STUDIES IN SPORT, PHYSICAL EDUCATION AND HEALTH
222

Tahir Masood

Calf Muscle Activation Strategies in Healthy and Injured Achilles Tendon Conditions

JYVÄSKYLÄN YLIOPISTO

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To the loving memories of my father (*Abdul Haque*: 1950 – 2014)

&

My mother (*Sughra Begum*: 1954 – 2015)

ABSTRACT

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Achilles tendon transmits triceps surae muscle force to the foot and is one of the strongest tendons in human body. Despite its strength, it is not immune to injuries leading to disruption of normal calf muscle activation strategies and leg function. The objective of this series of studies was to investigate 1) plantarflexor muscle use during submaximal isometric plantarflexion contractions, 2) electrical and metabolic activity patterns of superficial and deep ankle plantarflexors in Achilles tendinopathy and Achilles tendon rupture, and 3) effects of eccentric calf myotendon rehabilitation on skeletal myotendon glucose uptake and myoelectric activity patterns of ankle plantarflexors. Isometric plantarflexion force, surface electromyography and positron emission tomography measurements were performed on 19 - 35 year old subjects and both longitudinal and cross-sectional study designs were used. Myoelectric activity and myotendon glucose uptake during submaximal isometric plantarflexion were quantified at baseline, and after eccentric rehabilitation in Achilles tendon injury patients. Results indicated that in healthy individuals the triceps surae accounted for 70% and 80% of cumulative myoelectric and metabolic activities respectively. Additionally, although muscle glucose uptake was similar to healthy controls, myoelectric activity of soleus was greater in the symptomatic leg of the Achilles tendinopathy patients. Similarly, Achilles tendon glucose uptake in both legs of the tendinopathy patients was higher than that of healthy controls. The significant reduction in the maximal plantarflexion force caused by Achilles tendinopathy was eliminated by 12 weeks of heavy-load eccentric rehabilitation. Furthermore, the rehabilitation caused a greater glucose uptake in both soleus and lateral gastrocnemius of the symptomatic leg, while medial gastrocnemius and flexor hallucis longus had higher uptake in the asymptomatic leg. Conversely, the Achilles tendon glucose uptake was not affected by eccentric rehabilitation. Regarding electro-myography, significant rise in the activity of lateral gastrocnemius was evident after the rehabilitation. Eccentric rehabilitation was also effective in reducing self-reported severity of Achilles tendinopathy. In the Achilles tendon rupture patient, all plantarflexors and Achilles tendon displayed substantially higher glucose uptake than in the control subject followed by considerable reduction due to eccentric rehabilitation.

Keywords: Myoelectric activity, glucose uptake, surface electromyography, positron emission tomography, eccentric rehabilitation, isometric force.

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Where to start? Years ago when I got enrolled in the PhD program, I noticed in the 'acknowledgement' section of my supervisor's PhD dissertation a note of gratitude for a professor for recommending her for PhD. The same professor, after 10 years or so, recommended me for postgraduate studies to her. Hence, I owe Professor Janne Avela two-fold thanks and appreciation. Surely, my gratitude towards you does not end there.

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Sargodha, March 2015
Tahir Masood

LIST OF ABBREVIATIONS

[^{18}F]-FDG	[^{18}F]-fluorodeoxyglucose
µmol	Micromole
3-D fmMRI	three-dimensional muscle functional magnetic resonance imaging
ADC	Analog-to-digital converter
AMPK	Adenosine monophosphate-activated protein kinase
AOFAS	American orthopaedic foot and ankle society
AT	Achilles tendon
ATR	Achilles tendon rupture
CED	Cambridge electronic design
CTRL	Control subjects
dB	Decibel
DC	Direct current
EMG	Electromyography
EMG_{MVIC}	Electromyography during the maximal isometric contraction effort
ES	Effect size
FHL	Flexor hallucis longus
FUR	Fractional uptake rate
GLUT1	Glucose transporter type 1
GLUT4	Glucose transporter type 4
GU	Glucose uptake
IED	Inter-electrode distance
ISEK	International society of electrophysiology and kinesiology
LC	Lumped constant
LG	Lateral gastrocnemius
MC-SEMG	Multi channel surface electromyography
MG	Medial gastrocnemius
MPF	Median power frequency
MRI	Magnetic resonance imaging
mRNA	Messenger ribonucleic acid
MVIC	Maximal voluntary isometric contraction
n	Number of subjects
Na^{22}	An isotope of natrium (sodium)
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NO-PAIN	Asymptomatic leg
OPER	Operated leg
PAIN	Symptomatic leg
RCT	Randomized controlled trial
PET	Positron emission tomography
RMS	Root mean square
ROI	Region of interest
SD	Standard deviation
SEMG	Surface electromyography

SENIAM	Surface electromyography for the non-invasive assessment of muscles
SF-36	Short form-36
Sol.	Soleus
SUV	Standardized uptake value
TD	Tissue density
TS	Triceps surae
UNOP	Unoperated leg
VAS	Visual analogue scale
VISA-A	Victorian institute of sports assessment – Achilles tendon
VO_{2max}	Maximal oxygen uptake/consumption

LIST OF ORIGINAL PAPERS

This dissertation is based on the following original manuscripts, which are referred to in the text by their Roman numerals.

I. Masood T., Bojsen-Møller J., Kalliokoski K.K., Kirjavainen A., Äärimaa V., Magnusson S.P., and Finni T. (2014). Differential contributions of ankle plantarflexors during submaximal isometric muscle action: A PET and EMG study. *J Electromyogr Kinesiol* 24: 367–374.

II. Masood T., Kalliokoski K.K., Bojsen-Møller J., Magnusson S.P., and Finni T. (2014). Plantarflexor muscle function in healthy and chronic Achilles tendon pain subjects evaluated by the use of EMG and PET imaging. *Clin Biomech* 29: 564–570.

III. Masood T., Kalliokoski K.K., Magnusson S.P., Bojsen-Møller J., and Finni T. (2014). Effects of 12-wk eccentric calf muscle training on muscle-tendon glucose uptake and SEMG in patients with chronic Achilles tendon pain. *J Appl Physiol* 117: 105–111.

IV. Masood T., Kalliokoski K.K., Bojsen-Møller J., and Finni T. (2014). Muscle-tendon glucose uptake in Achilles tendon rupture and tendinopathy before and after eccentric rehabilitation: A case-control report. *Submitted for publication.*

CONTENTS

1 INTRODUCTION

Most voluntary synovial joint movements in humans are accomplished by the activation of a group of skeletal muscles rather than an individual muscle. These muscle groups, called agonists or prime movers, act in tandem to generate muscle force which is transmitted via individual tendons (e.g., hamstring muscles), a common tendon (e.g., quadricpes muscle), or both (e.g., ankle plantarflexors). Specifically, ankle plantarflexion involves combined action of superficial and deep plantarflexor muscles of the posterior compartment of leg. Supericial muscles comprise soleus, medial gastrocnemius, and lateral gastrocnemius – collectively termed triceps surae (TS) – which all insert on to calcaneus through a common tendon; the Achilles tendon. Deep muscles include flexor hallucis longus, tibialis posterior, flexor digitorum longus, and plantaris which exert force via their individual tendons. The delicate interplay among such muscles within a group can be termed as activation strategies. These strategies ensure the production of either a smooth joint movement or merely muscle fascicle shortening as in the case of isometric efforts.

Insight into how different muscles within a group activate, in relation to each other, during a motor task is vital to fully comprehend the pathomechanics of a musculoskeletal injury such as Achilles tendinopathy. Since muscles utilize metabolic energy, undergo shape deformation, and generate electrical signal during activity, these characteristics can be exploited to explore the extent of their contribution during a wide variety of muscle actions. In the case of ankle plantarflexion, differential contributions of various plantarflexors, both superficial and deep, have been studied using a number of techniques. These approaches include force recodrings with an in-situ buckle-type force transducer on the Achilles tendon (Gregor et al. 1991), cadaver estimations of moment arm length (van Zandwijk et al. 1996), measurement of tendon forces with in-vivo optic-fiber technique (Finni et al. 2000), and evaluation of individual muscle contraction velocities with velocity-encoded cine phase-contrast magnetic resonance imaging (Finni et al. 2006).

Despite wide spread use and potential abuse of surface electromyography (SEMG) to study muscle function (de Luca 1997), there is a paucity of literature

on its application regarding evaluation of ankle plantarflexor muscle activation strategies. The inherent limitation that the conventional bipolar SEMG entails is the provision of selective and limited information about electrical activity of muscles (Knight & Kamen 2005; Hodson-Tole et al. 2013). Positron emission tomography (PET), enabling exploration of a whole muscle, has also not been used to investigate how ankle plantarflexors activate in relation to each other.

Musculoskeletal injury has been shown to exhibit an altered pattern of muscle activation (Finni et al. 2006) although it is difficult to say whether altered activation patterns precede such injury or a clinical manifestation of it. The importance of a normally functioning tendon cannot be over-emphasized as they remain the primary medium of muscle force transmission to the skeleton. Although the Achilles tendon is one of the longest and strongest tendons in human body, it too has an "Achilles heel" or two. It is not immune to either abrupt rupture or injury due to repetitive, cyclic loading over time (Maganaris et al. 2004). Normal functioning of AT is vital to a wide variety of physical activities including locomotion. However, any disorder affecting the tendon would lead to compromised muscle force transmission thus altering the normal mechanism of ankle plantarflexion.

Major problems affecting the AT are tendinopathy and complete rupture of the tendon. A number of factors, both intrinsic and extrinsic, have been blamed for the pathogenesis of Achilles tendinopathy in athletes (Maffulli & Kader 2002; Paavola et al. 2002; Lesic & Bumbasirevic 2004; Damuth et al. 2008, Longo et al. 2009). Achilles tendinopathy can be either mid-portional or insertional type. Rupture of the AT, on the other hand, is the third most common major tendon disorder after those of the rotator cuff and knee extensor mechanism. Although most AT ruptures are unilateral, there is a 200-fold greater risk of contralateral rupture in such patients (Aroen et al. 2004). Conservative management of such injuries include various physical rehabilitation regimes, such as eccentric rehabilitation. Eccentric calf muscle training has been reproted to be beneficial in Achilles tendinopathy and is commonly used to treat both mid-portion and insetional type Achilles tendinopathies (Alfredson et al. 1998; Jonsson et al. 2008). The effectiveness of a given physical rehabilitation regimen can be evaluated by investigating how effectively it restores the normal activation pattern of a particular muscle group during a certain motor task.

Prior to the current study, to the best of author's knowledge, no report has surfaced concerning evaluation of the use of ankle plantarflexors during submaximal isometric plantarflexion using SEMG and PET in healthy or injured Achilles tendon conditions. In addition, although eccentric rehabilitation has been tested for its efficacy in treating tendinopathies, use of objective measures, such as myoelectric activity and glucose uptake, to study its effects is scarce, if not totally absent. This study provides novel and valuable insights into calf muscle function during submaximal intermittent isometric plantarflexion. It is hoped that future research will benefit from the reference values reported in this study.

2 REVIEW OF THE LITERATURE

Muscles can be regarded as the engines which use chemical energy obtained from the food as the fuel to power various body systems. The fundamental role of skeletal muscles as part of the musculoskeletal system is to generate force through activation of their fibers thus enabling us to perform wide ranging tasks of daily living including locomotion. The force generated by working muscles is transmitted to the skeleton through the tendons which attach muscles to the bones of their origin and insertion. Hence tendons can be considered as the primary force-transmitting gateways of musculoskeletal system.

Conventionally viewed, all the muscle force produced is transmitted longitudinally via tendons to the skeleton, which in most cases, results in joint movement. However, the phenomenon of 'lateral myofascial force transmission' has also been reported albeit in in-vitro animal studies (Huijing 1999a,b; Purslow 2002; Yucesoy et al. 2003; Huijing et al. 2007; Huijing & Baan 2008). Human studies, on the other hand, do not follow the same direct approach and the results are based mainly on imaging and cadaver studies which have yielded evidence of nonuniform strain in human soleus aponeurosis-tendon complex attributable to force transmission along intrasoleus connective tissue (Finni et al. 2003; Bojsen-Møller et al. 2004; Bojsen-Møller et al. 2010). Whether or not muscle force is transmitted laterally in humans, the importance of normally functioning, healthy tendons can not be over-emphasized as they remain the primary medium of muscle force transmission to the skeleton.

The following sections will address the ankle plantarflexor muscle function in both health and disease, methods of investigating muscle function, and the rehabilitation of triceps surae-Achilles tendon complex.

2.1 Overview of ankle plantarflexion

Ankle plantarflexion in humans is accomplished by a combined action of various muscles of the posterior compartment of leg or the posterior crural muscles. These muscles can be divided into two groups, separated by the deep transverse fascia of the leg. The superficial group mainly comprises the primary muscles of plantarflexion namely the medial gastrocnemius, the lateral gastrocnemius, and the soleus. The deep group consists of flexor digitorum longus, flexor hallucis longus, tibialis posterior, and popliteus.

2.1.1 Triceps surae-Achilles tendon complex

The three superficial or primary plantarflexors can be collectively termed as the triceps surae, referring to the three distinct muscle-to-bone insertions the group constitutes. The distal ends of these three muscles unite together to form a common structure to be inserted on to the calcaneus bone; the Achilles tendon (AT) or the tendo calcanei. Muscle force produced by the triceps surae is transmitted to the skeleton through the Achilles tendon which is one of the longest and strongest tendons in the human body. Loading of AT has been reported to be as high as 9 kN, equivalent to 12.5 times the body weight, in some cases (Komi 1990). Repetitive maximal isometric contraction leads to a reduction in the plantarflexion torque (Kawakami et al. 2000), but submaximal muscle contractions could be carried out even after the onset of muscle fatigue (Enoka & Duchateau 2008).

Several studies have investigated the distribution of loading within the compartments of the triceps surae muscle. Some of the notable ones come from the work of Arndt and colleagues. In a series of in vitro human experimental studies, it was demonstrated that inhomogeneous force distribution across the Achilles tendon was caused by the tensile loading of different triceps surae components. For instance, when medial gastrocnemius was loaded alone, the medial tendon forces were found to be significantly greater. Conversely, the loading of both medial and lateral gastrocnemii significantly increased the lateral tendon forces, as did the loading of all three components of the triceps surae (Arndt et al. 1999a). Furthermore, an evaluation of differential moments at the calcaneus bone due to force input from different triceps surae components has also been reported. It was shown that force input in medial and lateral gastrocnemii together lead to significantly higher plantarflexion moments compared to soleus alone. Additionally, loading of the lateral gastrocnemius resulted in eversion moment as opposed to inversion moment caused by the combined loading of the medial gastrocnemius and soleus while ankle abduction moment was observed in all cases (Arndt et al. 1999b).

The Achilles tendon, like any other tendon, demonstrates a viscoelastic behavior instead of rigidly connecting the triceps surae muscle to the calcaneus. The breakdown of tendon structure is shown in Fig. 1. As advancement to the traditional in vitro design used by Arndt and coworkers, in vivo techniques

have been devised to overcome the limitations and disadvantages associated with in vitro testing. For example one in vivo study involving Achilles tendon force and strains calculations during graded maximal isometric plantarflexion contractions found that the distribution of strain along the triceps surae aponeurosis is homogeneous. However, this study also cautioned against neglecting small joint angular rotations and antagonistic coactivation since it could have significant influence in stiffness estimations (Magnusson et al. 2001).

Real-time ultrasonography is widely used to study the Achilles tendon behavior in vivo. Such studies have indicated that the material properties of tendons are not dependent on the physiological loading and function (Maganaris & Paul 2002). Moreover, the distribution of strain in the triceps surae aponeurosis and tendon complex may not be uniform. Evidence has been presented that shows a preferential loading of the tendon side free from injury in the early stages of tendinopathy thus stress-shielding the injured side, given the material properties are homogeneous throughout the Achilles tendon (Finni et al. 2003; Maganaris et al. 2008). This may demand utmost caution while collecting specimen for investigating the presence of inflammatory process since the tendinopathic changes might be confined to a certain area especially in the early stages of the disease. Additionally, the strains within the proximal and distal regions of the aponeurosis, and between the aponeurosis and the Achilles tendon are similar (Muramatsu et al. 2001). Concerning tissue displacement, in the case of human soleus aponeurosis, the distal and middle regions of the aponeurosis have been shown to behave quite differently using cine phase-contrast magnetic resonance imaging. It was reported that the mid region lengthened 2.2% while the distal aponeurosis shortened 2.5% at 40% maximal isometric contraction force (Finni et al. 2003). However, it must be noted that in vivo experiments are not immune to a different set of inherent flaws, such as heat losses by the tendon-muscle and tendon-bone interfaces, which should be considered while interpreting the results of such studies (Maganaris et al. 2008).

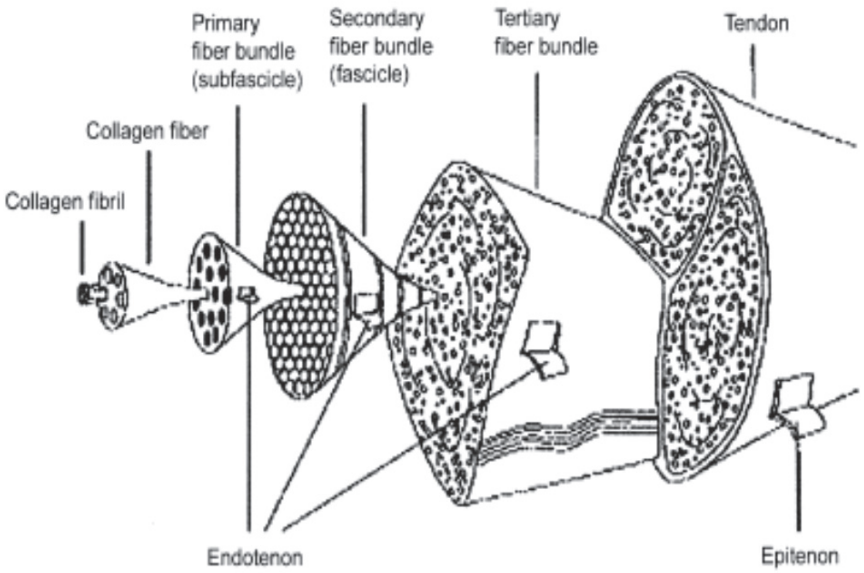

FIGURE 1 The organization of tendon structure from collagen fibrils to the entire tendon (reproduced from Kannus 2000).

While tendon strain studies show a reasonable consensus, the investigation into the vascularization of the Achilles tendon exhibit great variability. For example, the reported area of most vascularization ranged from the tendon origin, to the midsection, to the tendon insertion (Theobald et al. 2005). An insight into the internal structure of the human Achilles tendon has revealed that it may comprise different parts similar to those in many lower mammals. It has been reported that the posterior layer of the Achilles tendon is formed by the medial fibers of the medial gastrocnemius while the lateral fibers compose the lateral border of the tendon. Similarly, the anterior border of the tendon is constituted by the fibers from the lateral gastrocnemius muscle (Szaro et al. 2009) (Fig. 2).

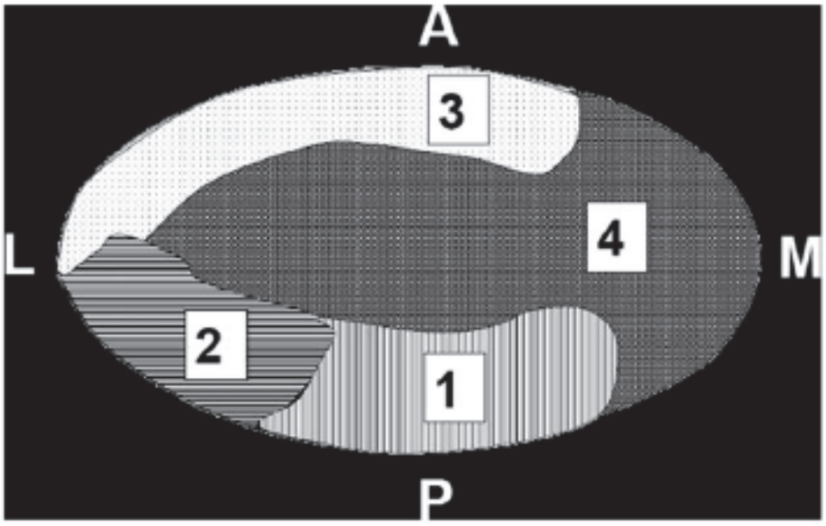

FIGURE 2 Transverse cross-section through the left Achilles tendon, 1 cm above tuber calcanei. (1) The fibers from the medial part of the medial head of the gastrocnemius, (2) the fibers from the lateral part of the medial head of the gastrocnemius,(3) the fibers from the lateral head of the gastrocnemius and (4) the fibers from the soleus, A:anterior,P:posterior,M:medial,L:lateral. (Reproduced from Szaro et al. 2009).

The understanding of how inflammation influences the critical interplay between mechanical signalling and biochemical changes in the tendon matrix is also important. While animal studies have shown that mechanical loading regulates tendon collagen homeostasis, core tissue in adult human Achilles tendon is more difficult to explain. It has been suggested that the outer tendon region might be the primary location of tendon adaptation in response to loading. This peritendinous tissue has shown a rise in inflammatory mediators following physiological mechanical loading which may have a role in augmented peritendinous collagen synthesis and tendon blood flow due to exercise (Kjaer et al. 2013). It is commonly known that Achilles tendon heals poorly and slowly. Whether the underlying cause was a poor tissue turnover was not known until the use of ^{14}C bomb-pulse method. The retention of ^{14}C at the levels comparable to the atmospheric levels of several decades prior to the sampling signified that the core tendinous tissue turnover was indeed very limited (Heinemeier et al. 2013).

2.1.2 Deep plantarflexors

All deep plantarflexors possess their individual tendons which transmit muscle force to the foot. The contribution of individual deep plantarflexors depends on the muscle cross-sectional area and moment arm, among other parameters. It has been shown that FHL is the most important contributor among the deep plantarflexors, in terms of their moment arm, nearly 3.5 times more than that of

the tibialis posterior (Klein et al. 1996). Similarly, according to Goldmann & Bruggemann (2012):

"*The flexor hallucis longus muscle has the largest physiological cross-sectional area (muscle volume divided by fiber length) of long and short toe flexor muscles [TFM] (Friederich & Brand, 1990; Kura et al. 1997) and therefore might produce the largest forces*".

With respect to the triceps surae, the average moment arm (1.43 cm), in relation to the ankle joint, of deep plantarflexors is about 3.5 times smaller in human cadavers (Klein et al. 1996). Furthermore, the total cross-sectional area of these muscles is approximately half that of the triceps surae (Yamaguchi et al. 1990).

2.1.3 Relative activation of plantarflexors

Several attempts have been made to evaluate the distribution of activation between the primary and deep ankle plantarflexors during various activities. One study reported the contribution of the triceps surae to the total torque generated at the ankle joints during maximal isometric plantarflexion by comparing a leg with excised triceps surae to the healthy contralateral leg. The input from the triceps surae and the deep plantarflexors was 62% and 38% of the net ankle joint torque respectively (Murray et al. 1976). Based on the physiological cross-sectional area of human leg muscles calculated from magnetic resonance imaging, the role of triceps surae to plantarflexion moment has been estimated to be 77% (Fukunaga et al. 1992). On the other hand, calculations based on the cadaver moment arm lengths and total muscle cross-sectional areas from other studies, triceps surae might be responsible for at least 88% of the plantarflexion moment with only 12% input from all the deep plantarflexors combined (van Zanwijk et al. 1998). Gregor et al. (1998) also investigated and compared the moment produced by the triceps surae muscle and the residual muscle moment at the ankle during cycling at three different power outputs. Myoelectric activity and changes in muscle-tendon length were used to estimate the contribution of individual triceps surae components while a buckle-type force transducer was surgically embedded in the Achilles tendon. It was found that the triceps surae moment accounted for nearly 65% of the residual muscle moment at the ankle joint. More recent studies have used techniques such as an in vivo optic-fiber technique to record tendon forces (Finni et al. 2000), and velocity-encoded cine phase-contrast magnetic resonance imaging to calculate individual muscle contraction velocities (Finni et al. 2006).

Studies examining the relative of primary and deep plantarflexor muscles have also found significant inter-individual differences denoting heterogeneity in how individuals activate various plantarflexors to achieve a given voluntary plantarflexion task (Finni et al. 2006; Bojsen-Møller et al. 2010). One example of such pattern is illustrated in the figure 3.

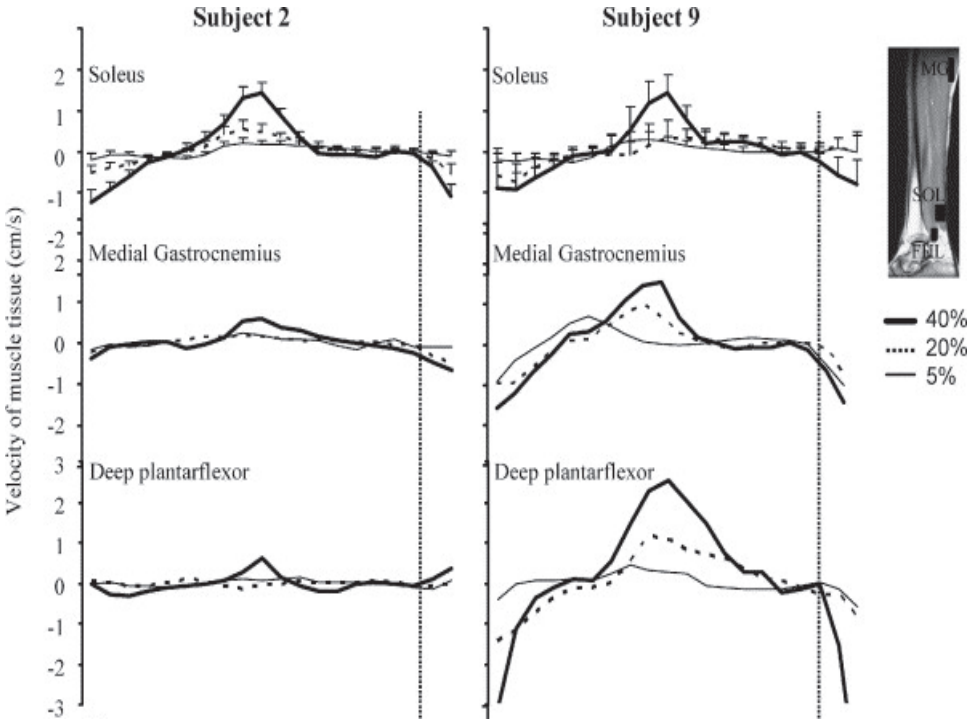

FIGURE 3 Plantarflexor muscle contraction velocity patterns during plantarflexion cycles at 40%, 20% and 5% maximal torque levels from two subjects displaying considerably different strategies. (Modified from Finni et al. 2006)

2.2 Achilles tendon injury

With the rise in recreational and competitive exercise and sport participation, there is an accompanied and continued rise in the prevalence of sports overuse injuries as well. Despite the strength and ability of the Achilles tendon to cope with high pressures, it is vulnerable to over-loading during strenuous physical training. In fact, the rupture of AT is the third most common major tendon disorder preceded only by those of the rotator cuff and the knee extensor mechanism with a rising incidence (Leppilahti et al. 1996; Möller et al. 1996; Lesic & Bumbasirevic 2004). In addition to the acute disruption, inflammation and chronic AT disorders are also widespread. A number of factors, both *intrinsic* (age, gender, systemic disease, endocrine and metabolic disturbances, leg misalignment, muscular imbalance and weakness, etc.) and *extrinsic* (overuse, repetitive strain, cold weather, hard running surface, medication, and steroids, etc.) have been blamed for the pathogenesis of Achilles tendinopathy in athletes (Maffulli & Kader 2002, Paavola et al. 2002, Lesic & Bumbasirevic 2004, Damuth et al. 2008, Longo et al. 2009). Overuse has also been reported as a major pathologic stimulus for tendinopathy, especially in athletes (Longo et al. 2009).

Plain soft-tissue *radiography* is useful in diagnosing associated or incidental bony abnormalities (Maffulli & Kader 2002). *Ultrasonography* correlates well with the histopathologic findings and is considered a primary imaging method (Longo et al. 2009). Ultrasound with Doppler flow has also been used to examine the vascular response of the tendon to the disease and exercise (Boesen et al. 2006). *Magnetic resonance imaging* (MRI) provides extensive information about the internal morphology of tendon and the external anatomy. Velocity-encoded cine phase-contrast MRI has been used to investigate muscle synergism, both in Achilles tendon rupture patients and healthy subjects, during isometric ankle plantarflexion (Finni et al. 2006). Similar methods have also been used to study the force-length relationship and stiffness of Achilles tendon, as well as the strain of soleus aponeurosis-tendon unit during submaximal voluntary muscle contractions (Shin et al. 2008; Finni et al. 2003). One of the more recent advancements in the imaging of the tendinopathy is the use of positron emission tomography (PET) (Kalliokoski et al. 2005, 2007; Huang et al. 2006).

2.2.1 Achilles tendinopathy

Achilles tendinopathy is a broad term that can be applied to any disorder affecting the Achilles tendon. More specifically, Achilles tendinopathy can be categorized as insertional and noninsertional, a distinction that is necessary because the two conditions are distinct disorders with different underlying pathophysiologies and treatment options (Clain & Baxter 1992). Insertional type refers to the tendinopathy affecting the region where the Achilles tendon inserts onto the calcaneus bone. Conversely, the noninsertional type could involve the Achilles tendinous tissue anywhere between its proximal and distal attachments. In most cases the noninsertional tendinopathy involves the mid-portion of the Achilles tendon and is usually classified as mid-portional type. Traditionally seen, it is a musculoskeletal disorder and is dealt with as one. However, there is evidence that suggests a direct relationship between obesity and mid-portion Achilles tendinopathy (Gaida et al. 2009). These findings may fuel the debate whether Achilles tendinopathy is really a musculoskeletal problem or would it be more appropriate to classify it as a cardiovascular disorder (CVD).

Noninsertional Achilles tendinopathy can be chiefly grouped into either paratendinopathy or intratendinous disease (tendinosis). Achilles paratendinopathy (peritendonitis/paratendonitis) is defined as an inflammation of the tissues surrounding the Achilles tendon with histologic specimens showing acute inflammatory features. Clinically, this describes Achilles pain with tenderness to palpation with no intratendinous involvement clinically or on imaging investigations (Khan et al. 2002; Maffulli 1998). Tendinosis is described as the chronic intratendinous degeneration of the tendon with the histologic presence of coalesced collagen fibers, cystic mucoid changes, calcification, and vascular degenerative changes. Despite the label "degenerative," Achilles tendinosis is thought likely to be reversible (Järvinen et al. 2005). While chronic tendinosis exhibits no histologic findings of inflammation, it is unclear whether inflammatory changes are seen in the acute phase. The distinction between the

two often cannot be made clinically on history and examination alone (Åström & Rausing 1995).

A focused but detailed history should identify the onset, frequency, and duration of symptoms. Any contributing factors such as changes in activity level, foot wear, potential training errors, and previous treatment modalities should be elicited. It is imperative to recognize the patient's expectations regarding his desired level of activity. Classically, noninsertional Achilles tendinopathy presents as a pain with activation occurring 2 to 6 cm proximal to the Achilles insertion in essentially the same location as Achilles tendon ruptures. While noninsertional Achilles tendinopathy is typically experienced only during physically demanding sporting activities, the pain can progress to eventually affect daily activities. There is a correlation between severity of tendinopathy and the degree of morning stiffness. Runners complain of pain at the beginning and end of training, but often with a characteristic pain-free period in the middle of the activity (Nunley 2009).

Although disorders of the Achilles are described as distinct entities, many disorders exhibit a variety of symptoms and may reflect the presence of more than one disorder simultaneously (Table 1). Clinical examination includes physical inspection and palpation. Two routinely administered physical tests to diagnose Achilles tendinopathy are the *painful arc sign* and *Royal Victorian Hospital* test (Maffulli et al. 2003; Longo et al. 2009). Victorian Institute of Sports Assessment - Achilles or (VISA-A) is used to measure the severity of Achilles tendinopathy (Robinson et al. 2001). Imaging is used to delineate the extent and severity of intratendinous degeneration in addition to differentiating between intrasubstance tendinopathy and paratendinopathy. Imaging modalities commonly used in the diagnosis of Achilles tendinopathy include plain radiographs (X-rays), ultrasound, and magnetic resonance imaging.

TABLE 1 Physical examination findings in Achilles tendon disorders.

Swelling
Acuity of onset (gradual/sudden)
Morning stiffness/pain
Palpable gap
Crepitus
Thompson test
Painful arc sign
Royal London hospital test

(reproduced from Easley & Le 2009; Chap. 13 in J.A. Nunley (ed.), *The Achilles Tendon: Treatment and Rehabilitation*)

2.2.2 Achilles tendon rupture

Other major disorder of the Achilles tendon is complete or partial rupture. Although the precise pathogenesis of Achilles tendon rupture is unknown, con-

tributing factors identified in the literature include tendon degeneration, failure of the normal inhibitory mechanism of triceps surae myotendon complex, drugs, systemic disease, genetics, foot deformity, and pre-existing Achilles tendon pathology (Leppilahti & Orava 1998). Ruptures are nearly always unilateral although there are reports of rare and unusual incidences of bilateral Achilles tendon rupture (Garneti et al. 2005). There is an enormously increased, up to 200-fold, risk of contralateral Achilles tendon rupture in patients who have previously suffered a rupture on one side. Finally, nearly half of the patients experience post-rupture tendon problems in the long run (Aroen et al. 2004). Diagnosis of the acute AT rupture can be made by means of a thorough history in many cases. *Thomson's test* or the calf-squeeze test and *O'Brian's test*s are positive in the case of AT rupture (Lesic & Bumbasirevic 2004).

2.2.3 Effects of Achilles tendon injury on muscle function

Achilles tendon injuries caused by overuse impair the function of the calf myotendinous unit. For instance, unilateral Achilles tendinopathy can cause significant reduction in the leg stiffness likely by an increase in the ankle joint compliance in athletes (Maquirriain 2012). Leg stiffness was tested by modelling the vertical ground reaction force on a contact mat and measuring flight and contact time during hopping (Maquirriain 2012). Similarly, Achilles tendinopathy causes not only pain and symptoms but also leads to impaired lower leg muscle-tendon function (Silbernagel et al. 2006). These effects include significant differences between the injured and the uninjured legs in terms of hopping, drop countermovement jumps, and concentric and eccentric-concentric toe raise performance. Further, the pain level while carrying out most of these tasks was also greater in the symptomatic leg (Silbernagel et al. 2006).

In one study investigating the neuromotor control of the triceps surae in runners with Achilles tendinopathy, it was found that offset times of soleus and lateral gastrocnemius during running were significantly different whereas no differences were evident in the offset times of healthy control muscles. The EMG activity of the three triceps surae muscles was recorded using surface electrodes during a running task to calculate these offset times (Wyndow et al. 2013). Furthermore, Achilles tendinopathy has also been shown to cause debilitating pain, thus hindering the running activity completely. The pain is also associated with significantly lower concentric and eccentric plantarflexion strength using isokinetic dynamometer (Alfredson et al. 1998). Similarly, other studies have also described disabling pain during walking and jogging (Mafi et al. 2001; Roos et al. 2004).

2.3 Management of Achilles tendon injury

Management of the acute and chronic AT injuries includes conservative and surgical treatments (Lesic & Bumbasirevic 2004). Conservative management

includes physical therapy, rest, training modification, splintage, taping, cryotherapy, nitric oxide, electrotherapy, shock wave therapy, hyperthermia, pharmaceutical agents such as non-steroidal anti-inflammatory drugs (NSAIDs), and various types of peritendinous injections. Surgical options range from minimally invasive stripping to open surgery, and include muscle transfer to the body of tendon (Longo et al. 2009).

2.3.1 Eccentric training in Achilles tendinopathy

According to the Medical Dictionary for the Health Professions and Nursing, an eccentric muscle contraction is: "*a lengthening action in which a muscle's attachments are drawn away from one another by an external resistance, even though the muscle is activated*". Eccentric loading of the calf muscles has been regarded as the foundation of conservative rehabilitation of mid-portional chronic Achilles tendinopathy. Traditionally, they are referred to as strengthening exercises but argument in favor of classifying them as stretching techniques has arisen (Allison & Purdam 2009). Furthermore, there is evidence to suggest that such exercise is more effective in treating the mid-portional tendinopathy than the insertional tendinopathy (Fahlström et al. 2003). Insertional Achilles tendinopathy patients may not respond to a typical eccentric training as well as individuals with mid-portion tendinopathy do. Therefore, modification (no loading into the dorsiflexion) in the training method is necessary in such cases because of a potential impingement of insertion between tendon, bursa, and bone in dorsiflexion (Jonsson et al. 2008).

The effects of eccentric training on Achilles tendinopathy have been evaluated using methods such as ultrasonography and power Doppler (Öhberg & Alfredson 2004), magnetic resonance imaging (Shalabi et al. 2004), isokinetic muscle testing (Yu et al. 2013), etc. Although heavy-load eccentric exercise has been an integral part of conservative management of Achilles tendinopathy over the past few decades, the precise underlying mechanism of its action remains unclear (Maffulli & Longo 2008; Kjaer & Heinemeier 2014). It has been suggested that heavy-load eccentric contractions induce beneficial effects by causing Achilles tendon hypertrophy, changes in elastic characteristics of the tendon, and increased tendon tensile strength (Alfredson & Lorentzon 2000). Similarly, evidence has been provided that an eccentric rehabilitation program alters the mechanical properties of the plantar flexor muscles. These changes lead to significant improvement in the dorsiflexion range of motion while significantly decreasing the passive resistive torque of the plantar flexors at the same time. These alterations are associated with structural modifications rather than to stretch tolerance (Mahieu et al. 2008). Another mechanism of eccentric training action is proposed by Öhberg & Alfredson (2004) wherein the blood flow in the pathological neovessels ceased during ankle dorsiflexion as depicted by dynamic ultrasound and colour Doppler examination. Regaining of a more or less normal tendon structure and reversal of the neovascularization were deemed good clinical outcomes of eccentric rehabilitation in patients with chronic painful mid-portional Achilles tendinosis. Other explanations of under-

lying mechanism as reviewed by Enoka (1996) are (1) maximization of force exerted and muscle work performed, (2) association with a greater mechanical efficiency, (3) attenuation of the mechanical effects of impact forces, (4) enhancement of the exercise-induced tissue damage, and (5) unique activation strategies by the nervous system.

Eccentric training has been shown to improve the Achilles tendon's biomechanical properties in animals as well as in humans. A rat model study demonstrated that the eccentric training resulted in improvement of the mechanical properties of tendons and suggested that eccentric mechanical loading could heal the tendon (Kaux et al. 2013). In human studies, Alfredson et al. (1998) who proposed and first tested the heavy-load eccentric training reported a significant reduction in pain scores and significant improvement in the concentric plantarflexion torque in the symptomatic leg after the rehabilitation. Eccentric training has also been shown to be superior to the concentric training in terms of patient satisfaction rates and visual analogue scale (VAS) pain scores in both the short-term (Mafi et al. 2001) and the long-term (van der Plas et al. 2012). Eccentric training also results in decreased tendon volume and intratendinous signal on proton density–weighted magnetic resonance images in the tendinopathic Achilles tendon. These findings were significantly correlated with the level of pain (Shalabi et al. 2004; van der Plas et al. 2012). Significant improvements in the Victorian Institute of Sports Assessment-Achilles (VISA-A) scores has also been reported after 12 weeks of eccentric rehabilitation (Herrington & McCulloch 2007) and at a 5-year follow-up (van der Plas et al. 2012). Petersen et al. (2007) reported a significant improvement in VAS pain, American Orthopedic Foot and Ankle Society (AOFAS), and short form-36 (SF-36) scores following 54 weeks of eccentric calf muscle training.

A systematic review and meta-analysis reviewing physical therapies for Achilles tendinopathy concluded that eccentric training provided significantly beneficial effects and recommended the use of such training as an initial rehabilitation tool in Achilles tendinopathy (Sussmilch-Leitch et al. 2012). A randomized controlled trial (RCT) investigating the effects of eccentric strength training on pain, muscle strength, endurance, and functional fitness factors in Achilles tendinopathy patients found significant improvement in the eccentric training group along all parameters except dexterity which was similar to the control group (Yu et al. 2013). A similar but more recent RCT study found a significant reduction in the active part of the series elastic component stiffness of plantarflexors with no changes in the passive part. Moreover, stiffness of the Achilles tendon during passive ankle joint motion was significantly increased. However, no significant changes were observed in the geometry of either the plantarflexors or the Achilles tendon. It was suggested that alterations in the intrinsic mechanical properties of myotendinous tissues were responsible for these specific changes in the muscle-tendon complex (Foure et al. 2013).

However, it is imperative to note that although eccentric training has shown the best evidence of effectiveness in treating the chronic Achilles tendinopathy, it is not the only beneficial training program available. A recent re-

view determined that while eccentric training influences tendon mechanical properties and matrix protein synthesis, the up-regulation of collagen mRNA was not dependent upon muscle contraction type. This signified lesser sensitivity of tendons to differences in the nature and/or intensity of mechanical loading compared to the skeletal muscles in terms of collagen expression, collagen regulatory factors, and cross-link regulators. Slow concentric loading might have benefits similar to those of eccentric exercise in Achilles tendinopathy (Kjaer & Heinemeier 2014).

2.3.2 Management of Achilles tendon rupture

Management of acute and chronic Achilles tendon rupture - partial and complete - includes both the surgical and non-surgical conservative options (Cetti et al. 1993). While conservative, non-operative management has been shown to be fairly effective in healing the tendon (Lea & Smith 1972; Saleh et al. 1992; Blake & Ferguson 1991), prolonged immobilization, higher risk of re-rupture, calf muscle atrophy, and danger of tendon lengthening render it less preferable though still an acceptable alternative (Cetti et al. 1993). Open surgical repair, despite higher costs and potential surgical complications, has been growing as a treatment of choice due to lesser incidence of reruptures and a faster restoration of normal function (Leppilahti & Orava 1998). Other surgical treatment options include percutaneous repair of the Achilles tendon and can be regarded as compromise between conservative and open surgical managements. It has been shown to be a safe and reliable method of managing ruptured Achilles tendons especially in patients with lower sporting demands. Advantages of this method are a lower incidence of surgical wound complications compared to open surgery and being cosmetically more acceptable. Disadvantage with this method is a slightly higher incidence of re-rupture. Although there is a risk of sural nerve injury with this method, it can be avoided by careful placement of the incisions (McClelland & Maffulli 2002).

Post-operative physical rehabilitation plays a vital role in full return to pre-rupture physical activity level and sport (Mortensen et al. 1999). Main types of post-surgical regimes can be classified as delayed rehabilitation and functional rehabilitation. The delayed rehabilitation involves placing the leg in a cast to immobilize the tendon after surgery for 4 to 6 weeks with no weight bearing. Physical therapy is usually allowed only after the cast has been removed (Haji et al. 2004). Although this approach completely protects the surgical repair from re-rupture and repair site gapping, it entails certain complications. These include arthofibrosis, leg muscle atrophy, tissue adhesions and contractures, deep vein thrombosis, and articular cartilage degeneration (Booth 1987). Functional rehabilitation, on the other hand, emphasizes early weight bearing to overcome the adverse effects of prolonged immobilization and provide conditions to promote better tendon healing (Mandelbaum et al. 1995). A prospective, randomized, clinical study comparing the delayed rehabilitation and functional rehabilitation (early motion) regimes has demonstrated that the latter lead to better isokinetic calf muscle strength (Kangas et al. 2003).

Although surgical intervention is gaining more popularity for AT rupture management, caution must be observed in the rehabilitation of athletes younger than 30 years of age since the likelihood of rerupture is significantly higher in younger population than the older individuals (Rettig et al. 2005).

2.4 Surface electromyography in investigating muscle function

Conventional bipolar surface electromyography (SEMG) has widely been used in biomechanics as a non-invasive way to measure the electrical activity of skeletal muscles during various physical activities (de Luca, 1997; Hermens et al. 2000). Despite the issues of optimal electrode positioning and signal reliability, SEMG is still believed to provide valuable, consistent, representative information which corresponds to the skeletal muscle work done (Merletti & Conte 1997; Kleissen et al. 1997). A high level of repeatability was found in surface EMG data collection from human quadriceps femoris muscle during voluntary isometric contractions (Rainoldi et al. 2001). Same had been shown to be true for biceps brachii muscle with various levels of voluntary isometric contractions (Rainoldi et al. 1999). A more advance form of surface electromyography which uses linear electrode arrays, instead of only two bipolar surface electrodes, has been successfully tested for characterization of muscles (Merletti et al. 2001). SEMG has also been used to study muscle function during functional movement, such as, cycling (Gregor et al. 1991).

2.5 Positron emission tomography in investigating muscle function

Positron emission tomography (PET) is a noninvasive nuclear imaging technique which involves the use of radionuclides that decay through positron emission. The radionuclides are useful in labelling various biologically desirable chemical compounds. These labelled compounds are administered into the body, in variable quantities, usually through intravenous injection. A positron emits from the nucleus upon decay of a radioactive atom resulting in production of photons which can be detected by a scanner consisting of multiple detectors. These detections can subsequently be corrected and reconstructed in high-resolution images available for further quantification in the three-dimensional tissue volume. The most commonly used quantifiers are standardised uptake value (SUV) and fractional uptake rate (FUR).

PET instrumentation is an area that has continued to evolve rapidly, especially over the last two decades although the technology has been used since the 1950s. In addition to being subjected to careful scrutiny, more than any other diagnostic technology, PET imaging has been reviewed to evaluate its cost ef-

fectiveness in performing the diagnoses. The economic modelling performed in different health care settings has suggested that PET is cost-effective, or even cost-saving, depending on the criteria devised. PET with [^{18}F]-fluorodeoxyglucose (PET-FDG) is now being routinely used before several types of surgeries so that unnecessary surgery can be avoided and only necessary surgery is performed. Clinical PET imaging, mostly with FDG, is being used in the following important areas of clinical diagnosis and management: cancer diagnosis and management, cardiology and cardiac surgery, neurology, and psychiatry.

Besides proving useful in clinical diagnoses, PET scanning has also been used in musculoskeletal research. It is one of the more recent advancements in the imaging of the tendinopathy and skeletal muscle glucose uptake since skeletal muscles take up glucose as a result of increased metabolism due to exercise. PET, combined with other tracers like [^{15}O]-H_2O, has been used to measure perfusion and perfusion heterogeneity in human skeletal muscle during various leg exercises (Nuutila & Kalliokoski 2000; Kalliokoski et al. 2000, 2001; Laaksonen et al. 2003). Additionally, [^{18}F]-FDG has also been increasingly employed in high resolution PET to image and quantify glucose uptake as a result of exercise not only in skeletal muscles (Hargreaves 1998; Pappas et al. 2000; Fujimoto et al. 2000; Kemppainen et al. 2002; Hannukainen et al. 2005; Kalliokoski et al. 2007) but also in tendinous tissue (Kalliokoski et al. 2005; Bojsen-Møller et al. 2006; Huang et al. 2006). However, it should be noted that even high-resolution PET imaging technique is not perfect and has limitations (Schöder & Gönen 2006).

2.5.1 Glucose transport, delivery, and uptake in muscles

It was over 125 years ago that first report on contraction-induced skeletal muscle glucose uptake was published. It was based on the measurements of differences between the concentrations of glucose in the arterial and venous blood outflow of horses after chewing. The significance of glucose as a fuel for endurance exercise in humans has been identified through the physiological studies conducted nearly a century ago. These studies also revealed the links between hypoglycemia and fatigue followed by other animal studies confirming the notion of increased muscle glucose uptake as a result of contractions (Richter & Hargreaves, 2013). It has been shown that the muscle blood flow is closely related to the oxygen demand of the exercising muscles and skeletal muscle blood flow can increase up to 20-fold from rest to intense, dynamic exercise (Andersen & Saltin 1985).

Glucose serves as an important fuel during muscle contraction and significance of normal glucose metabolism cannot be overemphasized. Entry of glucose into the muscle cell is accomplished through facilitated diffusion by the glucose transporter 4 (GLUT4). Muscle contraction leads to translocation of GLUT4 from intracellular reservoirs to the plasma membrane and T-tubules occurs (Richter & Hargreaves, 2013). Although there is no consensus on the precise mechanism through which the translocation of GLUT4 to plasma mem-

brane happens, it is thought to take place via intracellular signalling involving Ca^{2+}-calmodulin-dependent protein kinase, 5'-AMP-activated protein kinase, and likely protein kinase C (Rose & Richter 2005). The regulation of gene transcription and metabolism in skeletal muscle, in response to oxidative, energetic, and mechanical stresses, takes place mainly via mitogen-activated protein kinases (MAPKs) and NF-kB (Kramer & Goodyear 2007).

The three main sites and processes that can be regulated in the control of skeletal muscle glucose uptake during exercise are: *1*) glucose delivery, *2*) glucose transport, and *3*) glucose metabolism (Fig. 4). It is generally believed that the process which limits muscle glucose uptake during rest is glucose transport. This happens because expression of GLUT1 is relatively low while nearly all of the GLUT4 is located inside the cellular storage locations and hence isolated from the sarcolemma and T-tubules. In contrast, during exercise this rate-limitation is removed due to increase blood flow to the skeletal muscles, recruitment of the capillary bed, and translocation of GLUT4 to the sarcolemma and T-tubules. On the other hand, glucose phosphorylation becomes the new obstacle particularly at high exercise intensities (Katz et al. 1986; Wasserman 2009).

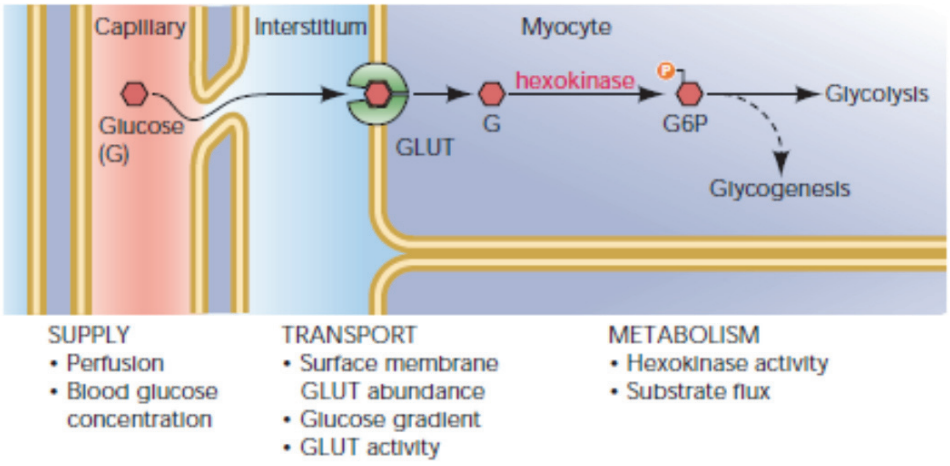

FIGURE 4 Rate-limiting steps of glucose uptake by skeletal muscle and potential sites of regulation of muscle glucose uptake during exercise (reproduced from Rose & Richter 2005).

Skeletal muscle glucose uptake is increased during exercise due to a coordinated rise in glucose delivery rate, surface membrane glucose uptake, and intracellular substrate flux through glycolysis (Rose & Richter 2005). Glucose uptake is a product of tissue blood flow and difference in the glucose concentration of arterial and venous blood. Since the arterio-venous glucose difference rises only two- to four times with exercise, the biggest contributor to the exercise-induced increments in muscle glucose uptake is improved muscle blood flow (Richter &

Hargreaves 2013). The relationship between plasma glucose concentration and exercise-induced muscle glucose uptake is virtually linear as long as the glucose concentrations remain within the physiological range. This signifies that changes in plasma glucose concentrations with exercise leads to nearly equal changes in the muscle glucose uptake (Richter 1996). GLUT4 overexpression, without hexokinase II (HKII) overexpression, had little effect on muscle glucose uptake during exercise. Similarly, the full effect of HKII overexpression on glucose uptake was dependent on an increase in GLUT4 expression (Fig. 5)

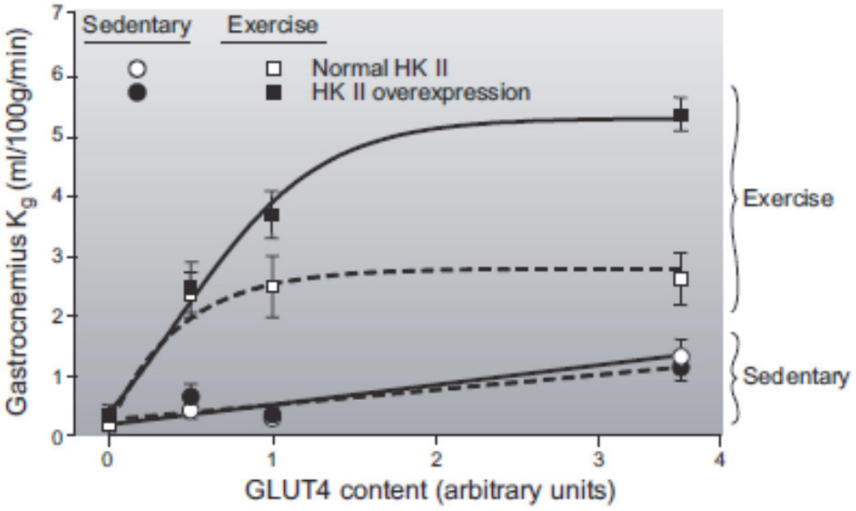

FIGURE 5 GLUT4 and hexokinase II (HKII) as determinants of skeletal muscle glucose uptake during exercise. The figure shows that at rest, overexpression of GLUT4 leads to increased glucose uptake independently of HKII expression. During exercise, HKII overexpression leads to increased glucose uptake at normal and increased levels of GLUT4 expression. Furthermore, GLUT4 overexpression does not in itself lead to increased glucose uptake during exercise. On the abscissa, 1 arbitrary unit denotes the average WT level (n = 8–11 per data point) (from Wasserman 2009 as adopted by Richter & Hargreaves 2013)

2.5.2 Exercise-induced skeletal myotendon glucose uptake

Although most of the studies employ localized PET imaging, investigators have also used whole-body FDG PET scanning to study muscle metabolic activity in exercising and non-exercising musculature (Fujimoto et al. 1996; Tashiro et al. 1999; Gradinscak et al. 2003; Jackson et al. 2006). It has also been reported that the distribution of leg skeletal muscle glucose uptake as a result of one-legged knee extension exercise stimulation is heterogeneous in obese population (Larmola et al. 2000). Application of PET for neuroimaging and sport and exercise science is both advantageous and feasible (Tashiro et al. 2008).

Bojsen-Møller et al. (2006) reported small glucose uptake values for Achilles tendon in their study. They reported the values of 0.13 ± 0.05 µmol*100g^{-1}*min^{-1} and 0.12 ± 0.01 µmol*100g^{-1}*min^{-1} at the calcaneal insertion and "free

tendon" levels respectively in the exercising tendon. The exercise was performed at an estimated ~13% maximal voluntary isometric contraction (MVIC) levels. However, it must be noted that Achilles tendon glucose uptake may not increase with increasing exercise intensity (Hannukainen et al. 2005). Although, the Achilles tendon glucose uptake was reported following intermittent isometric contractions, no triceps surae glucose uptake values were published. A case study involving a 30-year old male reported a 3-fold increase in MG glucose uptake while Achilles tendon uptake increased two times compared to the resting contralateral leg. No actual values were reported though (Kalliokoski et al., 2007). Additionally, even though Hannukainen et al. (2005) used bicycle ergometer and different submaximal target force levels, they did report a significant increase in muscle glucose uptake due to exercise while tendon GU behaviour did not change with rising exercise intensity.

There is a paucity of literature concerning the glucose uptake behavior of primary and deep ankle plantarflexors during submaximal isometric conditions in health and among patients with lower leg musculoskeletal problems. Only one study reported an abnormal, enhanced Achilles tendon glucose uptake in the case of Achilles tendonitis (Huang at al. 2006). Some studies have used whole body (Fujimoto et al. 1996; Kilgore & Watson 1998) or only upper extremities (Pappas et al. 2001). Yet another group of studies is where no particular exercise was performed at all (Jackson et al. 2006) or abnormal uptake was a result of muscle exertion happened 48 hours prior to the scanning (Gradinscak et al. 2003).

3 OBJECTIVES OF THE STUDY

The present study aimed to reveal the magnitude and relativity of superficial plantarflexors' contribution - with respect to a deep plantarflexor - during a submaximal isometric plantarflexion task using SEMG and PET in an attempt to obtain a better understanding of their role in health and injury. Furthermore, effects of eccentric rehabilitation on plantarflexion strength, muscle-tendon glucose uptake rate, and muscle electrical activity were also examined in injured Achilles tendon conditions to gauge its effectiveness in healing Achilles tendon and restoring muscle function.

The main objectives of the present series of studies were to:

1. Evaluate plantarflexor muscle use during submaximal isometric plantarflexion contractions, by SEMG and PET, in young healthy adults (paper I).
2. Investigate the electrical and metabolic activity patterns of various ankle plantarflexors in unilateral, chronic Achilles tendinopathy patients compared with healthy controls (paper II).
3. Examine the effects of eccentric calf myotendon rehabilitation on skeletal myotendon glucose uptake and myoelectric activity patterns of various plantar flexors in unilateral chronic Achilles tendinopathy patients (paper III).
4. Compare calf myotendon glucose uptake in Achilles tendon rupture (ATR) patient with a healthy individual and to explore the effects of eccentric rehabilitation on myotendon metabolic activity in ATR with reference to Achilles tendinopathy patient (paper IV).

The specific hypotheses of the study were:

1. The metabolic and electrical activity patterns of ankle plantarfelxors in healthy subjects would not be comparable due to inherently different nature of SEMG and PET.

2. Chronic Achilles tendinopathy will result in altered activation strategies of ankle plantarflexors.
3. The relative contribution of various ankle plantarflexors would be different between the two legs of the unilateral Achilles tendinopathy patients.
4. Plantarflexion strength in the symptomatic leg would be lower due to Achilles tendinopathy despite a compensatory rise in deep plantarflexor's activation.
5. The eccentric rehabilitation would restore the loss of plantarflexor strength accompanied by an increased glucose uptake rate in triceps surae of the symptomatic leg.
6. The eccentric rehabilitation would also affect the contributions of ankle plantarflexors relative to each other.

4 MATERIALS AND METHODS

4.1 Subjects

All participants of the study were recruited through public advertisements for the following three study groups.

Achilles tendinopathy (ATP): Twenty individuals responded to the advertisement. The desired age for the subjects was 18 to 35 years. The criterion set by Józsa and Kannus in 1997 was used to select the subjects. It necessitated Achilles tendon pain lasting at least 6 weeks prior to the measurements. After screening assessments, nine were not found eligible for the study. The remaining eleven subjects – four women and seven men – subsequently participated in the comparison study (paper II). As a result of one drop out (1 female), only ten subjects were included in the rehabilitation study (paper III). The mean ± SD age of the participants was 28 ± 4 years, body mass 66 ± 6 kg, and height 174 ± 6 cm. Five subjects suffered from chronic tendon pain in the right leg while the remaining six had the left leg involved. All subjects were physically active, recreational athletes involved in distance running, long jumping, high jumping, and ice-hockey etc. Their average exercise frequency was 4.7 times a week, in terms of days, prior to the study. The average duration of Achilles tendon pain at the time of baseline measurements was 9.8 ± 8 months (range: 2–25). The self-documented VISA-A score registered by the subjects was 64 ± 18 (range: 27–86) out of a maximum score of 100.

Healthy controls (CTRL): A total of twelve anthropometrically matched healthy individuals volunteered to serve as control subjects. They reported no history of major leg injury or Achilles tendon pain over the last year. Their mean ± SD age, height, and body mass were 28 ± 4 years, 173 ± 4 cm, and 67 ± 6 kg respectively. All twelve subjects were included in the first paper but only eleven became part of the comparison study (paper II). The background physical activity level for the control group was 2.4 days per week on average.

Achilles tendon rupture (ATR): To gain novel insight into the calf muscle activation strategies after Achilles tendon rupture, a 27-year old male with post-

surgical complete mid-portion Achilles tendon rupture was evaluated. The subject was a recreational ice hockey player with history of complete, acute left Achilles tendon rupture while playing badminton. The tendon was surgically repaired 3 months prior to the participation in the study. Before the baseline measurements the subject was cleared by the operating surgeon for full weight-bearing and did not report any other systemic or musculoskeletal disorder. His body mass and height were 79 kg and 183 cm respectively. Both operated (OPER) and unoperated (UNOP) legs were examined in this study.

4.2 Study design

Approval of the study was granted by the Ethics Committee of the Hospital District of South-Western Finland. All risks associated with the measurements were explained to the participants who provided written consent before the study commenced. The procedures of this study conformed to the Declaration of Helsinki guidelines.

Each subject participated in a series of tests at the Turku PET Centre, University of Turku, Finland. For any given subject, all components of the measurements were completed on the same day. A schematic diagram of the experimental design can be seen in figure 6. At least 8 hours of fasting was required before the PET scans to ensure stable metabolic condition between the subjects. Achilles tendinopathy and tendon rupture subjects were tested twice; before and after the eccentric rehabilitation. On the contrary, the healthy controls were tested only once at the baseline because of the restrictions imposed by the ethics committee regarding the exposure to radiation.

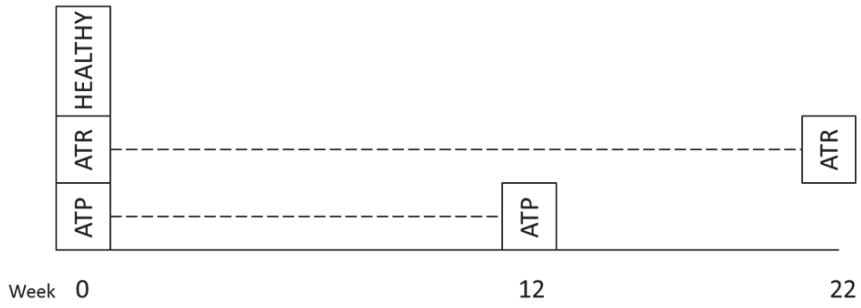

FIGURE 6 Chronology of the study events. ATP: Achilles tendinopathy, ATR: Achilles tendon rupture. (- - -) denotes length of interval between pre- and post-rehabilitation measurements. Note that healthy subjects were tested only once.

Paper I involved the investigation of bilateral differences between the two legs of the healthy controls using a simply cross-sectional study design. It also involved the comparison of the outcomes from the two investigative modalities employed. Paper II also utilized cross-sectional (between-group) study design involving a patient group (ATP) and healthy controls to seek effects of Achilles tendinopathy on the calf muscle activation strategies. Paper III used a "mixed factorial" study design comprising both cross-sectional and longitudinal (repeated measures design) aspects (intervention effect). Lastly, paper IV provided findings from an Achilles tendon rupture patient in the context of a healthy and an ATP patient.

4.3 Study protocol

Subject preparation for surface electromyography (SEMG) comprised the shaving, abrading, and cleaning of skin. Conventional bipolar surface electrodes were positioned on both legs and an electronic goniometer was secured to the ankle. In addition, intravenous catheters were inserted into the antecubital veins of both arms: one for venous blood sampling and the other for [^{18}F]-Fluorodeoxyglucose ([^{18}F]-FDG) tracer administration. Subsequently, the subjects were positioned in the exercise apparatus for force and SEMG data collectioon. Familiarization with the equipment and the plantarflexion motor task was achieved by performing submaximal plantarflexion contractions from each leg. Following warm-up, unilateral maximal voluntary isometric contraction (MVIC) of ankle plantarflexors was recorded three times with a rest period of one minutes between efforts. The highest force value of the three trials was used to determine the submaximal target force level for individual leg to be used in the plantarflexion task ahead.

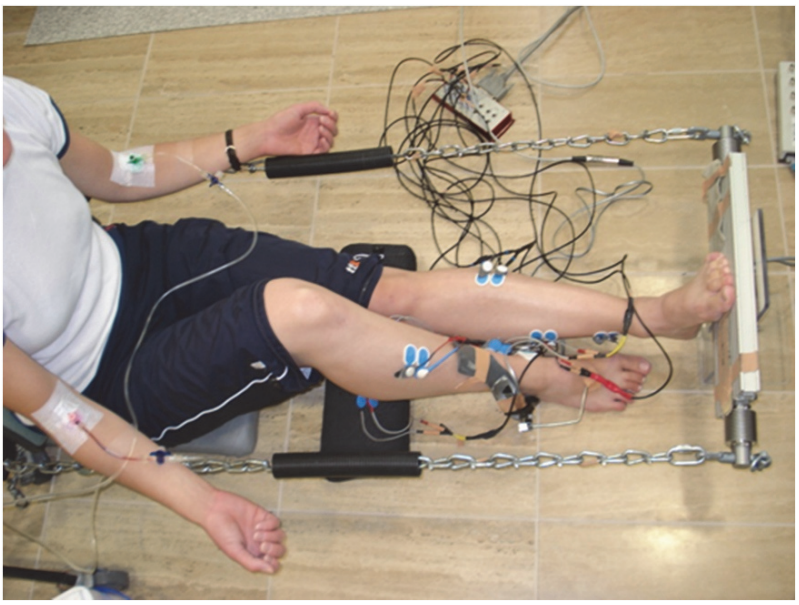

FIGURE 7 Subject preparation and experimental setup. A subject can be seen pressing with her left foot against the force transducer during a submaximal contraction. Intravenous catheters are visible on both arms for blood sampling and [^{18}F]-FDG tracer injection. Also visible are some of the SEMG electrodes connected to the acquisition device, along with an electronic goniometer around the right ankle.

The task was performed while sitting on a seat placed on the floor with hip flexed at right angle, knee in full extension, and ankle in neutral position (Fig. 7). The exercise protocol comprised sets of five unilateral submaximal, isometric voluntary contractions at 30% of respective MVIC force. The contractions lasted for 5 seconds each and were separated by a 5-second rest period. The legs were switched at the end of each set. The subjects were able to watch both the target force and the actual force exerted by them on a monitor display in real time. Additionally, verbal cues were provided to perform the task correctly. After two sets of warm-up contractions for each leg, ~150MBq of [^{18}F]-FDG tracer was injected. This was followed by execution of 8 more sets with each leg, alternatingly. The total exercise and rest time before tracer injection was ~6–7 min while the post-injection exercise and rest time was ~15 min (Fig. 8). The subjects did not report tendon pain or discomfort at any stage of the exercise protocol.

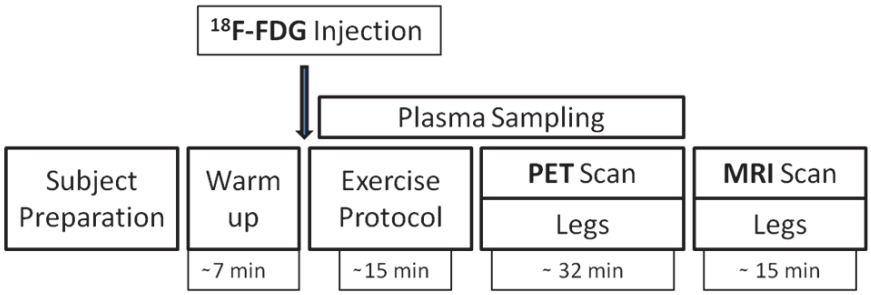

FIGURE 8 Schematic diagram of the experimental protocol.

4.4 Data acquisition and analyses

4.4.1 Plantarflexion force

Isometric ankle plantarflexion force was measured with an in-house custom-built portable force transducer (*University of Jyväskylä*, Finland) one leg at a time (Fig. 7). The force transducer plate was held in place using steel chains, which were secured to the seat-back thus creating a rigid frame. The length of the steel chains was adjusted according to individual subject's requirement.

During subsequent analyses, the mean absolute ankle plantarflexion force during the submaximal isometric contractions was calculated along with the maximal (MVIC) force. Analogue force signal was converted to digital form with Power1401 ADC (CED Ltd., Cambridge, England). Force data recording was accomplished via Signal 4.0 software (CED Ltd., Cambridge, England) in sync with electromyography. Since plantarflexion force did not show a significant decline during the exercise protocol, the average force from beginning, middle, and end of the protocol was considered to represent each leg's force generation (Fig. 9).

4.4.2 Electromyography

Electromyographic data were recorded using conventional bipolar SEMG electrodes from both legs. Ambu Blue Sensor N electrodes (*Ambu* A/S, Ballerup, Denmark) with high quality Silver–Silver Chloride sensors were used for this purpose. The electrodes were located, with an inter-electrode distance (IED) of 22 mm, over soleus, medial gastrocnemius (MG), and lateral gastrocnemius (LG) muscles according to the SENIAM recommendations (Hermens et al. 1999):

Soleus: at 2/3 of the line joining the medial femoral condyle to the medial malleolus.

Medial gastrocnemius: over the bulkiest part of the muscle, in line with the leg.

Lateral gastrocnemius: at 1/3 of the oblique line connecting the fibular head and the heel.

The electrodes on flexor hallucis longus (FHL), however, were positioned after locating the muscle behind the medial malleolus by manual palpation. In order to minimize crosstalk from nearby muscles, and due to limited surface accessibility of FHL, the electrodes were slightly trimmed (IED: 16 mm). This procedure was in line with an earlier study (Bojsen-Møller et al. 2010). All electrodes had a gel area of 95 mm^2 and a sensor area of 15 mm^2. Furthermore, an indifferent electrode was secured on the right medial malleolus to improve the signal quality by reducing noise.

SEMG data (bandwidth: 10 Hz to 1 kHz per 3 dB) were detected online via EISA electromyography detection system (model: 16–2, *University of Freiburg*, Germany) at a measurement frequency of 1000 Hz. The signal pre-amplification, by a factor of 200, was achieved with an integrated preamplifier in the shielded cables. Analogue-to-digital conversion of SEMG data was accomplished via a Power1401 high-performance multi-channel data acquisition interface (*CED Ltd*., Cambridge, England). Compatible Signal 4.0 software (*CED Ltd*., Cambridge, England) was used to record, reduce, and subsequently analyse the data. Myoelectric signals from a set of five contractions were stored on a computer individually for each leg during beginning, middle, and end of the exercise protocol. That amounted to data comprising three sets of five submaximal isometric contractions each for either leg.

Subsequently, the acquired SEMG data was differentiated with a high-pass filter (second-order Butterworth filter, 12 dB/octave) using a cutoff frequency of 10 Hz to remove noise signal and correct DC offset. Root mean square (RMS) amplitude of each muscle was obtained from a 3-second time window during the middle of a 5-second submaximal isometric contraction. This RMS was then normalized to the RMS amplitude from a 1-second epoch during MVIC effort of the respective leg. Median power frequency (MPF) analysis of the power spectra of EMG waveforms was conducted to investigate muscle fatigue in accordance with ISEK "Standards for Reporting EMG Data". Since fatigue was not present, as shown by MPF analysis, an average of the three data sets (beginning, middle, and end) was calculated to characterize the myoelectric activity of a given muscle. Unprocessed SEMG myoelectric signals from the three triceps surae components, along with plantarflexion force, are shown in figure 9. In an attempt to evaluate contributions of triceps surae muscle components with respect to the deep plantarflexor, SOL-to-FHL, MG-to-FHL, and LG-to-FHL ratios were computed by dividing the respective normalized RMS during submaximal isometric plantarflexion task. These calculations were based on the assumption that all plantarflexors were maximally activated during MVIC efforts.

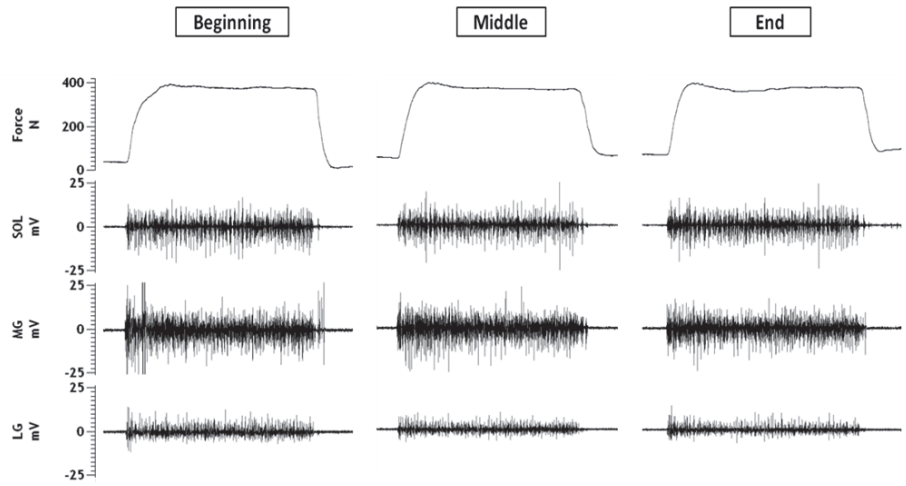

FIGURE 9 Raw SEMG and force signal (SOL: Soleus, MG: Medial gastrocnemius, LG: Lateral gastrocnemius)

4.4.3 Positron emission tomography (PET)

High-resolution positron emission tomography (PET) scanning was achieved with a CTI-Siemens ECAT EXACT HR+ (*Siemens*, Knoxville, TN, USA) PET scanner. The participants were transported on a wheelchair to the PET scanner and were asked to lie down supine in the scanner tray with radioactive spot markers (Na^{22}) taped on both lateral tibial malleoli and medial femoral condyles to enable later alignment of PET and magnetic resonance images during the analyses. The legs were scanned in four adjacent regions, addressing the whole leg, from the toes to the lower thigh. The emission scan time of each region was approximately 5 minutes and the subsequent transmission scan took about 2 minutes per region. Overall, the scanning of the legs, including transition time between the regions, lasted approximately 32 minutes.

The acquired static PET images were corrected for decay with Ecattime 2.0.3 software (*Turku PET Centre*, University of Turku, Finland). Subsequently, parametric fractional uptake rate (FUR) images were computed using the PET image data and the individual input function (plasma radioactivity data) with Imgfur 1.0.3 software (*Turku PET Centre*, University of Turku, Finland) as described previously (Kemppainen et al. 2002, Fujimoto et al. 2003). These FUR images were then superimposed on the magnetic resonance images (described later). Consequently, the regions of interest (ROIs) were drawn on the transverse plane FUR images using Carimas 2.0 software (*Turku PET Centre*, University of Turku, Finland). ROIs were drawn at an interval of 1 cm of muscle and tendon thickness and included the whole individual muscle and tendon length. All analyses were conducted by the same investigator (author) to avoid inter-

observer differences. FUR values were thus obtained for soleus, medial and lateral gastrocnemii, FHL, and the Achilles tendon. Finally, these values were further converted to glucose uptake (GU) rate values using the following formula:

$$Glucose\ uptake\ rate = \frac{FUR \quad \text{x} \quad Plasma\ glucose}{Lumped\ constant\ \text{x}\ Tissue\ density}$$

Plasma glucose value was obtained from the repeated plasma sampling during the study. The lumped constant (LC) - a correction factor - was used to deduce glucose metabolic rate from ^{18}F-FDG metabolic rate by taking into account the differences in the tissue glucose uptake and ^{18}F-FDG from the blood (Graham et al. 2002). LC has been reported to be 1.2 for skeletal muscle (Kelley et al. 1999; Peltoniemi et al. 2000). Tissue density was acquired from "Report of the Task Group on Reference Man" (Snyder et al. 1975).

Similar to electromyography SOL-to-FHL, MG-to-FHL, and LG-to-FHL muscle GU ratios were calculated in order to examine the relative contribution of various plantarflexors.

4.4.4 Magnetic resonance imaging (MRI)

Bilateral magnetic resonance imaging (MRI) scanning was performed with 1.5 T Philips Intera MRI (*Philips Healthcare*, Eindhoven, The Netherlands) for specific determination of muscle locations. Lipid markers (cod liver oil capsules) were secured to the same anatomical landmarks as were used in the PET scanning to provide anatomical reference during later superimposition of PET and MRI data images. MR images only served as anatomical references to delineate the studied muscles during the drawing of ROIs on the FUR images (Fig. 10).

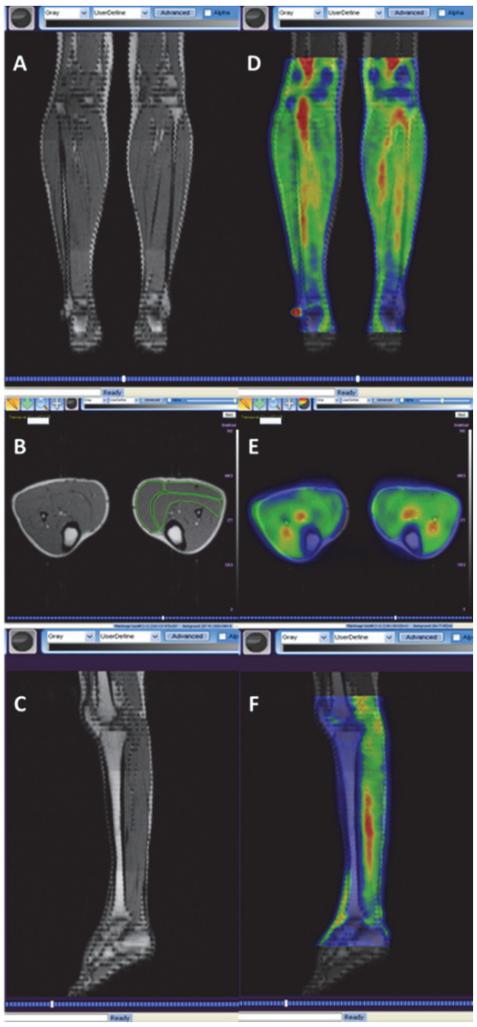

FIGURE 10 Representative data images from a subject in the study. MRI images from (**A**) coronal (anterior), (**B**) transverse, and (**C**) sagittal sections and (**D–F**) the same images superimposed with PET images. Region of interest drawings can be seen on the triceps surae muscle of the left leg in B and a calibration marker is visible on right lateral malleolus in (D).

4.5 Eccentric rehabilitation program

The heavy-load eccentric training regimen - proposed and first investigated by Alfredson and colleagues (1998) - was used as a rehabilitation program for both tendinopathy and tendon rupture patients. It recommended eccentric loading for calf muscles of the injured leg performed twice a day, every day, for an elongated period of time (Alfredson et al. 1998). Each session comprised 3 sets of 15 eccentric contractions each, amounting to a total of 90 dynamic plantar-

flexion contractions of the injured leg every day. Slight modification in the loading technique was made for one insertional type tendinopathy patient, as proposed in the literature. This alteration suggested against the loading of calf muscles into dorsiflexion to avoid impingement between Achilles tendon, retrocalcaneal bursa, and calcaneus (Jonsson et al. 2008). Tendinopathy subjects underwent the training for 12 weeks while the tendon rupture patient exercised for 5 months.

Each subject was individually instructed about the correct training technique through practical demonstrations and written instructions were provided for future reference. It was advised to lift the body weight using concentric muscle action of the uninjured leg followed by lowering down with the injured Achilles tendon predominantly bearing the body weight (Fig. 11). All subjects were advised to maintain a training journal documenting training time of the day, level of pain after exercise, and loading intensity of the exercise, as well as other daily physical training and activities performed during the rehabilitation period. The training began by using only the body weight, and subsequently additional external weights (2.5 kg/week on average), in the form of backpack loads, were added during the course of the rehabilitation as a mean of progression. Reassessment of the exercise loading intensity, tendon pain and swelling was made fortnightly, and necessary adjustments, in terms of adding or removing weight, were suggested accordingly. Virtual analogue scale (VAS) pain level was registered at the end of each eccentric training session by the subjects. It must be noted that the healthy control subjects did not undertake the eccentric rehabilitation program.

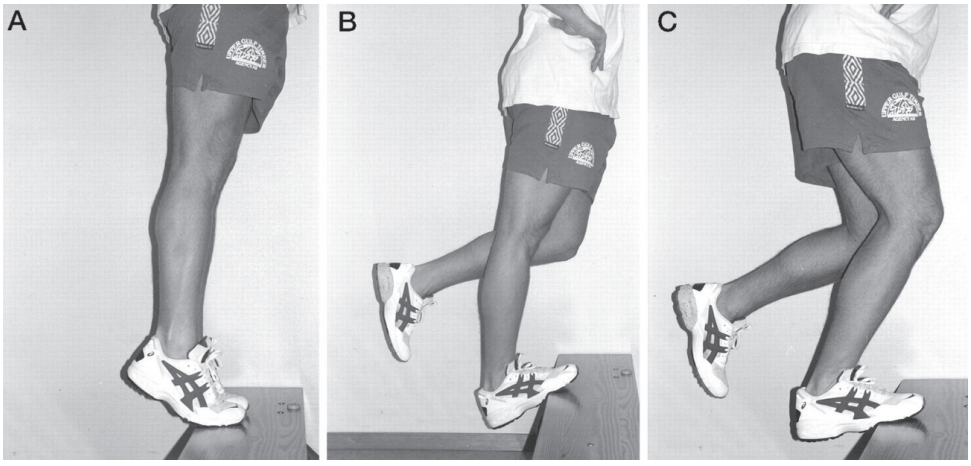

FIGURE 11 Prescribed way of performing the eccentric exercise. Standing upright with all body weight on the forefoot and the ankle joint in plantar flexion lifted by the uninjured calf muscles (A), eccentric loading of the calf muscle on the injured side by asking the patient to lower the heel with a straight knee (B) and with the knee bent (C). (Reproduced from Alfredson et al. 1998)

4.6 Statistics

4.6.1 Healthy reference study (Paper I)

Normality of the data was checked using Shapiro–Wilk test which revealed that the distribution of data was predominantly non-normal. Therefore, Wilcoxon signed-rank test - a nonparametric test - was used to compare the skeletal muscle glucose uptake rate and myoelectric activity of the two legs in healthy individuals. Further, statistical correlations among the investigated muscles in terms of their metabolic and myoelectric activity (Pearson's *r*) were explored. Similarly, correlations were also checked between metabolic and myoelectric activity of individual muscles (Spearman's rank).

4.6.2 Comparison study (Paper II)

Shapiro–Wilk test, a test of normality in statistics, showed that some variables had a normal distribution while others displayed a non-normal distribution. Mann–Whitney U test or independent samples T-test was used, according to the normality of the data, to compare the skeletal muscle-tendon glucose uptake and myoelectric activity of the Achilles tendinopathy and healthy groups. On the other hand, inter-leg comparison within a group was performed with either Wilcoxon signed rank test (non-parametric) or paired samples T-test (parametric). Additionally, effect size (ES) was calculated for quantifying both inter-group and inter-leg differences. Effect size was computed by subtracting the symptomatic leg value from that of asymptomatic leg and subsequently dividing the result with the standard deviation of healthy control subjects.

$$Effect\ size = \frac{(Mean\ of\ symptomatic\ leg)\ -\ (Mean\ of\ asymptomatic\ leg)}{Standard\ deviation\ of\ controls}$$

4.6.3 Intervention study (Paper III)

Dependent (paired) samples *T*-test was used for inter-leg comparisons within the two study groups for all GU and SEMG variables both before (PRE) and after the rehabilitation period (POST). Paired-samples *T*-test was also utilized to perform the longitudinal analysis of VISA-A scores over time. Conversely, independent or unpaired samples *T*-test was used for inter-group analyses exploring the differences between the two groups. In order to compare different muscles within a leg, repeated measures analysis of variance (RM-ANOVA), with Bonferroni confidence interval adjustment, was used. Moreover, statistical correlations (Pearson's *r*) were explored between changes in the submaximal exercise target force and changes in the GU rate parameters of individual muscle/tendon resulting from rehabilitation. Similar correlations were checked between target force level changes and changes in normalized SEMG parameters.

All statistical analyses were accomplished with IBM SPSS 20.0 (*IBM Corporation*, New York, USA) predictive analytics software package. Alpha (α) level of significance was set at a *P* value of 0.05. The results are expressed as mean ± S.D (standard deviation).

5 RESULTS

5.1 Plantarflexion force

Although there were significant bilateral and individual differences, the mean plantarflexion force during MVIC from right and left legs (1133 ± 236 N vs. 1129 ± 192 N) of the healthy individuals was virtually similar. Since the target force level during the submaximal exercise protocol was calculated based on MVIC force, both legs on the healthy control group exercised at a comparable absolute force level during the protocol (352 ± 71 N vs. 347 ± 55 N). Therefore, while evaluating the effects of tendinopathy on ankle plantarflexors muscle function, an average of the force values from the two legs was taken to represent the control value.

In the symptomatic (PAIN) leg of the tendinopathy patient group, MVIC plantarflexion force production was significantly lower than that of the asymptomatic (NO-PAIN) leg ($P < 0.01$; 1101 ± 176 N vs. 1250 ± 192 N; ES = 0.8). Mean of control subjects' legs (CTRL) did not differ significantly from either PAIN or NO-PAIN legs. For apparent reasons, 30% MVIC target force level used during the submaximal exercise reflected the same trend. PAIN leg exercised at a significantly lower force level compared to NO-PAIN leg ($P < 0.01$; 325 ± 46 N vs. 369 ± 52 N; ES = 0.8). The average force level achieved by CTRL legs during the exercise protocol (349 ± 56 N) was not significantly different from those of either patient leg (Fig. 12).

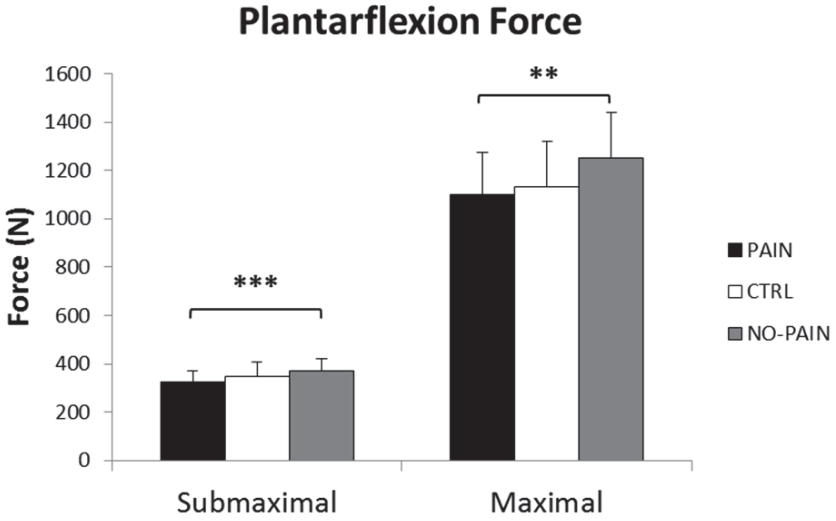

FIGURE 12 Maximal and submaximal isometric plantarflexion force from symptomatic (PAIN), asymptomatic (NO-PAIN), and healthy control (CTRL) legs at 0 weeks. ** P<0.01; *** P<0.005

As a result of the eccentric rehabilitation, significant improvement was observed in the PAIN leg ($P < 0.005$; 1104 ± 185 N vs. 1298 ± 253 N). Similarly, NO-PAIN leg produced significantly more plantarflexion force compared to the baseline value ($P < 0.05$; 1262 ± 373 N vs. 1343 ± 408 N) (Fig. 13). These increments resulted in both PAIN and NO-PAIN legs exercising at significantly higher force levels during the post-rehabilitation submaximal exercise protocol versus the baseline session ($P < 0.01$ and $P < 0.05$ respectively).

Consequently, during the post-rehabilitation measurements, PAIN and NO-PAIN legs were not significantly different from each other anymore regarding plantarflexion strength. Additionally, no differences were found between the two groups. It also meant that both legs exercised at the same absolute submaximal force level during testing following the rehabilitation. CTRL group legs did not show bilateral within-group or between-group differences with respect to maximal and submaximal isometric plantarflexion force (Fig. 13).

In the Achilles tendon rupture patient, MVIC force from the operated (OPER) leg was nearly 75% lower than that of the unoperated leg (UNOP) at baseline, even three months after the reconstruction surgery (360 N vs. 1355 N). The leg of healthy control subject was 260% stronger than OPER while being similar in strength to the UNOP leg (Fig. 14). Therefore, the operated leg exercised at a much smaller submaximal force level compared to the UNOP (107 N vs. 402 N). Eccentric rehabilitation resulted in over three-fold increase in plantarflexion force production of OPER (360 N vs. 1188 N). On the contrary, the UNOP leg demonstrated a slight decline in the force level after the rehabilitation period.

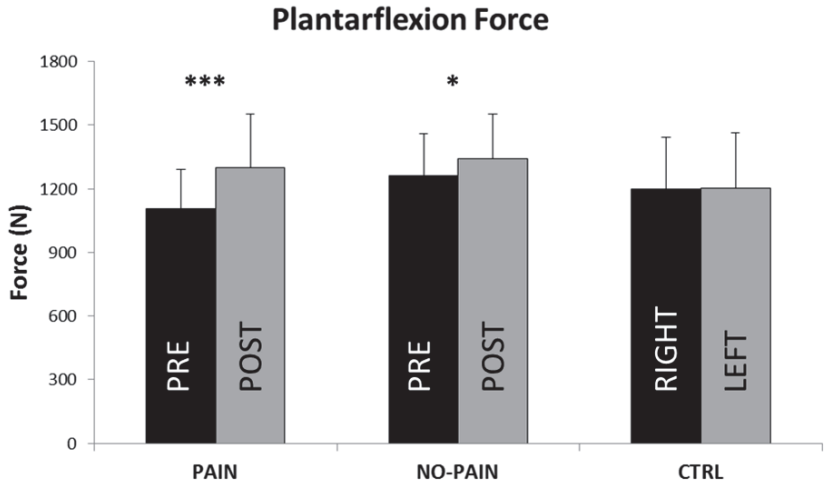

FIGURE 13 Maximal isometric plantarflexion force from both symptomatic (PAIN) and asymptomatic (NO-PAIN) legs of the tendinopathy patients before (PRE) and after (POST) the eccentric rehabilitation. For reference, force values from both legs of the control (CTRL) are also provided. * P<0.05; *** P<0.01

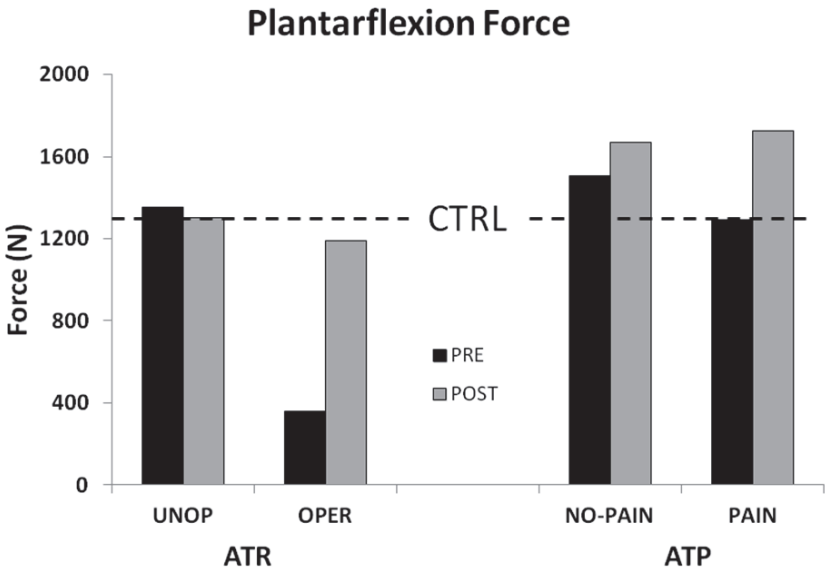

FIGURE 14 Maximal isometric plantarflexion force before (PRE) and after (POST) the eccentric rehabilitation. UNOP: unoperated and OPER: operated legs of Achilles tendon rupture (ATR) subject undergoing 5-month rehabilitation. NO-PAIN: asymptomatic and PAIN: symptomatic legs of the Achilles tendinopathy (ATP) subject undergoing 12-week rehabilitation. Horizontal interrupted line denotes the force level from the healthy control subject.

5.2 Myoelectric activity

5.2.1 Muscle specific values

Since EMG values during the submaximal exercise protocol were normalized to those during the MVIC effort, the results are reported here as $\%EMG_{MVIC}$. In the healthy individuals, both right and left legs displayed comparable myoelectric activity patterns. Highest activity was evident in flexor hallucis longus (34.1 ± 25 %) and medial gastrocnemius (33.3 ± 12 %) muscles. The activity of soleus was 24.5 ± 7 % while lateral gastrocnemius demonstrated the lowest activity level (20.7 ± 12 %). No significant correlation was observed between the myoelectric activities of different muscles.

Compared to the control group, soleus in PAIN leg of the tendinopathy patients was significantly more active ($P < 0.05$; 25.5 ± 9 % vs. 38.3 ± 15 %; ES = 1.4). On the other hand, FHL of NO-PAIN leg was less active than controls ($P < 0.05$; 21.1 ± 19 % vs. 33.2 ± 24 %; ES = 0.5). Within the tendinopathy group, soleus on PAIN side displayed greater activity than that of NO-PAIN ($P < 0.05$; 38.3 ± 15 % vs. 22.9 ± 6 %; ES = 1.7). Similarly, FHL was also more active in PAIN leg ($P < 0.05$; 25.6 ± 13 % vs. 21.1 ± 19 %; ES = 0.2) (Fig. 15).

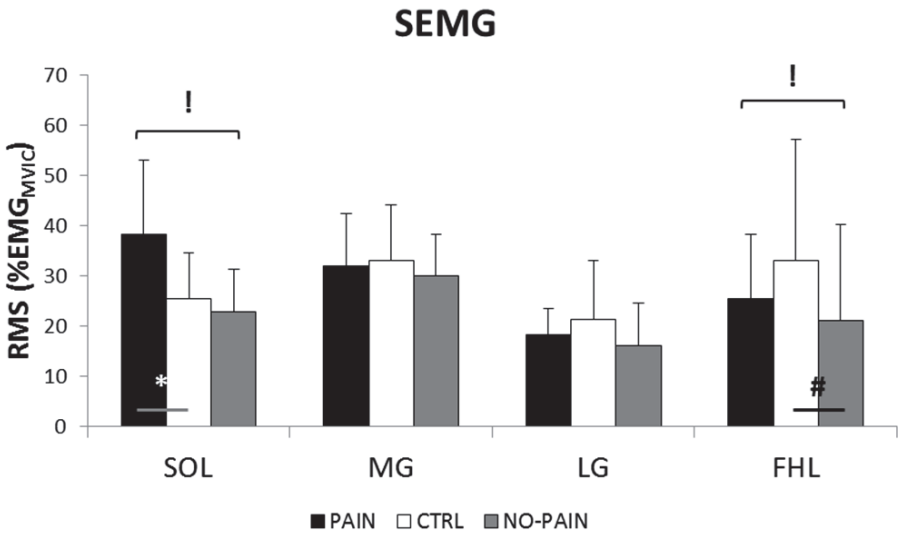

FIGURE 15 Normalized root mean square values of EMG ($\%EMG_{MVIC}$) during submaximal isometric plantarflexion task for Achilles tendinopathy and control groups (Sol: soleus, MG: medial gastrocnemius, LG: lateral gastrocnemius, FHL: flexor hallucis longus). *P<0.05; # P<0.01

As a result of eccentric rehabilitation, significant increase was evident in the myoelectric activity of lateral gastrocnemius in PAIN leg of the tendino-pathy patients ($P < 0.01$; 19.2 ± 5 % vs. 26.5 ± 10 %) (Fig. 16). The changes in the activity of other muscles were not significant. Normalized SEMG values before and after the rehabilitation, along with quantitative changes, are presented in Table 2.

During the post-rehabilitation testing, myoelectric activity of LG was significantly greater in PAIN than of NO-PAIN ($P < 0.005$) (Fig. 17). Activity of other muscles was not significantly different between symptomatic and asymptomatic legs. Similarly, muscle SEMG in neither PAIN nor NO-PAIN was different from CTRL (Table 2). In regard to intermuscle comparison, MG in the symptomatic leg was significantly more active than FHL ($P < 0.05$). No intermuscle differences were seen in NO-PAIN and CTRL legs.

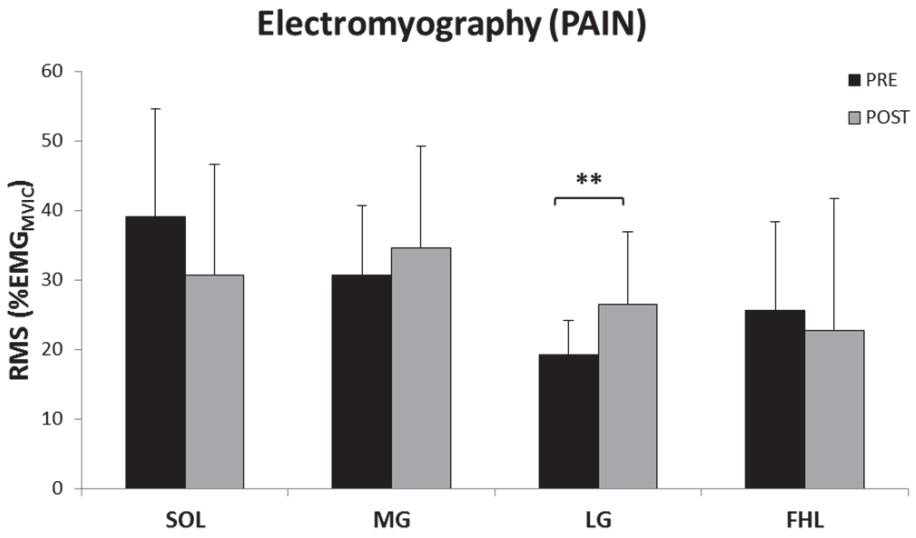

FIGURE 16 Normalized SEMG activity in the muscles of symptomatic leg (PAIN) of the tendinopathy patients before and after the eccentric rehabilitation. ** $P<0.01$

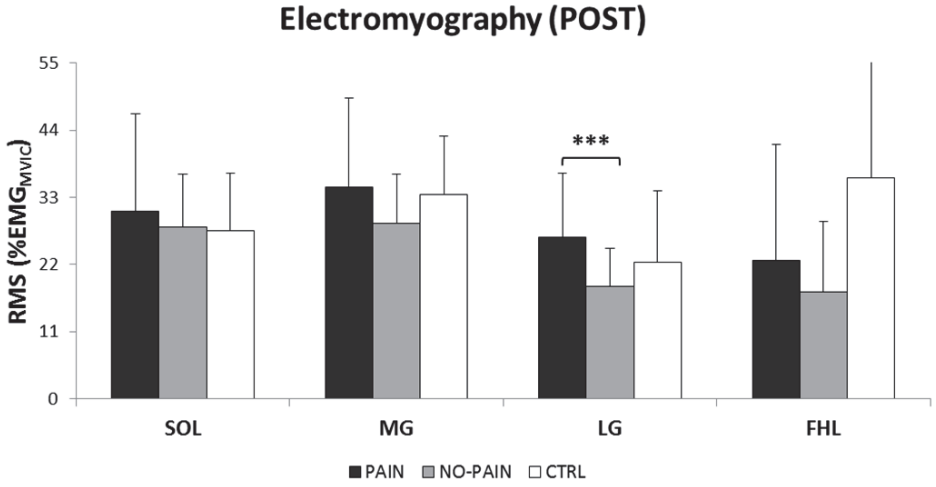

FIGURE 17 Normalized SEMG activity after the eccentric rehabilitation in the symptomatic (PAIN) and asymptomatic (NO-PAIN) legs of the tendinopathy patients. Average of healthy controls (CTRL) is given for reference. *** P<0.005

TABLE 2 Submaximal normalized surface electromyography root mean square values from Achilles tendinopathy patients before and after eccentric rehabilitation. Healthy control values are also provided and compared.

	PAIN			NO-PAIN			CONTROLS (CTRL)	
	PRE	POST	% Δ EMG	PRE	POST	% Δ EMG	RIGHT	LEFT
Soleus	39.16 ± 15.51 (¤)(ǂ)	30.66 ± 16.04	-12.87 ± 26.10	23.55 ± 8.85	28.2 ± 8.54	28.48 ± 42.38	24.09 ± 4.77	27.51 ± 9.49
Medial Gastrocnemius	30.74 ± 10.05	34.64 ± 14.57	18.71 ± 43.46	29.10 ± 8.21	28.7 ± 8.14	09.21 ± 44.72	29.82 ± 10.06	33.37 ± 9.71
Lateral Gastrocnemius	19.17 ± 4.95 (**)	26.47 ± 10.52	38.38 ± 39.32	16.5 ± 8.95	18.43 ± 6.15 (¤¤¤)	64.26 ± 137.54	22.41 ± 11.65	22.41 ± 11.65
Flexor Hallucis Longus	25.58 ± 12.81	22.67 ± 19.03	0.86 ± 49.19	21.48 ± 20.74	17.42 ± 11.59	22.69 ± 92.00	36.60 ± 18.01	36.12 ± 34.68

EMG values are Means ± S.D (%MVC EMG). Due to missing values, N is different in the statistical analyses from that used to calculate mean values here.

% Δ means percent change from PRE to POST

* Significantly different between PRE and POST. ¤ Significantly different between PAIN and NO-PAIN. ǂ Significantly different from CTRL

5.2.2 Relative muscle ratios

In the healthy controls, MG showed the highest EMG activity relative to FHL in both right (1.3 ± 0.5) and left (1.2 ± 1.2) legs (Fig. 18). Considerable individual variation was evident.

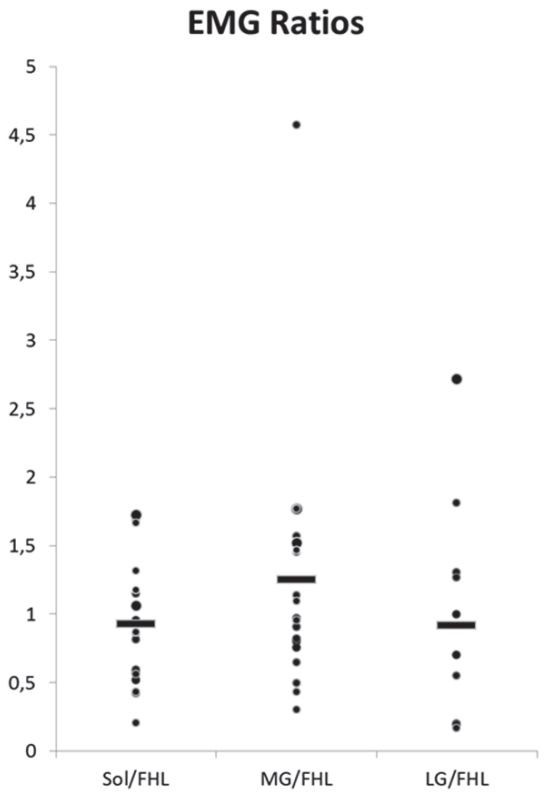

FIGURE 18 Comparison of triceps surae-to-flexor hallucis longus SEMG muscle ratios during submaximal isometric contractions. Each individual leg is represented by a dot and mean value by a horizontal line. (MG: Medial Gastrocnemius, Sol: Soleus, LG: Lateral Gastrocnemius, FHL: Flexor Hallucis Longus).

The combined contribution of the three triceps surae components in terms of evident myoelectric activity was 69 ± 13 % of the cumulative activity of all the four investigated muscles while FHL accounted for the other 31 ± 13 % (Fig. 19A).

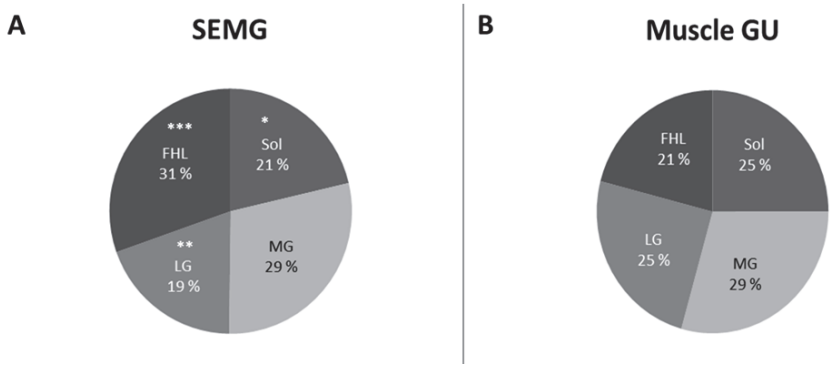

FIGURE 19 Relative contributions of examined ankle plantarflexors during submaximal isometric plantarflexion task based on surface EMG (**A**) and high-resolution PET (**B**). The values represent the percent contribution of each muscle to the cumulative SEMG or GU. * denote significant difference between the methods for a given muscle * P<0.05; ** P<0.01; *** P<0.001

When compared to the control group, the tendinopathy patients demonstrated significantly bigger SOL-to-FHL (SOL/FHL) ratio in the PAIN leg ($P < 0.05$; ES = 1.7). Additionally, MG-to-FHL (MG/FHL) ratio was significantly higher in the NO-PAIN leg versus the healthy controls ($P < 0.05$; ES = 0.5). Within the tendinopathy patients, MG/FHL ratio in NO-PAIN was significantly greater than that of PAIN ($P < 0.05$; ES = 0.6) (Fig. 20).

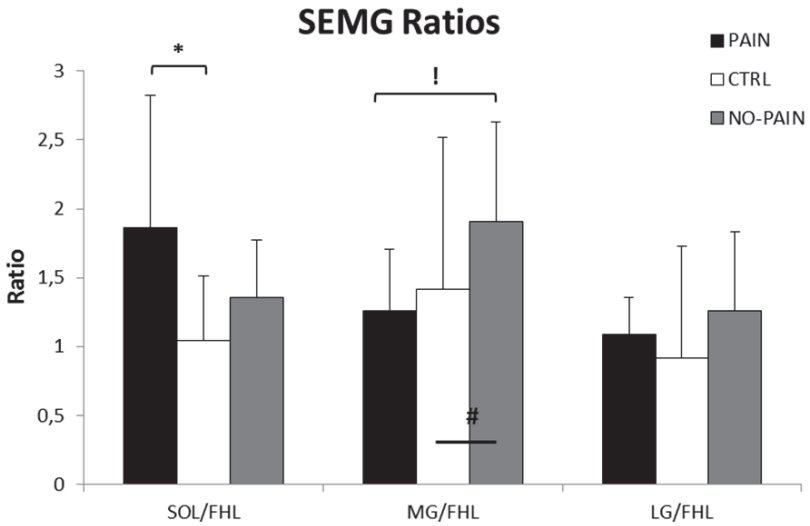

FIGURE 20 Comparison of triceps surae-to-FHL muscle SEMG ratios during submaximal isometric plantarflexion task in healthy and Achilles tendinopathy subjects. P<0.05

Significant increments in the MG/FHL ($P < 0.05$; 1.3 ± 0.4 vs. 2.2 ± 1.3) and LG/FHL ($P < 0.005$; 1.1 ± 0.3 vs. 1.8 ± 1.1) ratios were observed in the PAIN leg as a result of eccentric rehabilitation (Fig. 21). No significant differences were seen in the case of asymptomatic leg.

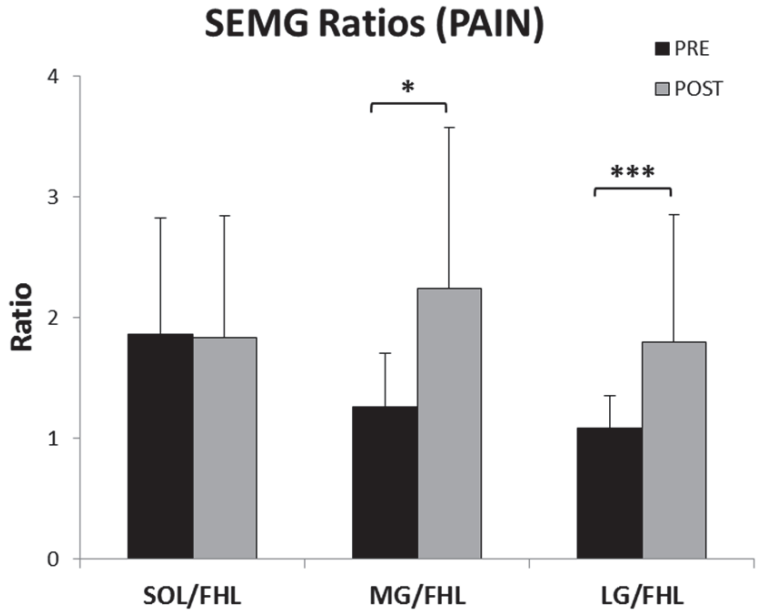

FIGURE 21 Triceps surae-to-FHL muscle SEMG ratios from the symptomatic leg of the tendinopathy patients before (PRE) and after (POST) the eccentric rehabilitation. * $P < 0.05$; *** $P < 0.005$

Subsequently, during the post-rehabilitation measurements, no major differences between the PAIN and NO-PAIN legs, in terms of SEMG ratios, were present except for LG/FHL which was significantly larger in PAIN ($P < 0.05$). However, compared to the control group, SOL/FHL ratio was greater in both PAIN and NO-PAIN ($P < 0.05$). Similar differences were found for MG/FHL ratio ($P < 0.05$). In the case of LG/FHL, only PAIN leg had significantly larger ratio than CTRL ($P < 0.01$) (Fig. 22).

The relative contribution of soleus, as a percentage of cumulative SEMG of all four muscles, was decreased while that of MG increased after the rehabilitation ($P < 0.05$) (Fig. 23 A and B).

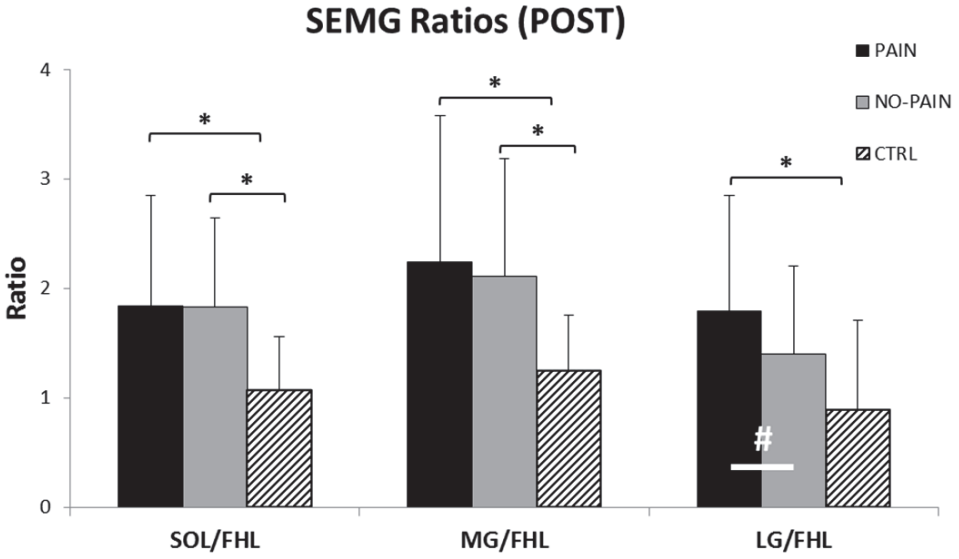

FIGURE 22 Triceps surae-to-FHL muscle SEMG ratios from both legs of tendinopathy patients. Mean of control legs (CTRL) is shown for comparison. $P<0.05$

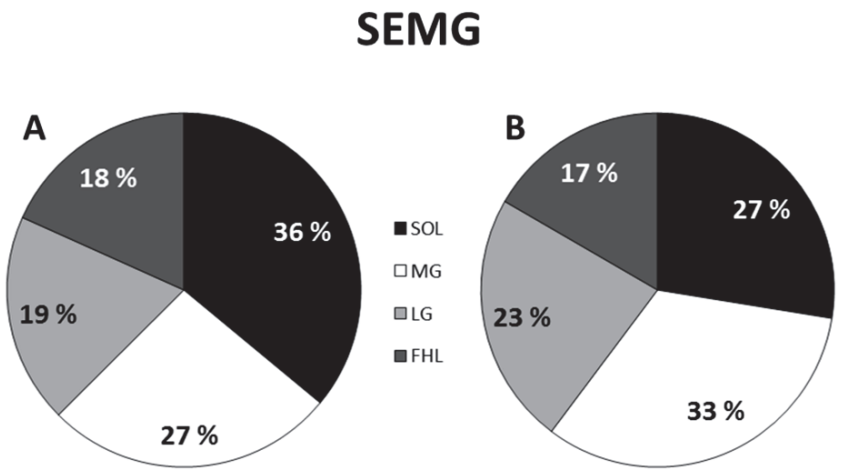

FIGURE 23 Relative myoelectric contributions of individual muscles as a percentage of cumulative value of all four muscles in the symptomatic (PAIN) leg of Achilles tendinopathy patients before (**A**) and after (**B**) eccentric rehabilitation.

The changes in the triceps surae SEMG and the changes in submaximal plantarflexion target force were not significantly correlated in either leg of the Achilles tendinopathy group.

5.3 Myotendon metabolic activity

5.3.1 Muscle specific GU rate

The unit for glucose uptake rate reported here is μmol * 100 g^{-1} * min^{-1}. In the healthy controls, the average glucose uptake rate for the four muscles and the Achilles tendon was quite similar for both legs. MG demonstrated the highest rate among the muscles in both right and left legs (2.4 ± 0.8 and 2.6 ± 0.8). On the contrary, the lowest uptake rate was detected in FHL (right: 1.8 ± 0.6, left: 1.8 ± 0.6) which was significantly different from both SOL ($P < 0.01$) and MG ($P < 0.005$). Compared to the muscles, the GU rate of Achilles tendon was significantly smaller ($P < 0.01$). Other GU rate values can be seen in Table 3. A significant positive correlation ($P < 0.005$) was observed among the GU rate of all muscles.

Although the GU rate of all muscles in both PAIN and NO-PAIN legs of Achilles tendinopathy patients tended to be higher versus the healthy controls, the differences were not significant. However, in the case of Achilles tendon, both tendinopathy patient legs showed greater GU rate than the control tendons ($P < 0.05$; ES = 1.0-1.2). No significant differences were evident in the myotendon GU rate of PAIN and NO-PAIN legs (Fig. 24).

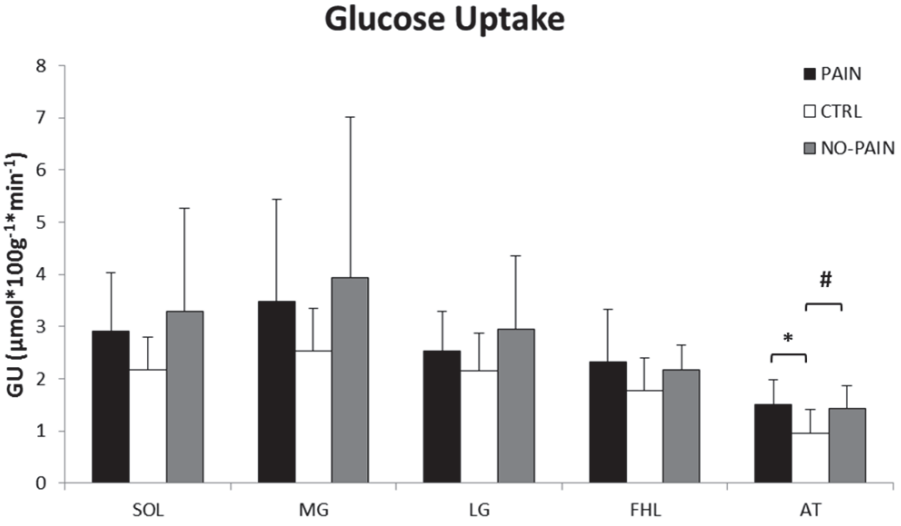

FIGURE 24 Muscle glucose uptake rates for Achilles tendinopathy group and healthy control group. $P<0.05$

TABLE 3. Myotendon glucose uptake values from Achilles tendinopathy patients before and after eccentric rehabilitation. Healthy control values are also provided and compared.

	PAIN			NO-PAIN			CONTROLS	
	PRE	POST	% Δ GU	PRE	POST	% Δ GU	RIGHT	LEFT
Soleus	2.64 ± 0.74 [b]	3.47 ± 0.98 [g]	39.65 ± 52.07	3.03 ± 1.85	3.50 ± 1.07 [f]	31.04 ± 43.90	2.07 ± 0.67	2.04 ± 0.65
Medial Gastrocnemius	3.08 ± 1.54	3.56 ± 0.80 [f]	32.82 ± 54.72	3.53 ± 2.94 [a]	4.13 ± 2.27 [e]	31.91 ± 35.79	2.48 ± 0.86	2.31 ± 0.80
Lateral Gastrocnemius	2.43 ± 0.76 [c]	3.20 ± 0.74 [f]	38.65 ± 37.58	2.78 ± 1.39	3.06 ± 0.91 [e]	20.16 ± 34.94	2.03 ± 0.68	2.05 ± 0.91
Flexor Hallucis Longus	2.22 ± 1.0	2.55 ± 0.66 [f]	24.59 ± 40.35	2.08 ± 0.41 [a,e]	2.40 ± 0.55 [d,f]	18.02 ± 31.55	1.63 ± 0.41	1.66 ± 0.45
Achilles Tendon	1.50 ± 0.51 [e]	1.73 ± 0.64 [e]	22.81 ± 48.39	1.39 ± 0.45 [f]	1.63 ± 1.00 [e]	15.74 ± 41.54	1.00 ± 0.50	0.86 ± 0.32

Values are means ± SD of glucose uptake (GU) in μmol·100 g^{-1}·min^{-1}. PAIN, symptomatic leg; NO-PAIN, asymptomatic leg; PRE, before rehabilitation; POST, after rehabilitation; %Δ, percent change from PRE to POST. Significant difference between PRE and POST: [a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.005$. [d]Significant difference between PAIN and NO-PAIN, $P < 0.05$. Significantly different from control: [e]$P < 0.05$, [f]$P < 0.01$, [g]$P < 0.005$.

As a result of 12-week eccentric rehabilitation, GU rate of both soleus and LG increased significantly in the symptomatic leg of the Achilles tendinopathy patients ($P < 0.005$) (Fig. 25). GU rate of MG, FHL, and the Achilles tendon also demonstrated a non-significant rise. On the other hand, in NO-PAIN leg, significant increments in GU rate were seen in MG and FHL muscles ($P < 0.05$) (Table 3).

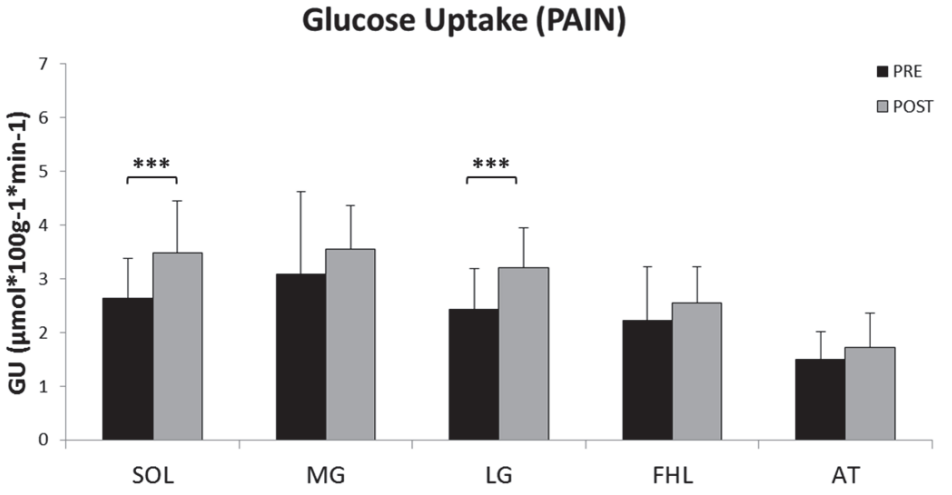

FIGURE 25 Myotendon glucose uptake rate in the symptomatic leg of the Achilles tendinopathy patients before (PRE) and after (POST) eccentric rehabilitation. *** P<0.005

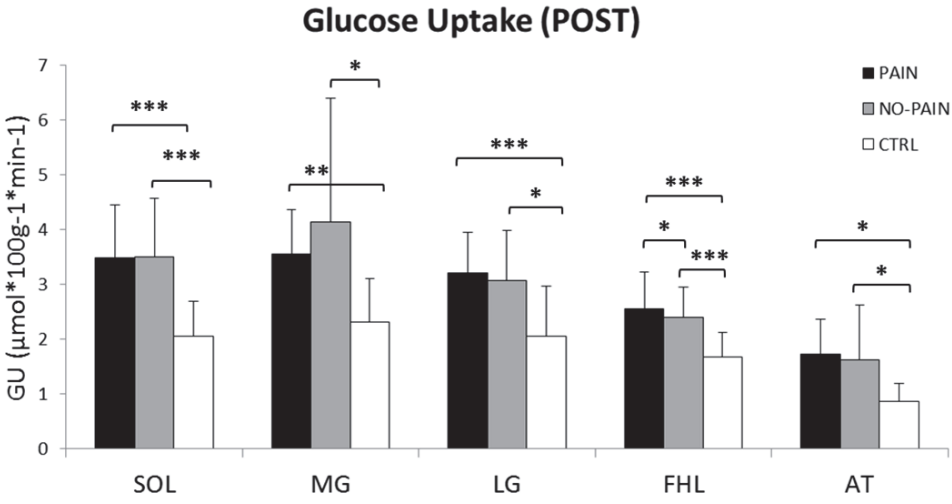

FIGURE 26 Myotendon GU rate in tendinopathy patients during post-rehabilitation measurements compared with healthy reference (CTRL) values. * P<0.05; P<0.01; *** P<0.005

During the post-rehabilitation measurements, GU rates of all muscles and the tendon were significantly different between the healthy and tendinopathy groups (Fig. 26).

In terms of intermuscle differences, in PAIN leg, both soleus and MG showed greater GU rates than FHL ($P < 0.05$) at POST. Similarly, all components of TS muscle (SOL, MG, LG) and FHL displayed significantly higher GU rate than that of AT ($P < 0.05$). In NO-PAIN leg, there were no major intermuscle differences (SOL > FHL: $P < 0.054$). However, all TS components had greater GU compared to AT ($P < 0.05$).

Glucose uptake PET images from both legs of the ATR subject, before and after the rehabilitation, are shown in figure 27. At baseline, all components of triceps surae in OPER leg had much higher glucose uptake than those of UNOP. In the case of Achilles tendon, OPER leg had nearly 11 times higher GU rate than the unoperated leg.

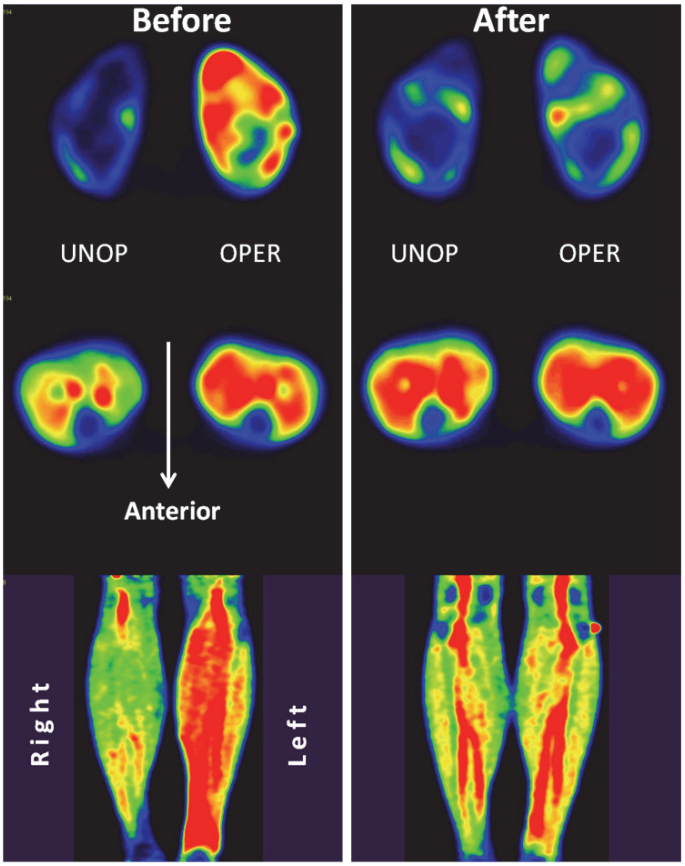

FIGURE 27 PET images from both unoperated (UNOP) and operated (OPER) legs of the Achilles tendon rupture patient before and after eccentric rehabilitation. The top row represents the level at 2 cm above calcaneus, middle row represents mid-leg level, and bottom row shows coronal plane images on the same absolute scale.

As a result of the eccentric rehabilitation, GU rate of all muscles was reduced to half or less in OPER despite an increased absolute force produced during the submaximal plantarflexion task. Achilles tendon demonstrated over 65% decline in GU rate but was still remained more than 3-fold higher than that of the contralateral leg. In UNOP, the myotendon GU remained mostly unchanged after rehabilitation except for soleus which displayed 30% reduction. Numerical values are presented in Table 4.

TABLE 4 Myotendon glucose uptake rates from operated (OPER) and unoperated (UNOP) legs of the Achilles tendon rupture (ATR) patient before (PRE) and after (POST) eccentric rehabilitation.

	ATR patient			
	OPER		UNOP	
	PRE	POST	PRE	POST
Soleus	5,25	3,45	3,16	2,46
Medial Gastrocnemius	4,52	3	2,77	2,52
Lateral Gastrocnemius	3,94	2,52	2,4	2,31
Flexor Hallucis Longus	5,58	3,7	2,98	3
Achilles Tendon	12,08	4,19	1,12	1,19

All values are (µmol*100g-1*min-1).

5.3.2 Relative muscle ratios

Similar to absolute GU rate, no significant differences were present in the relative muscle GU between the healthy control legs with respect to muscle ratios. Ratio above one suggested that triceps surae components were metabolically more active compared to FHL. MG/FHL ratio was (1.4 ± 0.3) while both soleus and LG had a very similar ratio with FHL (~1.2 ± 0.3). When the data from both legs were combined, the collective TS muscle GU rate constituted 79 ± 4 % of total GU by all four plantarflexors. Compared with SEMG findings, both soleus ($P < 0.05$) and LG ($P < 0.01$) showed significantly more relative contribution towards overall plantarflexion effort regarding metabolic activity. Conversely, the contribution of FHL was significantly ($P < 0.005$) smaller than that revealed by SEMG (Fig. 19B).

When healthy controls were compared with the Achilles tendinopathy patients, no sigificant differences were seen between the GU muscle ratios. Similarly, PAIN and NO-PAIN legs were not significantly different (Table 5).

TABLE 5 Muscle glucose uptake ratios from Achilles tendinopathy and control subjects.

	Achilles tendinopathy		Healthy controls
	PAIN	NO-PAIN	Leg Average
Sol-to-FHL	1.3 ± 0.3	1.5 ± 0.7	1.2 ± 0.3
MG-to-FHL	1.6 ± 0.7	1.7 ± 1.1	1.4 ± 0.3
LG-to-FHL	1.2 ± 0.4	1.3 ± 0.5	1.2 ± 0.3

All values are means ± S.D

Resulting from eccentric rehabilitation, both SOL/FHL and LG/FHL ratios showed significant increments in PAIN leg ($P < 0.05$). In the case of NO-PAIN leg, the ratios did not change significantly. At the end of rehabilitation, the relative contributions were not significantly different between the symptomatic and asymptomatic legs of the tendinipathy patients. Similarly, they were comparable to the healthy references values (Table 6).

TABLE 6 Muscle glucose uptake ratios from both legs of the control subjects and Achilles tendinopathy patients before and after eccentric rehabilitation.

	PAIN		NO-PAIN		Controls	
	PRE	POST	PRE	POST	RIGHT	LEFT
Sol-to-FHL	1.26 ± 0.31	1.38 ± 0.26	1.42 ± 0.67	1.48 ± 0.38	1.22 ± 0.24	1.25 ± 0.34
MG-to-FHL	1.49 ± 0.74	1.44 ± 0.31	1.63 ± 1.10	1.74 ± 0.82	1.37 ± 0.33	1.48 ± 0.33
LG-to-FHL	1.18 ± 0.39	1.31 ± 0.33	1.31 ± 0.48	1.31 ± 0.37	1.23 ± 0.48	1.22 ± 0.29

All values are means ± S.D

The relative contribution of any individual muscle, as a percentage of cumulative GU rates of all four muscles, remained unchanged after the rehabilitation (Fig. 28 A and B).

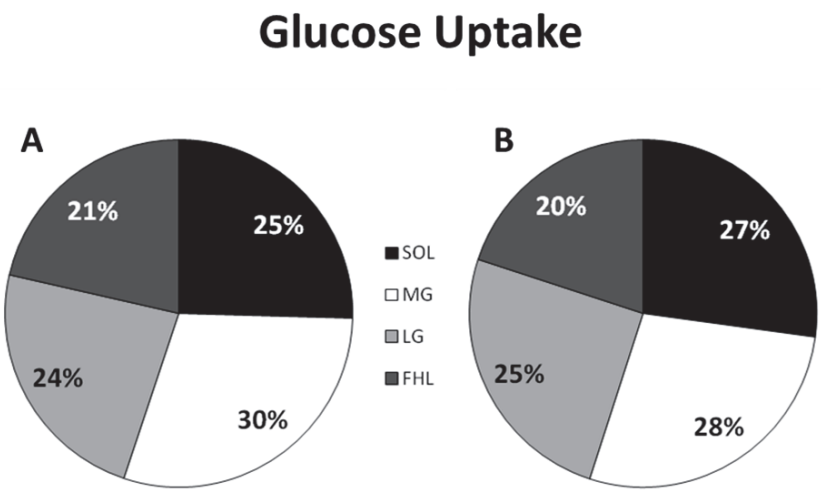

FIGURE 28 Relative metabolic contributions of individual muscles as a percentage of cumulative value of all four muscles in the symptomatic (PAIN) leg of Achilles tendinopathy patients before (**A**) and after (**B**) eccentric rehabilitation.

No significant correlation was found between the rehabilitation-induced changes in GU of any muscle and changes in submaximal target force levels over time in either leg of the Achilles tendinopathy patients. However, significant positive correlation was seen between the changes in GU of Achilles tendon and changes in submaximal target force levels over 12 week of eccentric training in PAIN leg ($r = 0.70$, $P < 0.05$).

In the Achilles tendon rupture patient, all muscle GU ratios were less than 1 at baseline in the operated leg. In the unoperated leg, only soleus showed a higher GU relative to FHL. Following rehabilitation, all ratios stayed similar in OPER leg while reductions were observable in UNOP (Table 7).

TABLE 7 Muscle GU ratios from the Achilles tendon rupture patient.

	ATR patient			
	OPER		UNOP	
	PRE	POST	PRE	POST
SOL-to-FHL	0,94	0,93	1,06	0,82
MG-to-FHL	0,81	0,81	0,93	0,84
LG-to-FHL	0,71	0,68	0,81	0,77

5.4 Other results

The average VISA-A questionnaire score in Achilles tendinopathy patients at baseline was 63.8 ± 19 (range 27 – 86). As a result of 12-week heavy-load eccentric calf muscle rehabilitation, the score increased significantly ($P < 0.05$) to 79.6 ± 17 (range 52 – 100). However, VISA-A questionnaire score of individual patients followed a heterogeneous trend (Fig. 29).

The VAS pain score, recorded after each eccentric exercise session, showed a non-significant decline as a result of rehabilitation. Self-reported training compliance, established on training journals, was 90% in terms of days and 81% with respect to overall training sessions. The average eccentric contractions performed by each patient were ~6,050.

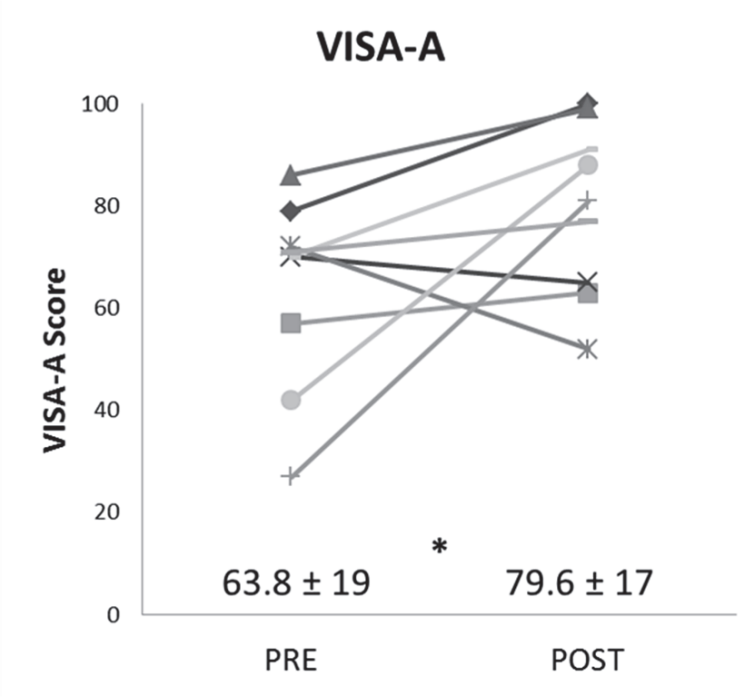

FIGURE 29 Mean and individual VISA-A scores of Achilles tendinopathy patients before (PRE) and after (POST) eccentric rehabilitation.

6 DISCUSSION

6.1 Plantarflexion force

This study demonstrated that the average maximal isometric plantarflexion force production was similar in the right and left legs of the healthy individuals, even though significant bilateral and inter-individual variability was observed. The force levels maintained during the submaximal exercise protocol were high enough to reveal appreciable muscle glucose uptake, and low enough to enable the completion of the task without the onset of fatigue. The fatigue was ruled out after the subjective reporting of the subjects and the objective median power frequency (MPF) analysis of the power spectra of EMG waveforms. One assumption made in this study is that all muscles were fully activated when MVIC was recorded. Therefore, caution must be observed while making inferences based on the findings. Similarly, contractions at 30% MVIC level do not imply that each muscle was activated at 30% of its capacity.

In the Achilles tendinopathy patients, the maximal isometric plantarflexion force was significantly greater on the asymptomatic side compared to the painful leg. This finding confirms earlier reports on the undermining effect of pain associated with Achilles tendinopathy on plantarflexion strength (Arya & Kulig 2010; Wang et al. 2012). A similar difference was expected between the PAIN and control legs but no difference was evident. On the other hand, instead of showing similar force levels, NO-PAIN leg was substantially stronger than the CTRL legs. One explanation to this is that the subjects in the patient group were physically more active and had therefore about 10 % stronger legs than the control group despite being age-weight-height matched. The differences in MVIC force generation were reflected in the target force levels for the submaximal isometric exercise too for obvious reasons.

In line with the hypothesis, plantarflexion strength of the symptomatic leg of tendinopathy patients improved significantly from baseline level as a result of the eccentric rehabilitation. Consequently, the MVIC force from the two legs of the patients was not significantly different any longer. Both these findings

are consistent with an earlier report (Alfredson et al. 1998). A similar pattern was observed in the Achilles tendon rupture patient wherein the absolute improvement in force production was even greater leading to comparable plantarflexion strength post-rehabilitation.

6.2 Myoelectric activity in healthy and tendinopathy patients

In the healthy individuals, this study has shown that during the submaximal exercise, normalized myoelectric activity of all muscles was similar in both right and left legs. On average, FHL and MG were the most active (~33%), followed by the soleus (~24%) and the LG (~21%) in regard to their respective root mean square EMG_{MVIC}. Behavior of the triceps surae muscle regarding EMG RMS during submaximal isometric contractions has previously been reported in the literature. In one study, average RMS of soleus, MG, and LG at the beginning of a sustained unilateral submaximal (40 % MVIC) isometric exercise was shown to be ~43%, ~33%, and ~28% (%EMG_{MVIC}) respectively in older healthy male subjects (Mademli & Arampatzis 2005). In our much younger healthy controls, values for the soleus were considerably lower in contrast. In the past, myoelectric activity of both the gastrocnemius and the soleus has been shown to increase significantly over time during sustained unilateral submaximal isometric exercise at 10-40% MVIC (McLean & Goudy 2004; Löscher et al. 2008; Pereira et al. 2011). Since we used intermittent contractions instead of sustained, no significant changes in the RMS were evident from beginning to end of the exercise protocol as revealed by the median power frequency analysis. The combined EMG activity of the three TS components made up ~70% of the total contribution from the targeted muscles in this study while FHL was responsible for the remaining 30 percent (Fig. 19 A).

Past studies have also shown a heterogeneous distribution of muscle activation within the triceps surae muscle. Five sets, of ten single leg calf-raise exercises (2 seconds) each, resulted in the activation of various TS components at different intensities as evaluated by three-dimensional muscle functional magnetic resonance imaging (3-D fmMRI) (Kinugasa et al. 2005). During this submaximal exercise, only ~46% of MG, in terms of muscle volume, was activated while the activation of soleus and LG was ~35%. These activation levels correlated well (r = 0.84) with the EMG results. Another important finding of that study was that no significant differences between the activation of superficial and deep portions of any muscle were found. This is important because it may counter the proposed limitation of SEMG technique (Knight & Kamen 2005) to only the superficial regions of the studied muscle. However, the difference in the nature of muscle contractions in the two studies must be noted. Kinugasa and colleagues reported the findings from an isometric exercise study while Knight and Kamen published the results from dynamic exercise.

Furthermore, this study evaluated the relative contribution of different superficial plantarflexors to the deep plantarflexor (FHL) during the submaxi-

mal isometric task by calculating Sol-to-FHL, MG-to-FHL, and LG-to-FHL ratios using normalized EMG RMS of the corresponding muscles. Considerable individual variations were seen in how various plantarflexors were activated in the healthy subjects. For instance, activity of the soleus ranged from as low as 1/5th of, to as high as nearly twice the electric activity of FHL. Previously, muscle ratios in terms of peak muscle displacement have been investigated using velocity-encoded cine phase-contrast MR imaging (Finni et al. 2006). Finni and colleagues reported that Sol-to-FHL muscle displacement ratios from healthy control legs displayed a large discrepancy between the subjects, ranging from 0.6 to 9.6 at 20% MVIC and 1.1 to 4.7 at 40% MVIC. In addition, they suggested that the inter-individual differences in the muscle coordinative strategies may affect the calculation of plantarflexion forces generated by individual muscles. Similarly, a more recent study also found large inter-individual variations in the relative activation of triceps surae and the FHL. The study, by dividing the subjects in FHL activators and non-activators, reported that three of the seven participants exhibited excessive myoelectric activation and proximal displacement of the FHL. The EMG was nearly 50% of the EMG_{MVIC} in these subjects. Conversely, the other four subjects were characterized by a minimal FHL activation in terms of EMG and proximal displacement. Myoelectric activity in these subjects was merely 12% EMG_{MVIC} (Bojsen-Møller et al. 2010). The findings of the present study confirm these earlier reports that contribution of FHL to an overall plantarflexion effort during a task is highly individual.

Compared to the healthy controls, the Achilles tendinopathy patients exhibited significant differences in the myoelectric activation of ankle plantarflexors. It was expected that FHL would be more active in the symptomatic legs in an attempt to compensate for the reduced input from the triceps surae muscle. Predictably, therefore, FHL did demonstrate greater relative myoelectric activity in the symptomatic leg versus the asymptomatic leg. However, unexpectedly, soleus also demonstrated significantly greater activity (~67%) in the painful leg compared to the healthy contralateral leg. The reason underlying higher soleus activity is open to interpretation and may need further investigation. More importantly, however, there was no significant difference between the two legs regarding SOL-to-FHL ratio. This finding stemmed from a simultaneous occurrence of higher myoelectric activity in both the soleus and the FHL. Furthermore, soleus was also the most active muscle among the four in the symptomatic in contrast to controls subjects wherein FHL showed highest activity. In the asymptomatic leg, MG was found to be the most active muscle. Soleus was also significantly more active than its healthy control counterpart (Fig. 15) while the other three muscles did not show significantly different activity between the symptomatic and control legs. On the other hand, all three compartments of triceps surae in the asymptomatic were comparable to those of healthy controls with regard to myoelectric activity. Hence, the assumption that TS muscles of the asymptomatic leg in the tendinopathy group would behave similarly to those of healthy individuals was proven correct. The results of this study also indicate that MG had presented the most consistent behaviour while soleus was

the least predictable muscle in terms of myoelectric activity during submaximal exercise.

Following the rehabilitation, the normalized myoelectric activity of the soleus declined significantly in the symptomatic leg of the tendinopathy patients. On the other hand, the activity of both gastrocnemii displayed increments, of which that of LG was statistically significant. Thus the most comparable muscle between the two investigative techniques was LG exhibiting not only significantly higher metabolic activity but also myoelectric activity during the post-rehabilitation measurements. The SEMG of FHL remained unchanged, which is in agreement with the PET findings. During post-rehabilitation session, MG showed significantly more activity than FHL. It is reasonable to state that eccentric training resulted in an apparent redistribution of myoelectric activity of TS components in the symptomatic leg. The reduction in the activity of soleus was accompanied by a compensatory increase in the input by the gastrocnemii (Fig. 23). An alternative explanation could be that the tendinopathy might have decreased the myoelectric activity of gastrocnemii, which resulted in a compensatory increase in soleus activity, as seen at baseline, only to be ultimately normalized by the eccentric exercise.

It is plausible that a painful Achilles tendon may cause some components of the TS muscle to contribute relatively more during submaximal effort under reduced overall plantarflexion strength situation. In the present study it can be exemplified by a considerable higher soleus activity than that of LG at baseline, followed by more homogenous contributions from all three TS components after the rehabilitation. Since the activity of LG increased significantly following rehabilitation in the symptomatic leg, while staying unchanged in the asymptomatic, LG on the symptomatic side was significantly more active after the rehabilitation. In fact, all muscles of the asymptomatic leg tended to have a slightly lower activity compared to the painful leg.

6.3 Metabolic activity

6.3.1 Muscle glucose uptake

In the healthy subjects, the average muscle glucose uptake was found to be similar in both legs for all four muscles. MG had the highest GU (~2.5 µmol*100g^{-1}*min^{-1}). Both the soleus and LG displayed a very similar GU behaviour (~2.1 µmol*100g^{-1}*min^{-1}) while FHL had the lowest GU among all muscles. The GU of all muscles were significantly correlated with each other and a rise in one was directly associated with an increase in others. In the past, Kemppainen et al (2002) measured muscle glucose uptake per unit area of mass (µmol*kg^{-1}*min^{-1}) for quadriceps femoris muscle under both resting and exercising conditions. Resting muscle GU was found to be very low and it increased significantly with the increase in exercise (cycle ergometry) intensity (30%, 55%, and 75% VO_2max.). At 30% VO_2max, (91 ± 24 W) the uptake of 7.5 µmol*100g^{-1}*min^{-1} was

reported which is more than twice the GU of plantarflexors in our study. Another study (Hannukainen et al. 2005) reported the values of ~4.5 µmol*100g^{-1}*min^{-1} using the same protocol as Kemppainen et al, at (76.9 ± 15.6 W). Yet another study, comparing GU response to exercise in trained and untrained men, reported quadriceps femoris GU of ~5 µmol*100g^{-1}*min^{-1} in untrained men during cycle ergometry at 30% VO_2max (Fujimoto et al. 2003).

One reason behind the discrepancy in the findings could be the use of different exercise modality and muscle group. Most other studies are incomparable because of either a different exercise device/intensity was used (Oi et al. 2003; Kalliokoski et al. 2005; Reinking & Osman 2009) or the glucose uptake was reported in different units [SUV (Rudroff et al. 2013), glucose index (Bojsen-Moller et al. 2006)]. Some studies have used whole body (Fujimoto et al. 1996, Kilgore & Watson 1998) or only upper extremities (Pappas et al. 2001). Yet another group of studies exists where no particular exercise was performed at all (Jackson et al. 2006) or abnormal uptake was a result of muscle exertion happened 48 hours prior to the scanning (Gradinscak et al. 2003). A case study involving a 30-year old male reported a 3-fold increase in the glucose uptake of MG compared to the resting contralateral leg No actual values were reported although the exercise intensity and duration were comparable to the current study (Kalliokoski et al. 2007).

Similar to SEMG, in order to study the relative GU behavior of various TS configurations to the deep plantarflexor in healthy individuals, Sol-to-FHL, MG-to-FHL, and LG-to-FHL ratios were computed. All three ratios exceeded 1 denoting that every TS component had taken up more glucose than the deep plantarflexor. MG-to-FHL ratio was the largest among the three, consequent to the highest GU in MG. Although not as stark as was the case in SEMG, inter-individual differences were evident in the muscle GU ratios too. For example, both Sol-to-FHL and MG-to-FHL ratios ranged from ~0.8 to ~2. Cumulative TS muscle GU accounted for ~80% of the total GU of all four muscles (Fig. 19 B). In the past, muscle moment investigations have established the input of TS to the residual plantarflexion moment to be ~65% on average while pedalling at power outputs of 90, 180, and 270W (Gregor et al. 1991). In a separate study, Arndt et al (1998) found that directly measured AT moment was 121% of the resultant plantarflexion moment, under the forefoot, during isometric plantarflexion at 25% MVIC with nearly straight knee. This exceptionally high contribution, as explained by the authors, was due to opposing moment from the antagonistic dorsiflexors. Findings based on cadaver moment-arm length data and muscle cross-sectional area had suggested that TS components were responsible for at least ~88% of total plantarflexion moment (van Zandwijk et al. 1998).

No significant correlation was observed between the SEMG and glucose uptake parameters in the healthy participants concerning activation during the submaximal isometric plantarflexion task. The absence of a correlation only highlights the dissimilar nature of the two methods employed. A recent study also concluded that SEMG and PET yield heterogeneous findings with PET being more sensitive, in detecting the modulation of physical activity, than SEMG

during isometric knee extension tasks in young subjects (23 ± 4 yr) (Rudroff et al. 2013). These differences may originate from the fact that PET has an excellent spatial resolution and lower temporal resolution and vice versa for EMG (Holtermann et al. 2005; Hodson-Tole et al. 2013), which may result in variability and lack of correlation. Regarding the ability of these findings to serve as a reference for other studies, we consider that because there was no correlation between SEMG and PET, it means that electrical activity and metabolic activity provide different results. For example, if using an EMG driven model where surface EMG is measured, it could be converted to represent the entire muscle's contribution using the differences that was found in this study.

The Achilles tendinopathy patients: Compared to the healthy controls, in contrast to EMG findings, the Achilles tendinopathy patients did not show significant differences in individual muscle glucose uptake rates. This was unexpected since it was hypothesized that triceps surae of the symptomatic leg would take up appreciably lower glucose than healthy controls due to the effects of Achilles tendon condition on their activation. On the contrary, the glucose uptake in the healthy individuals tended to be lower than not only the asymptomatic leg but also the symptomatic leg. This pattern can be explained by the fact that the tendinopathy patients were relatively more physically active than the controls. Similarly, the relative contribution of the primary plantarflexors to that of FHL was also similar between the groups. Within the tendinopathy group, it was expected that triceps surae of the symptomatic leg would have significantly lower glucose uptake than the asymptomatic leg because of detrimental effect of tendon injury. However, although the glucose uptake rate of the painful leg did tend to be slightly higher, the differences did not reach significant levels. This happened despite the fact that the asymptomatic leg had exercised at a significantly greater force level during the exercise protocol. On the other hand, a compensatory rise in the glucose uptake rate of FHL, and significant difference with the asymptomatic leg, was expected in the symptomatic leg. Again, even though the trend was according to the expectations, it was not statistically significant. To the best of author's knowledge, there are no previous reports on the glucose uptake behavior of ankle plantarflexors, under submaximal isometric conditions, in Achilles tendinopathy patients to compare the findings of the present study.

The Achilles tendon rupture patient: In the Achilles tendon rupture patient, all components of the triceps surae muscle in the operated leg showed much higher glucose uptake rate than those of unoperated and control legs. In the case of FHL, the uptake rate was even greater. While cachexia-related muscle atrophy is associated with muscle inflammation, studies on muscle disuse-atrophy have shown use of an alternative nuclear factor (NF-*k*B) pathway which does not involve activation of transcription factor p65 and, thus, is not pro-inflammatory (Hunter et al. 2002) or could even be anti-inflammatory (Lawrence 2009). Furthermore, physical inactivity may lead to a transition from slow-type to fast-type muscle fibers (Zhang et al. 2007) which typically have lower GLUT4 content, compared to type-1 slow fibers and hence theoretically

should have a lower glucose uptake rate. However, it has also been reported that associated with this muscle fiber-type transition is a shift in the metabolic fuel utilization towards glycolysis (Stein & Wade 2005) which may explain higher glucose uptake rate in the muscles of ATR patient at baseline. Alternatively, and possibly simultaneously, it seems reasonable to postulate that complete severance of the Achilles tendon and the resultant post-operative immobilization resulted in inefficient muscle metabolic activation wherein triceps surae muscle function at a much higher metabolic cost even at nearly 4 times lower force compared to the unoperated leg. In the FHL, greater GU rate at baseline, twice that of contralateral leg, may signify an increased contribution to plantarflexion torque production when Achilles tendon function is compromised. Concerning the relative activation of ankle plantarflexors, SOL-to-FHL, MG-to-FHL, and LG-to-FHL ratios were about 10% smaller in the operated leg as compared to those in the unoperated leg. Compared to the anthropometrically matched control subject, the ratios were 34 - 53% smaller in the operated leg and 25 - 46% smaller in the unoperated leg suggesting a greater relative contribution from FHL in the ATR patient. Similar to the findings of the present study, Finni et al. (2006) also found that the contribution of FHL, relative to that of soleus, was very high in both legs of the ATR patients, compared to the healthy control subjects. They used velocity-encoded cine phase-contrast MR imaging to evaluate the relative contribution of ankle plantarflexors through quantification of muscle displacements during submaximal isometric exercise in the operated and unoperated legs of ATR subjects (Finni et al. 2006).

Following 12 weeks of eccentric rehabilitation, the glucose uptake rate of triceps surae components saw a rise in the symptomatic leg of *tendinopathy patients*. It was expected to happen due to improvement in the plantarflexion strength. Although the up-regulation of TS glucose uptake was not significant, both the soleus and LG demonstrated increases of about 40% while that of MG was ~30%. Although these increments coincided with rise in plantarflexion force levels, there was no significant correlation between the two changes leaving unanswered questions. The heightened glucose uptake observed in the triceps surae may point towards a restoration of its normal contribution to the plantarflexion task. With the rehabilitation-induced pain relief, the normal force transmission through the tendon, and hence normal input of triceps surae, was restored. The smallest increment in muscle glucose uptake was noticed in FHL as expected. As shown by both SEMG and PET, the least active TS component at baseline was LG and showed greatest increments after 12 weeks of training.

Regarding the *tendon rupture patient*, it appears that after 5 months of eccentric strength training the muscles regained much of their metabolic efficiency back as demonstrated by substantial reduction in muscle GU rate despite over 3-fold increase in plantarflexion strength. Interestingly, the opposite was found in a matched Achilles tendinopathy patient where muscle GU rate increased in the symptomatic leg, along with increased strength after 12 weeks of eccentric rehabilitation. With the near restoration of normal triceps surae function with rehabilitation in the operated leg of ATR subject, the metabolic activa-

tion of FHL declined considerably and reached a level comparable to that of the unoperated leg.

6.3.2 Achilles tendon glucose uptake

In healthy control subjects, the Achilles tendon GU was significantly lower than any muscle. It averaged about 1 µmol*100g^{-1}*min^{-1} and was similar in both legs. Hannukainen et al (2005) published the Achilles tendon GU of well under ~1 µmol*100g^{-1}*min^{-1} during cycle ergometry at 30% VO2max and it stayed constant as the exercise intensity was increased to 75% VO2max. On the other hand, a case study involving a 30-year old male reported a 3-fold increase in MG glucose uptake while Achilles tendon uptake increased two times compared to the resting contralateral leg (Kalliokoski et al. 2007). No actual values were reported although the exercise intensity and duration were comparable to the current study. Use of other techniques, such as microdialysis, had shown the absence of appreciable GU in the peritendinous tissue of Achilles tendon during submaximal, intermittent isometric plantar flexion of the ankle (Langberg et al. 1999).

Compared to the healthy controls, the Achilles tendinopathy patients had significantly higher glucose uptake in the Achilles tendon in both legs. One explanation of higher GU in the asymptomatic leg could be the higher muscle force transmission through the tendon. Conversely, greater tendon metabolic activity on the symptomatic side is harder to explain fully. One possible mechanism behind this finding could be increased tendon cell count. There is evidence that Achilles tendinopathy leads to a proliferation of cells in the injured tendon (Pingel et al. 2012) which in theory could result in higher glucose uptake although there is no literature available supporting or refuting the hypothesis. Another explanation could be an increased vascularization of the tendon as a part of the normal healing process thus causing a greater glucose uptake as a result. Lastly, and most controversially, localized tendon inflammation could also the underlying cause. Theoretically, inflammation could play a role and FDG is a potent radiotracer for detecting inflammation (Love et al. 2005). What is not settled is whether inflammation exists in chronic Achilles tendinopathy or not. It must be noted that most histological (Movin et al. 1997), biochemical (Alfredson et al. 2001), and microdialysis (Alfredson et al. 1999) studies have concluded that inflammation is absent in Achilles tendinopathy. Only one study reported an abnormal, enhanced Achilles tendon glucose uptake in the case of an Achilles tendonitis patient (Huang at al. 2006). In the absence of immunohistological and biochemical data in the present study, it is not possibly to conclusively confirm or reject the presence of inflammation. Since FDG is considered one of the most effective radioactive tracers for the detection of an inflammation, had there been an active inflammatory process present in the AT of our patient group, there would be an increased resultant glucose uptake compared to the asymptomatic leg.

In the Achilles tendon rupture patient, the operated Achilles tendon demonstrated nearly 11-fold higher glucose uptake rate compared to the unoperated and healthy control legs. This could, for most part, stem from the pres-

ence of inflammation on the side of Achilles tendon rupture (Cetti et al. 2003). Additionally, since the baseline measurements took place just three months post-operatively, it seems reasonable to postulate that normal healing process and accompanying hyperemia must have played a considerable role in observed heightened glucose uptake rate.

After 12 weeks of eccentric rehabilitation, although there were not significant changes in the tendon GU of both legs of tendinopathy patients, it stayed significantly higher than that of control legs. Eccentric exercise has been associated with a reversal of neovascularization in Achilles tendinopathy (Öhberg & Alfredson 2004). Since glucose delivery rate is down-regulated by a reduction in the blood flow (Rose & Richter 2005), it may lead to reduced glucose uptake. The failure of eccentric exercise to lower the tendon glucose uptake in the present study may stem from a concomitant rise in the glucose uptake caused by strengthened plantarflexion. This hypothesis is supported by the evidence of significant correlation between changes in the glucose uptake rates and those of the plantarflexion force levels at which the legs exercised.

After 5 months of heavy-load eccentric training, Achilles tendon GU rate in the operated tendon demonstrated a reduction to one-third of the baseline level, but remained still almost four-fold higher than in the unoperated and control reference value. This finding either reflects persisting inflammation in the healing tendon or, alternatively, it could be a consequence of an abnormally lengthy physiological healing process. ^{14}C bomb-pulse method has been used recently to reveal that Achilles tendon has a very slow tissue turnover and the core of the tendon may not change in decades (Heinemeier et al., 2013). It is plausible that persistently high glucose uptake rate in both Achilles tendinopathy and tendon rupture patients is somehow associated with the lack of tissue renewal in the Achilles tendon.

6.4 Other results

As expected, the VISA-A questionnaire score (64 ± 19) in the Achilles tendinopathy group was substantially lower than the maximum score of 100 indicating considerable severity of the injury. Following the eccentric rehabilitation, there was a general trend towards a higher score with only two patients exhibiting a decline. In overall terms, there was a 25% improvement observed in the score after the rehabilitation. Simultaneously, the VAS pain score was thought to decline significantly with the tendon recovery but only a slight drop was evident. The apparent lack of correlation between the VISA-A and VAS scores could be explained by the difference in the nature of the two assessments. While VISA-A addressed the tendon condition during general physical activity bouts, VAS score was recorded only after the eccentric training sessions which were designed to be a little painful in principle. One of the biggest issues with such unsupervised, home training exercise programs is lack of compliance. In the present study, the patients demonstrated an acceptably high level of commitment

to the rehabilitation. In the tendinopathy group, the training was carried out on 90% of the days (range: 74–100%) while it was over 95% in the tendon rupture patient.

6.5 Methodological considerations

The deep musculature in the proximal leg, where majority of the muscle bellies are located, cannot be assessed reliably using PET because of their proximity to large blood vessels (peroneal artery & vein, posterior tibial artery & vein). There is always some spillover of radioactivity between the nearby regions in the final PET images, which limits the accuracy near very large blood vessels. Therefore it was decided to leave out the analyses of tibialis posterior and flexor digitorum longus muscles. The FHL is the most important contributor among the deep plantarflexors, in terms of their moment arm, nearly 3.5 times more than that of tibialis posterior (Klein et al. 1996). Additionally, FHL has the largest physiological cross-sectional area among the long and short toe flexor muscles and hence may exert the greatest muscle force (Goldmann & Bruggemann 2012). Due to the distal location of its muscle belly and accessibility for SEMG, flexor hallucis longus was chosen as a representative of the deep musculature in the present study.

Although the exercise protocol could theoretically be performed during the PET scan, we chose to do the exercise before the PET scan. Such a protocol, recently applied in several other experiments (Bojsen-Moller et al. 2010, Heinonen et al. 2012, Rudroff et al. 2013), has been made possible by the properties of [^{18}F]-FDG that enables entrapment into the cells. As there is some tracer still available in the plasma to be taken up by the cells after the cessation of exercise, it may affect the measure of glucose uptake during exercise. However, this effect has previously been estimated to be small (Kemppainen et al. 2002) and most probably in line with the relative usage of the muscles during the preceding exercise. Thus, the lapse between the cessation of exercise and image acquisition in our study is likely not to have affected the data, and this issue was considered when designing the protocol. On the positive side, performing the PET scan after the exercise eliminated motion artifacts during the scan and improved the spatial accuracy of the measurements which is a major advantage.

6.6 Future perspectives

Since the number of participants in the Achilles tendon rupture group was low, it was not possible to generalize the findings of the study to the overall Achilles tendon rupture population. Further investigations with adequate number of

study subjects are required to gain insights into not only the metabolic but also myoelectric activity patterns of such patients.

Conventional bipolar SEMG has inhrently lower temporal resolution. This limitation can be overcome by the application multi-channel surface EMG (MC-SEMG). Investigating the correlation between GU and MC-SEMG of a muscle, such as lateral gastrocnemius muscle, may yield important information regarding global myoelectric activity and its association with the metabolic activation.

The present study reported the chronic effects of eccentric exercise on muscle electric and metabolic parameters. What is not clear is how an acute bout of eccentric exercise would affect the activation. A future study with SEMG measurements during, and PET scan immediately follwing such exercise is highly recommended.

7 KEY FINDINGS AND CONCLUSION

The current series of studies demonstrated that surface electromyogrpahy and high-resolution positron emission tomogrpahy can be effectively used to investigate the electric and metabolic activation strategies of ankle plantarflexors in health and disease. Such evaluations provide insights into muscle function and help better understand the pathomechanics of tendon injury and mechanism of action of eccentric exercise rehabilitation.

The main findings and conclusions of this research are as follows:

1) Significant variability exists in the differential contributions of primary and deep plantarflexors in both healthy and injured Achilles tendon conditions.

2) Bipolar surface electromyography and high-resolution positron emission tomography do not provide comparable results in evaluating plantarflexion muscle function.

3) Chronic Achilles tendinopathy has significant detrimental effect on the plantarflexion force generation.

4) Heavy-load eccentric exercise is beneficial in restoring plantarflexion strength in both chronic Achilles tendinopathy and tendon rupture situations.

5) The effects of eccentric exercise on the myoelectric activity patterns of ankle plantarflexors are inhomogeneous and not always easy to interpret.

6) The glucose uptake rate of the Achilles tendon is significantly higher than the control values in both Achilles tendinopathy and complete tendon severance.

YHTEENVETO (FINNISH SUMMARY)

Pohjelihaksilla on tärkeä rooli jokapäiväisessä elämässämme. Pohjelihakset voidaan jakaa pinnallisiin, jotka käsittävät kaksipäisen ja leveän kantalihaksen, ja syviin pohjelihaksiin, joita ovat varpaiden pitkä koukistajalihas, isonvarpaan pitkä koukistajalihas (FHL, flexor hallucis longus), takimmainen säärilihas ja polvitaivelihas. Kaksipäisen pohjelihaksen lateraalinen ja mediaalinen aitio yhdessä leveän kantalihaksen kanssa muodostavat komipäisen pohjelihaksen (TS, triceps surae), joka kiinnittyy akillesjänteeseen. Pohjelihasten tehtävänä on ojentaa nilkkaa, ja ymmärtääksemme pohjelihaksiin ja akillesjänteeseen liittyvien vammojen patomekaniikkaa tarvitsemme tietoa siitä, miten eri pohjelihaksia käytetään. Tässä tutkimuksessa pohjelihasten sähköistä aktiivisuutta tutkittiin ihon pinnalta elektromyografiaa (EMG) käyttäen ja lihasten glukoosiaineenvaihdunnan aktiivisuutta (glukoosinkulutusta) tutkittiin positroniemissiotomografiaa hyödyntäen. Tutkimuksen tavoitteena oli selvittää kolmipäisen pohjelihaksen ja FHL lihaksen toiminnallista suhdetta terveillä, akillesjännekivuista kärsivillä tutkittavilla ja akillesjänteen repeämästä toipuvalla tutkittavalla. Akillesjännepotilailla tutkittiin lisäksi eksentrisen harjoittelun vaikutusta pohjelihasten voimantuottoon, lihasten ja akillesjänteen glukoosinkulutukseen sekä EMG-aktiivisuuteen.

Tutkittaviksi rekrytoitiin 18-35 -vuotiaita vapaaehtoisia miehiä ja naisia. Akillesjännekipupotilaat (N=11, ikä 28 ± 4 vuotta) olivat fyysisesti aktiivisia harjoitellen keskimäärin 4.7 kertaa viikossa. Antropometrisesti vastaavia terveitä verrokkeja oli 12 (ikä 28 ± 4 vuotta), ja he harrastivat liikuntaa keskimäärin 2.4 kertaa viikossa. Tapaustutkimuksen akillesjännevammapotilas oli 27-vuotias aiemmin liikuntaa harrastanut mies. Akillesjänteen kivuista kärsivillä tutkittavilla pohjelihaksen eksentristä harjoittelua sisältänyt kuntoutus kesti 12 viikkoa ja repeämästä toipuvalla tutkittavalla 22 viikkoa.

Tutkimuksen mittaukset toteutettiin Valtakunnallisessa PET-keskuksessa Turussa. Tutkittavat tulivat laboratorioon paastotilassa. Valmisteluihin kuului EMG elektrodien kiinnittäminen pohkeen lihaksiin, kanyylien asettaminen käsivarren laskimoihin ja maksimaalisen nilkan ojennusvoiman mittaaminen. PET-kuvantamista varten laskimoihin annettiin pohjelihasharjoituksen aikana toisen kanyylin kautta radioaktiivista glukoosimerkkiainetta. Samanaikaisesti toisen kanyylin kautta otettiin verinäytteitä tutkimuksen loppuun sakka veren merkkiainepitoisuuden määrittämiseksi. Tutkittavat tekivät isometrisiä nilkan ojennuksia 30 % nilkan maksimaalisesta ojennusvoimasta vuorotellen vasemmalla ja oikealla jalalla viiden sarjoissa noin 20 minuutin ajan. Samanaikaisesti rekisteröitiin lihasten EMG aktiivisuutta ja heti harjoituksen päätyttyä heidän jalkansa polven yläpuolelta jalkaterään saakka kuvattiin PET-laitteistolla. Jaloista otettiin myös anatomiset magneettikuvat samalta alueelta.

Tulokset osoittivat, että pohkeen lihasten käyttö isometrisessä nilkan ojennuksessa on hyvin yksilöllistä sekä terveillä että akillesjänteen kivuista kärsivillä henkilöillä. Joillain tutkittavilla löydettiin huomattavaa aktiivisuutta FHL lihaksessa, kun puolestaan toisilla tämän lihaksen käyttö oli vähäistä. Krooni-

sesta jännekivusta kärsivillä tutkittavilla nilkan ojennusvoima oli kipeässä jalassa huomattavasti tervettä jalkaa heikompaa. Eksentrisen harjoitusjakson jälkeen voimatasot paranivat sekä jännekipu- että jännerepeämäpotilailla. Arvioitaessa pohjelihasten suhteellista osuutta nilkan ojennusvoimaan tässä tutkimuksessa käytetty EMG menetelmä arvioi FHL-lihaksen roolin suuremmaksi kuin PET-menetelmällä mitattu glukoosinkulutus. Pohkeen toiminnan arvioimisessa EMG ja PET antoivat erilaista tietoa johtuen menetelmien periaatteellisista eroista.

Kuntoutuksen vaikutuksesta pohjelihasten väliseen koordinaatioon on vaikea tehdä yksiselitteistä tulkintaa. EMG:n perusteella kaksipäisen kantalihaksen suhteellinen osuus FHL-lihakseen verrattuna kasvoi, mutta glukoosinkulutuksen perusteella myös leveän kantalihaksen rooli nilkan ojennusvoiman tuottajana vahvistui. Akillesjänteestä analysoitu glukoosinkulutus oli huomattavasti suurempaa potilailla kuin terveillä tutkittavilla. Kahdentoista viikon eksentrinen harjoittelu ei muuttanut kipupotilaiden jänteen glukoosinkulutusta. Tämä voi johtua harjoittelun tuomasta pohjelihasten voiman kasvusta, jonka voidaan arvella kasvattavan glukoosintarvetta, kun samalla tulehduksesta johtuva glukoosinkulutus vähenee. Akillesjänteen repeämästä toipuvalla tutkittavalla jänteen glukoosinkulutuksessa havaittiin laskua kolmannekseen lähtöarvosta, vaikkakin se pysyi korkeammalla kuin terveessä jalassa.

Vaikka tutkittavat toteuttivat yksilöllistä kotiharjoitusohjelmaansa 90 prosenttisesti, kuntoutuksen aikana jännekiputuntemuksissa ilmeni vain hienoista laskua. Akillesjännepatologian kliinisestä asteesta kertovan VISA-A kyselyn tulos kuitenkin osoitti kuntoutuksen tuoneen helpotusta kipupotilaille.

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ORIGINAL PAPERS

I

DIFFERENTIAL CONTRIBUTIONS OF ANKLE PLANTARFLEXORS DURING SUBMAXIMAL ISOMETRIC MUSCLE ACTION: A PET AND EMG STUDY

By

Masood T., Bojsen-Møller J., Kalliokoski K.K., Kirjavainen A., Äärimaa V., Magnusson S.P., Finni T. 2014

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II

PLANTARFLEXOR MUSCLE FUNCTION IN HEALTHY AND CHRONIC ACHILLES TENDON PAIN SUBJECTS EVALUATED BY THE USE OF EMG AND PET IMAGING

By

Masood T., Kalliokoski K.K., Bojsen-Møller J., Magnusson S.P., Finni T. 2014

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III

EFFECTS OF 12-WK ECCENTRIC CALF MUSCLE TRAINING ON MUSCLE-TENDON GLUCOSE UPTAKE AND SEMG IN PATIENTS WITH CHRONIC ACHILLES TENDON PAIN

By

Masood T., Kalliokoski K.K., Magnusson S.P., Bojsen-Møller J., Finni T. 2014

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IV

MUSCLE-TENDON GLUCOSE UPTAKE IN ACHILLES TENDON RUPTURE AND TENDINOPATHY BEFORE AND AFTER ECCENTRIC REHABILITATION: A CASE-CONTROL REPORT

By

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