not explain any additional variance.

Discussion

In this study of healthy community-dwelling men aged 50 years and over, we found that femoral mid-shaft muscle cross-sectional area was a stronger predictor of tibial mid-shaft bone strength than tibial mid-shaft muscle cross-sectional area. This finding highlights the importance of careful consideration of loading modes on a given skeletal site when deciding on which loading surrogate to use as an indicator of site-specific bone loading effects.

A large body of evidence supports the concept of a functional muscle-bone interaction, with studies in both children and adults showing that muscle cross-sectional area or regional lean tissue mass[10,20-23] and muscle strength, which are all estimates of loads acting on bone, are associated with measures of bone mass, geometry and strength[20,21,24-26]. The strength of the associations vary from study to study, with the correlation coefficients typically ranging from 0.3 to 0.8[10,20-26]. Consistent with these findings, we found that there was a moderate but significant correlation (r=0.31 to 0.49) between both mid-femur and mid-tibia muscle CSA with tibial and femoral mid-shaft bone strength indices in middle-aged and older men. From a mechanical and proximity perspective, related bones and muscles have exhibited stronger associations than mechanically (and proximity) unrelated bones[20-22,27]. For instance, in middle-aged men it has been reported that grip strength is a significant independent predictor of ulnar and radial DXA-measured BMD, but is not related to femoral neck or lumbar spine BMD[27]. Even within a given bone, some sites are more closely related to the adjacent muscle than others[10,25,27]. A study using pQCT in young adults indicated a closer association between tibial muscle CSA (or maximum forefoot ground reaction force in one-legged hopping) and bone mineral content at the tibial shaft (14%, 38% or 66% of tibial length) than at the distal tibia (4% of tibial length)[8]. It has been suggested that the reason for this site specificity, even within a given bone, relates to the loading of a given bone site and/or its anatomical role[10,25,28].

There is a sound mechano-physiological reason underlying our finding that femoral mid-shaft muscle CSA was a stonger predictor of tibia mid-shaft bone strength than tibial mid-shaft muscle CSA. Tibial mid-shaft musculature consists primarily of muscles originating from the tibia and fibula, which consequently have their line of muscle pull parallel to the tibia, in all knee and ankle joint angles. Thus, one would expect that these muscles would primarily produce compressive loads on the tibia. However, there is evidence that loading from the tibial mid-shaft muscles is not purely compressive. The triceps surae muscle is likely to provoke some bending and compressive loading, as shown by the findings from an electrical stimulation study of the soleus of a complete T4 motor-sensory nerve paralyzed person[29]. In this individual, the soleus muscle was electrically stimulated with 500, less than 1 second long contractions, 5 days per week for 4 years. This led to amelioration of tibial bone loss at the distal tibia with the protective effect more pronounced posteriorly than anteriorly[29]. On the other hand, the attachment sites of some femoral mid-shaft muscles have their insertions at the proximal tibia, notably the quadriceps femoris through the patellar tendon. This would be expected to produce marked bending moments around the knee joint and the tibia, especially when the knees are flexed, as indicated by the close temporal association between patella tendon force during counter movement jumping[30] and the typical knee joint moment pattern around the knee joint in the same movement[31]. Notably, patella tendon forces explains nearly all of the measured torque over the knee joint (r^2=0.94), at least in the isometric knee extension[30]. Since bending is one of the primary loading modes at the tibial shaft[11-13], and because the shape of proximal tibial diaphysis seems particularly well adapted to bending moments[10,14], it is not unexpected that the femoral mid-shaft muscle CSA was a significant predictor of tibial shaft, even more so than tibial mid-shaft muscle CSA. The implications of these findings are that they support current international consensus guidelines which recommend targeted, site-specific interventions to maximise bone adaptations[32,33]. Moreover, examining the associations between a bone-site and functionally adjacent muscles may provide a more meaningful probe for site-specific loading, thereby enabling more targeted exercise interventions to maximise bone strength.

Despite the significant relationship between muscle and bone traits at the tibia, the regression models in the present study indicated that around 60% of the variability in bone traits remain unexplained. Genetics has been estimated to explain between 60-80% of variation in bone strength[34-36], with other lifestyle and environmental factors assigned to the remaining 20-40% of the variance[37]. Skeletal loading and nutrition can be considered two of the more important environmental factors. Indeed, the relative importance of these two environmental factors is highlighted in an interesting pair of observations provided in a study on paralyzed people, and women suffering from anorexia nervosa. In the case of the paralysis patient, when the loading imposed by muscles was removed/minimized both tibial and femoral shaft bone cross-sectional areas decreased by 30-40%, while distal bone sites lost 55-60% of their mineral mass[38]. On the other hand, severe malnutrition (anorexia nervosa) does not appear to diminish bone mass as markedly and some patients even exhibit normal bone strength[39]. To summarize, these results indicate that skeletal loading plays a central role in determining bone strength over and above that imposed by the genes and can thus be considered one of the most important modifiable factors for improving skeletal health.

In this study, we used whole muscle CSA alone as an indicator of skeletal loading. As discussed previously, there are several ways to estimate loading on bone *in vivo*. For example, there is some evidence that appropriate muscle performance measures may be more closely associated with bone strength than muscle CSA[8]. This would suggest that muscle CSA (or mass) may be a suboptimal surrogate of skeletal loading when considered in isolation. One of the reasons why muscle mass may only explain some, but not all of the variance in bone strength is illustrated in the myostatin knockout mice model, in which mice lacking myostatin have normal femoral size, shape and mass despite muscle mass being up to three times larger than those of wild type animals[40,41]. However, if the myostatin deficient animals were made to exercise, bone strength was increased to a similar extent or greater compared to wild-type animals, suggesting that loading and subsequent muscle forces are important[41]. Additionally, it has been reported that neither muscle mass nor CSA predicts isometric or dynamic force/torque production accurately in humans[42,43]. Thus, the mechanostat paradigm would predict that appropriate performance measures should predict bone structure and strength better than muscle mass or size alone. However, because the bone loading environment cannot be fully described by performance in a single test, predicting bone strength via appropriate muscle performance measures is not without problem[23]. That is, it is well established that bone adaptation is largely dependent on strain magnitude, rate, number of loading cycles, loading direction and temporal separation between loading bouts[44-46], all of which are not captured with a single measure of performance. Consequently, estimating the prevalent skeletal loading in a more accurate manner (e.g. with extended accelerometry measurements[47-51]) may well improve the ability to predict bone traits.

The strength of the study lies in the relatively large number of participants, which enabled the comparison between mid-femoral and mid-tibial muscle CSA as predictors of mid-tibial bone traits. However, there are a number of limitations. First, the cross-sectional design is not able to demonstrate causal relations and thus the findings remain hypothesis generating. Second, this study only included Causasian males aged 50-79 years recruited as part of a larger randomised controlled trial with distinct inclusion/exclusion criteria, and thus our findings may not be generalizable to other groups. Third, this study was limited to an assessment of muscle and bone traits at the 50% femur and tibial sites, and the muscle-bone relationship may vary along the length of a given bone[10]. Fourth, no effort was taken to separate the effects of extensor and flexor musculature, which could play a role in the examined associations e.g.through co-activation of agonists and antagonists, which may markedly affect skeletal loading[52]. Finally, thigh musculature comprises a larger proportion of body mass than tibial musculature and even though the regression models were adjusted for height and body mass, it cannot be ruled out that some of the observed association was driven by the effect of body size.

In conclusion, we found that femoral mid-shaft muscle CSA was a better predictor of tibial mid-shaft bone geometry and strength than tibial mid-shaft muscle CSA in middle-aged and older men. The finding suggests that it is important to carefully consider the loading modes of a given skeletal site rather than simply relying on spatial proximity in estimating the loading environment.

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Appendix

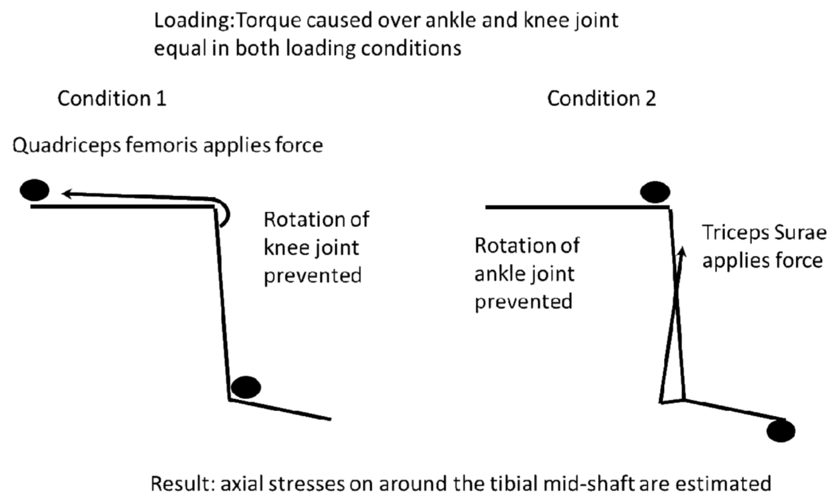

Figure A1. Schematic illustration of the numerical test cases for two tibial loading scenarios. Condition 1) loading induced by the quadriceps femoris muscle group; Condition 2) loading induced by the triceps surae muscle group.

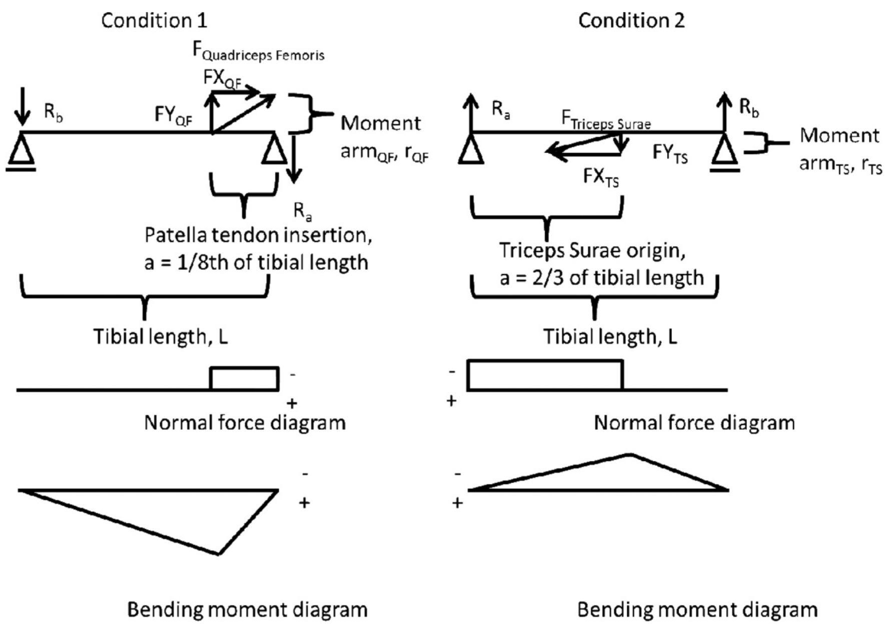

Figure A2. Simply supported beam diagram with the forces considered for each test case. QF denotes quadriceps femoris muscle group, TS triceps surae muscle group, R is the vertical component of the reaction force at the support. Negative sign indicates compression for the normal force diagram, whereas a bending moment with a negative sign will cause compression on the upper part of the beam.

To understand the role of muscles on tibial loading, two numerical cases are presented. In the first case (Figure A1, Condition 1) the hip joint is constrained from movement and the distal tibia is supported just above the ankle joint. It is assumed that the quadriceps femoris muscle group (QF) produces a force, which would extend the knee if the motion was not constrained. In the second scenario (Figure A1, Condition 2), the knee is constrained from motion and support is placed under the toes. In this case it is assumed that the triceps surae muscle group produces a force, which would plantarflex the foot if the

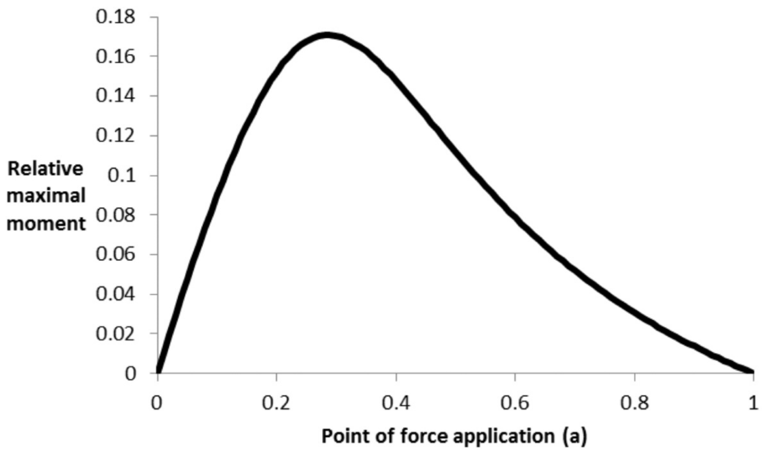

Figure A3. The maximal moment caused at the point of force application depending on the point of force application relative to the bone length. The plot is calculated for muscles with a moment arm of 1/8th the length of the bone.

motion was not constrained.

The problem is solved by simplifying the loading case to a simply supported beam. To solve the problem, four main assumptions are made:

- The force caused by the QF has the same moment arm relative to the knee joint as the force caused by the TS muscle group relative to the ankle joint.
- The moment arm (r) is 1/8th of the length of tibia.
- The insertion of the QF is 1/8th of the tibial length from the knee towards the ankle and the origin of the TS muscle group is 2/3rds of the tibial length from the ankle towards the knee.

The first assumption leads to a situation where in both cases the same muscle force will lead to the same torque around the actuated joint. The second assumption is based on a tibial length of 40 cm with a moment arm of 5 cm. The third assumption is needed to calculate the bending moments caused by either muscle.

The bending moment M in a given point (x) along the bone shaft can be calculated as (Figure A2):

$$M(x)=\begin{cases} R_a \cdot x, & x\le a \\ R_b \cdot (L\text{-}x) & x\ge a \end{cases}$$

$$R_a = FY \cdot \left(1\text{-}\frac{a}{L}\right)$$

$$R_b = FY \cdot \frac{a}{L}$$

$$FY = F \cdot \frac{r}{\sqrt{a^2+r^2}}$$

where a=point of force application, i.e. QF insertion or TS origin; r=moment arm; F=applied muscle force, either TS or QF; FY=muscle force component parallel to the bone; L=tibial length; R_a=the vertical component of the reaction force at the support that does not allow translation; R_b=the vertical component of the reaction force at the support, which does allow translation.

To solve the bending moments for the two conditions presented, the equations take the form:

$$M(x)=\begin{cases} F \cdot \dfrac{r}{\sqrt{a^2+r^2}} \cdot \left(1\text{-}\dfrac{a}{L}\right) \cdot x, & x\le a \\ F \cdot \dfrac{r}{\sqrt{a^2+r^2}} \cdot \dfrac{a}{L} \cdot (L\text{-}x), & x\ge a \end{cases}$$

For the first condition, x=1/2 L and a=1/8 L, so x>a and the upper equation is used. For the second condition, x=1/2 L and a=2/3 L, so x<a and the lower equation is used. F=1, L=0.4 m, and r=1/8 L is inserted in both conditions. Consequently for condition 1: M(1/2 L)=0.018 and for condition 2: M(1/2 L)= 0.012, giving QF a 44% higher loading magnitude (the moments actually have opposite signs) at the tibial mid-shaft than TS with the same moment imposed over the respective joint.

In the case of QF, no normal force is imposed at the tibial mid-shaft, but for TS there is a normal force, which causes compression at the mid-shaft. Assuming a tubular bone with a length of 40 cm, cortical cross-sectional area of 3.8 cm^2, and endo- and periosteal diameters of 2.58 cm and 1.34 cm, respectively, the normal force of a TS force of 1 unit causes a stress of 25.8 units/m^2, whereas the maximal stress caused by the bending moment of the same force is 7900 units/m^2. This indicates that the loading caused by the compressive force is negligible compared to the bending.

Let us extend the analysis to a more general solution. From the moment equations it can be seen that the maximum bending moment occurs at the point of force application ($R_a \cdot x$ gets larger with increasing x until a is reached, whereas $R_b \cdot (L\text{-}x)$ gets smaller with increasing x), so bending moment will next be considered only at x=a, i.e. the maximal bending moment caused by a given insertion site, while the moment produced over the joint remains constant. If we insert r=1/8 L, consider F as 1 and L as 1 (i.e. lengths are given as relative to the length of the bone), the equations simplify to:

$$M(a)= \frac{1/8 \cdot (1-a) \cdot a}{\sqrt{a^2+(1/8)^2}}$$

From the above equation it can be seen that the only remaining parameter is the point of force application and by varying the insertion point between 0 and 1 it can be seen that the highest maximal bending moment will be caused by a muscle that is inserted (or originates) to 0.29 of the bone length (Figure A3), which indicates that a muscle that is expected to bend the bone instead of compressing it, may be expected to impose the greatest loading.