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Voluntary activation of quadriceps femoris in patients with unilateral anterior cruciate ligament rupture within 6 months of injury: a cross-sectional observational study

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ABSTRACT

Background Deficits in quadriceps femoris strength and voluntary activation have been well documented in chronic anterior cruciate ligament (ACL) injuries, but less is known about the acute or early phase after injury.

Objectives The aim of this study was to evaluate and compare the levels of quadriceps voluntary activation (VA) and strength in both limbs of participants with unilateral ACL ruptures (complete tears) within 6 months of injury.

Design Cross-sectional observational study.

Method Seventeen participants, 12 male, mean age 30 (17-45) years, performed maximal voluntary isometric contractions with the interpolated twitch technique.

Results Mean (SD) peak VA was significantly lower in the injured limb 76.5 (15.0) % than the uninjured limb 85.9 (6.7) % (p=0.02). Mean (SD) peak torque in the injured limb was significantly lower 162.7 (74.1) Nm than the uninjured limb 240.5 (81.0) Nm (p<0.01).

Conclusions This between-limb difference in VA has not previously been observed in patients within 6 months of ACL rupture. Our findings suggest that early rehabilitation programs for adults with ACL rupture should focus on reducing VA deficits to facilitate improvement of the quadriceps femoris muscle strength in the injured limb to comparable values of the uninjured limb.

Key Words: voluntary muscle activation, quadriceps strength, anterior cruciate ligament

INTRODUCTION

Ruptures of the anterior cruciate ligament (ACL) are common during sport and other recreational activity (Gianotti et al. 2009). Subsequent to an ACL rupture both quadriceps weakness (Hurley et al. 1992; Chmielewski et al. 2004; Urbach et al. 1999; Keays et al. 2000; Tsepis et al. 2006) and muscle fibre atrophy occur (Booth 1982; Lieber et al. 1988). This can produce disability, prolong the rehabilitation process and delay return to sport and activities of daily living.

It has been widely reported that reflex inhibition of the musculature surrounding the knee joint exists following injury (Hurley et al. 1992, Newham et al. 1989) or simulated joint effusion (Spencer 1984, Hopkins 2002). This decrease in voluntary activation (VA), an inability to fully activate the muscle, has been termed arthrogenic muscle inhibition (AMI) (Hopkins and Ingersoll 2000) or reflex inhibition (Stokes and Young 1984). Iles et al. (1990) and Hopkins et al. (2001) concluded that joint effusion inhibits quadriceps alpha motor neurons due to excitation of slowly adapting Ruffini endings within the knee joint capsule and stimulation of the 1b inhibitory interneurons. Unless the AMI is reduced or suppressed this may limit rehabilitation (Hopkins and Ingersoll 2000).

Several studies have investigated quadriceps strength in the injured and uninjured limbs of people with unilateral ACL injury, and have found significant strength deficits in the injured limb as would be expected (Chmielewski et al. 2004; Urbach et al. 1999; Keays et al. 2000; Tsepis et al. 2006). Likewise, it is known that quadriceps VA is lower in the injured limb than in healthy control participants (Urbach et al. 1999). But in studies which have compared the injured and uninjured limbs of unilateral ACL ruptured patients, most studies report bilateral deficits in VA, and only two studies have observed between-limb differences in VA to be statistically significant. Newham et al. (1989) examined VA in 11 males with ACL deficiency, at a mean of 11 months post injury. Mean (SD) quadriceps activation in the uninvolved limb was 94.2 ± 2.3% and the involved limb 74.7 ± 5.4%. Hurley et al. (1992) observed similar findings in 10 males with unilateral ACL rupture, mean time since

injury 31 months. This is interesting because it could be logically presumed that the uninjured limb would exhibit lower levels of muscle inhibition, due to those reported differences in strength between limbs (Chmielewski et al. 2004; Urbach et al. 1999).

It is important to note that most ACL VA studies have focused on chronic injuries. Chronic ACL injury is often classed as over 6 months from injury, although it is noteworthy that there is variability in the literature in the use of acute/chronic descriptions, and these terms are often not defined (Flint et al. 2014). Nevertheless, there is a paucity of evidence regarding VA in the early stage of ACL injury, in the acute or subacute stages, 6 months or less from injury. Chmielewski et al. (2004) observed no significant difference in VA between the uninjured and injured limbs of 100 people with acute ACL rupture with a mean time since injury of 6 weeks (range 1-19 weeks). Mean VA in the uninjured limb was 92.8±10.3 (range 54-100%) and in the injured limb 92.6±10.4 (range 60-100%). Williams et al. (2005) observed similar findings in a cohort of 17 ACL deficient subjects at a mean time of 2 months since injury, reporting VA in the uninjured limb was 92±6% and in the injured limb 90±9%. This early stage of ACL injury is important as it is crucial during early rehabilitation that patients perform exercises that are effectively activating the quadriceps, in order to facilitate gains in strength and function following injury (Hart et al. 2010). In addition, early rehabilitation before ACL surgery is beneficial (Smith et al. 2014). An inability to fully activate the muscles of the injured limb could impact on the ability to regain strength and control. Better knowledge of VA in this early phase after ACL rupture could help improve the effectiveness of physiotherapeutic exercise.

To accurately assess VA it is necessary to determine whether the motor neuron pool is sufficiently excited during a voluntary contraction to evoke all the force the muscle is capable of producing (Herbert and Gandevia 1999). If compliance is obtained and maximal effort is made but maximal muscle strength is not achieved, it is likely that there is an underlying physiological reason as the cause, for example AMI (Hart et al. 2010). The twitch interpolation technique can be used to estimate the level of neural drive to a muscle. An electrical impulse is delivered in a controlled manner to a voluntarily contracting muscle (whilst recording force/torque output) and if a twitch-like increment in the force/torque produced by the muscle is observed then maximal force/torque is not being generated voluntarily (Gandevia et al. 1998). The size of

this twitch can be used to estimate the level of neural drive to the muscles (when compared to the force/torque generated from the same twitch in a resting muscle), and hence recruitment of the motor neuron pool. It can therefore be said that this interpolated twitch "is an index of the completeness of muscle activation" (Oskouei et al. 2003).

The variation of levels of VA reported in the previous ACL studies may be the result of methodological differences in the elicitation and measurement of the stimulated twitch. The methodologies described in several studies are questionable in terms of the level of stimulation delivered to the quadriceps. This level has often been under 100 mA which can be inadequate (Behm et al. 1996, Hart et al. 2010).

So it can be seen that some important aspects remain unclear. To the authors' knowledge, there is little research evaluating levels of VA and strength in patients within six months of ACL rupture. Furthermore, there is marked variation in the levels of muscle inhibition reported in studies, and this could be due to methodological differences and particularly inadequate stimulation. Therefore, the aim of this study was to evaluate and compare quadriceps VA and maximal voluntary strength in both limbs of people with unilateral ACL ruptures within six months of injury using an adequate level of stimulation. It was hypothesised that both VA and quadriceps strength would be lower in the injured limb than the uninjured limb.

METHODS

This was a cross sectional observational study. The primary outcome measures were the level of quadriceps VA and torque from both legs.

Participants

Approval was gained from the Teesside University School of Health and Social Care Research Ethics Committee, the South Tees Local Research Ethics Committee, and the South Tees Hospitals Research Approval Board. Patients with a unilateral ACL

rupture (i.e. complete tear) within 6 months of injury were recruited via an acute hospital orthopaedic outpatients clinic. All subjects were diagnosed with an ACL rupture by a consultant orthopaedic surgeon or Extended Scope Practitioner Physiotherapist, and diagnosis confirmed by MRI scan. To be included, participants had to be over the age of 16 years (or skeletally mature as determined by closure of epiphyses on plain X-ray) and they were excluded if they had bilateral injuries; previous injury or surgery to the same knee within the previous 2 years; underlying rheumatological, neurological, cardiovascular or degenerative / congenital condition affecting the lower limbs; history of steroid use (performance enhancing or medication); or were pregnant. Before taking part, each participant read an information sheet about the study and gave informed consent.

The study was time-limited as part of a PhD studentship and so recruitment was set for a fixed period of nine months. In this respect, as an exploratory study, no *a priori* sample size was set, but it was hoped to recruit approximately 20 participants in this within-subjects study to give an adequate degree of precision in estimates made from the results. Twelve male and five female participants were recruited to the study, mean (SD) age 30.2 (9.5) years and mean (SD) time since injury 83 (59) days. Full demographic data are presented in Table 1. No participants had any previous surgery to the injured knee.

Procedures

All participants gave standard demographic data and completed the Lysholm score (Tegner & Lysholm, 1985) and the International Knee Documentation Committee (IKDC) subjective knee form (Irrgang et al. 2001).

Quadriceps VA and torque were measured in both legs during maximal voluntary isometric contractions (MVICs) with the interpolated twitch technique (ITT). Standardised methods were used (Behm et al. 1996; Hurley et al. 1992; Newham et al. 1989) which had been shown previously to have high reliability (Behm et al. 1996). These were adapted with use of an increased level of stimulation to ensure this was adequate to elicit full activation (Babault et al. 2001; Babault et al. 2003) as set out below.

Participants were seated on a Biodex System 3 dynamometer (Biodex Medical systems, Shirley, New York), in an upright position hips at 90 degrees, with their knees flexed to 90º (as measured by the dynamometer). To isolate the quadriceps contraction and minimise use of other muscle groups, all participants were restrained by a thigh strap, pelvic strap and shin strap. Participants carried out practice submaximal contractions and MVICs before the main data collection for familiarisation purposes. Two self-adhesive electrodes (Axelgaard CF1020, 10x18cms) were positioned over the quadriceps, one on the upper lateral aspect of the thigh and the second on the distal medial aspect of the thigh as shown in Figure 1. A constant current high voltage stimulator (Digitimer DS7AH, Digitimer Ltd, England) with a trigger generator (Digitimer DG2A, Digitimer Ltd, England) was used to deliver electrical stimulus to the muscle.

Determination of adequate stimulus level:

A two minute data acquisition period was set on the dynamometer (sampling rate 1000 Hz), during which time a gradually increasing current of approximately 10mA increments, was delivered (frequency 0.2Hz, voltage 400 V) to the resting muscle, until the point at which the output torque reached a plateau. The value of the current at this point for each participant was then used for the subsequent interpolation technique during the MVICs (Babault et al. 2003). The stimulation values determined for use in the MVICs ranged between 180-350 mA.

Measurement of VA and MVIC:

Torque output was recorded from the dynamometer for a 10 second period whilst stimulating pulses were delivered to the quadriceps at a frequency of 1Hz, pulse width 200µs, at the pre-determined current for each participant. In this 10 second period, 3 pulses were first delivered to the resting quadriceps muscle, followed by 5 pulses during a 5 second MVIC. This was repeated for three MVIC attempts for each participant, each lasting 5 seconds, with a 120 second rest period between each (Callaghan et al. 2001) for both limbs (uninjured limb first). Verbal encouragement was given during the MVIC attempts as this has been shown to improve force output (McNair et al. 1996).

The following formula was used to calculate the VA for each MVIC (Babault et al. 2001):

VA (%) = [1- (superimposed twitch / control twitch)] x 100.

For each participant the highest VA value from the three MVICs was extracted and used for data analysis. Peak torque was determined from the Biodex software output data for each limb of each participant. For data analysis, the peak torque of the three MVICs was used to represent the quadriceps maximal voluntary strength of the limb.

Statistical analysis

Data were analysed for normal distribution using the Shapiro-Wilk test in SPSS for Windows v13.0 (SPSS Inc., Chicago, IL, USA). Differences between limbs in VA and quadriceps maximal voluntary isometric strength (peak torque) and were analysed using paired *t* tests. Correlations between appropriate variables were undertaken using the Pearson product-moment correlation coefficient. For all tests, the level of statistical significance was set at 0.05.

RESULTS

All data for both the injured and uninjured limbs were normally distributed ($p>0.05$). These are shown in Table 2. The paired t test revealed that VA was significantly lower in the injured limb than the uninjured limb (t 2.31, df 16, $p=0.034$) with a mean (95% CI) difference of 9.4 (0.8 to 18.1) %. Peak torque in the injured limb was also significantly lower than the uninjured limb (t 8.71, df 16, $p<0.01$) with a mean (95% CI) difference of 77.8 (58.8 to 96.7) Nm.

No significant relationships were identified for the injured limb between: the time since injury and VA ($r=0.24$, $p=0.36$); time since injury and peak torque ($r= -.05$, $p=0.85$); peak torque and Lysholm ($r=0.07$, $p=0.80$); peak torque and IKDC ($r=0.14$, $p=0.60$); VA and Lysholm ($r= -0.13$, $p= 0.62$); VA and IKDC ($r=0.27$, $p=0.30$). In the uninjured limb the same correlations were not statistically significant (all $p>0.05$).

DISCUSSION

The aim of this study was to evaluate and compare quadriceps VA and maximal voluntary strength in both limbs of people with a unilateral ACL rupture within six months of injury. The results showed that both VA and maximal voluntary strength were significantly lower in the injured limb compared to the uninjured limb.

The statistically significant difference observed in the level of quadriceps VA between the uninjured and injured limbs has not previously been reported in unilateral ACL ruptures within 6 months of injury. Both Chmielewski et al. (2004) and Williams et al. (2005) reported no significant side-to-side differences in their acutely injured samples. These previous studies have classed VA below 95% as voluntary activation failure, and have observed this failure in both limbs of unilateral ACL ruptures. The results of the current study agree with this bilateral failure (if set at the 95% level) but show clear side-to-side differences. The magnitude of the mean difference in our study, of about 9%, is potentially clinically meaningful. Non-significant differences between limbs have also been reported in chronic ACL (Chmielewski et al. 2004; Urbach et al. 1999; Urbach et al. 2001; Urbach & Awiszus 2002; Farquar 2005) while others have observed a significant difference (Newham et al. 1989; Hurley et al. 1992) with lower VA in the injured limb. It is notable that inadequate stimulation could lead to inaccurate twitch interpolation results, as the quadriceps muscle is not being stimulated fully (Behm et al. 1996; Bulow et al. 1993; Norregaard et al. 1997, Hart et al. 2010). This could explain why other studies have not found a significant side-to-side difference in VA in unilateral ACL patients.

When considering the between-limb differences in strength, the mean deficit in strength of 32% observed in the current study is larger than those reported in previous studies in ACL injuries: Hurley (1992) 20%, Urbach (1999) 20%, Williams (2005) 26%, and Chmielewski (2004) 13%. Indeed others have not observed a significant difference (Urbach 2001, Urbach 2002). The contrasting findings above

could potentially be due to differences in the time since injury, or methodologies used, or could also just be sampling variability.

The novel results of this study, of significant side-to-side differences in the levels of VA, have potential implications for clinical practice. The results indicate that both inhibition and strength deficits occur at this early stage and should be addressed early in the rehabilitation process, and with appropriate techniques. This level of VA deficit in the injured limb may inhibit recovery using voluntary exercises (Hart et al. 2010), and other techniques such as electrical stimulation may be needed. Indeed Hurley et al. (1992) showed that quadriceps exercises did not improve VA in ACL ruptures. In clinical settings without complex equipment it may be acceptable to use the non-injured limb strength as a target. However the findings from this study must be interpreted with some caution because it has been documented that the levels of VA observed from healthy populations can vary from 73% to 99% and the mean activation in this study in the injured limb was 76%, which falls within the levels observed in healthy populations. However, this study has utilised a sound methodology derived from extensive review of the literature (Bulow et al. 1993; Gandevia et al. 1998; Hurley et al. 1992; Newman et al. 2003;Norregaard et al. 1997; Urbach et al. 1999; Urbach et al. 2001) and expert opinion – including the use of a un-potentiated twitch to measure resting twitch height; the use of higher levels of stimulation than typically reported in the literature (typically between 180 and 350 mA in this study); and the use of large surface area stimulation pads. No other studies have used a combination of these methodologies.

The variation of levels of VA reported in previous studies may be the result of methodological differences in the elicitation and measurement of the stimulated twitch (Hart et al.2010). This issue is sometimes also compounded by inadequate reporting of methods of determining VA. There is currently no "gold standard" to use in comparing the validity and reliability of VA estimates. Direct nerve stimulation is required to evoke maximum force in all non-activated muscle fibres during an MVC however this method causes intolerable discomfort to participants and possible injury. Therefore percutaneous muscle stimulation was used in the current study as in others (Behm et al. 1996; Hurley et al, 1992). A limitation of this method is that it can activate only those muscle fibres in the vicinity of the electrodes. However, in

preliminary experiments, the size and location of the stimulating electrodes needed to generate the highest possible knee extension torque were determined by applying a twitch of a given intensity. Some studies have used stimulation under 100 mA which can be inadequate for this technique (Behm et al. 1996, Hart et al. 2010). In the current study levels were between 180 and 350 mA.

There are two methods of determining VA: that used in the current study ITT = (1 − superimposed stimulus torque / resting stimulus torque) × 100, and the central activation ratio (CAR) method. Krishnan and Williams (2010) demonstrated that activation estimates obtained in normal subjects with the ITT-based percent activation and CAR methods are significantly different in terms of magnitude, however the estimates are strongly associated. Furthermore Kean et al. (2010) observed excellent test-retest reliability of quadriceps VA measures in patients with knee OA with the ITT method. The current study used the ITT approach in order to compare the data obtained with the results of historical studies (Hurley 1992, Newham 1989, Urbach 1999, Urbach 2001, Urbach 2002) in which voluntary muscle activation was estimated using this approach. However other studies have used the CAR method (Chmielewski 2004, Farquar 2005, Williams 2002).

This study was limited by a small sample size and therefore the results should be interpreted with some caution. Nevertheless the sample size is similar to that of previous studies, such as 10 in Hurley et al. (1992), and indeed the majority of studies in this area have less than 30 participants (Hart et al. 2010). There was also no healthy control group in this study as participants acted as their own control. The results of this study were obtained with the participants in an open chain (non-weight bearing) non-functional position, seated with the knee at 90 degrees and under isometric conditions and all previous studies have used this position. In this regard it must be noted that muscle strength is joint position, speed and contraction type specific. It is currently not possible to determine VA during dynamic functional tasks. An alternative isometric test could have been performed in a weight bearing position but this presents difficulty in standardisation and maintenance of position during testing.

CONCLUSION

This study demonstrated that in a sample of ACL ruptured participants within six months of injury there is a statistically significant difference in the VA of quadriceps femoris between the injured and uninjured limbs, with lower levels of activation in the injured limb. In addition, there was a significant difference in quadriceps muscle strength, with the injured limb significantly weaker than the uninjured limb. This strength deficit may be attributable to the decrease in VA and unilateral muscle atrophy, and hence the importance of effective strengthening exercises in the early stages of rehabilitation is paramount. These findings suggest that rehabilitation programs for people early after ACL rupture should focus on reducing VA deficits to facilitate improvement of the quadriceps femoris muscle strength in the injured limb to comparable values of the uninjured limb.

This between-limb difference has not previously been observed in ACL ruptures within six months of injury. This may be because previous studies have used inadequate electrical stimulation which may have produced invalid estimates of VA. In future researchers should ensure robust and adequate stimulation methodologies are used when assessing VA.

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Tables

Table 1: Demographic data of study participants (n=17)

	Mean (SD)	Range	
		Lower	upper
Age (years)	30.2 (9.5)	17	45
Height (cm)	176.8 (10.1)	155	195
Time since injury (days)	83 (59)	16	172
IKDC subjective knee score	48.3 (15.4)	25.3	73.6
Lysholm score	54.2 (21.2)	30	91

SD standard deviation

Table 2: Voluntary activation and peak torque (n=17)

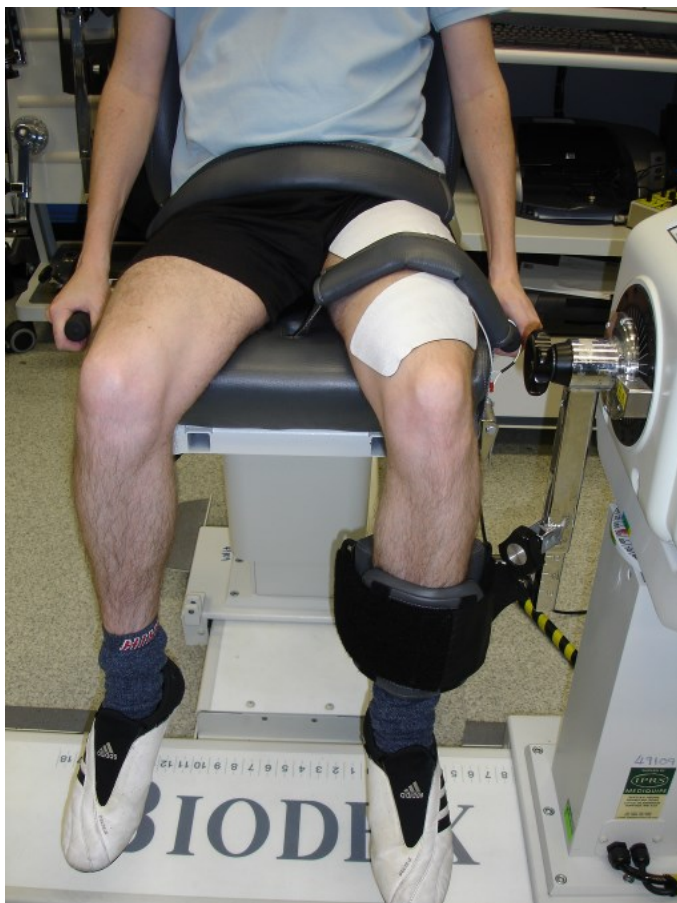|	Mean (SD)	Range	
		Lower	upper
VA injured limb (%)	76.5 (15.0)	36.3	100.0
VA uninjured limb (%)	85.9 (6.7)	70.7	95.3
Peak torque injured limb (Nm)	162.7 (74.1)	47.3	288.3
Peak torque uninjured limb (Nm)	240.5 (81.0)	114.6	380.5

% = percentage voluntary activation

Figure 1: Placement of electrodes for twitch interpolation