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Factors associated with arthrogenous muscle inhibition in patellofemoral osteoarthritis

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SUMMARY

Objectives: Arthrogenous muscle inhibition (AMI) is thought to contribute to quadriceps weakness in knee osteoarthritis (OA), but its relationship with structural changes of bone marrow lesions (BMLs), capsular distension and pain is unclear. This study's objective was to investigate the factors associated with AMI in subjects with symptomatic patellofemoral joint OA (PFJOA).

Design: 126 Subjects with predominant PFJOA were assessed for pain by the visual analogue scale (VAS) for a nominated aggravating activity. Their more symptomatic knee underwent a magnetic resonance imaging (MRI) scan which was used to assess BMLs and synovitis which were scored using the Whole Organ MRI score (WORMS). Quadriceps AMI was measured by calculating the activation deficit and quadriceps strength assessed by isometric maximum voluntary contraction. Multiple linear regressions were used to assess factors associated with AMI.

Results: We studied 124 subjects [mean age 55.5 (SD 7.5); 57.14% female]. In regression analyses, higher levels of AMI were significantly associated with more severe knee pain and with lower BML score.

Conclusion: Quadriceps AMI in knee OA is associated with severity of knee pain and surprisingly with lower BML scores.

Introduction

In patients with knee osteoarthritis (OA), quadriceps weakness is a common clinical feature which is considered to be an important determinant of disability and is probably due, in part, to arthrogenous muscle inhibition (AMI)[1,2]. Modulated by both presynaptic and postsynaptic mechanisms, AMI is a reflex inhibition thought to be elicited by abnormal afferents from a damaged joint resulting in decreased motor drive to muscles and limiting a muscle's potential to generate force[1].

Studies on AMI have found it exists in knee OA[1–6], in knees with effusion and pain[7], post knee trauma[8], and just prior to total knee arthroplasty for OA[9]. While triggers for AMI are not fully understood, causative factors could be pain[3,6] and structural changes to articular cartilage[5]. Intriguingly, AMI has been found in knee OA without pain or effusion, indicating that its causes might be complex[1]. To our knowledge, there have been no studies in knee OA examining whether pain severity is related to AMI. Furthermore, we are aware of no studies assessing whether AMI is related to structural lesions that can be detected by magnetic resonance imaging (MRI) assessments, even though a number of lesions in OA occur in innervated structures whose pathology might be expected to affect AMI.

The structures seen on MRI implicated in the genesis of painful knee OA in cross-sectional and longitudinal studies are bone marrow lesions (BMLs)[10,11] and capsular distension/synovitis[12]. BMLs reflect areas of bone trauma caused by increased stress; bone is richly innervated, in contrast to aneural hyaline cartilage. BMLs are common in moderate to severe OA and may reflect a marker of the severity of OA pathology. Their role in AMI is unknown.

Capsular distension consists of the combination of synovitis and effusion, both of which are frequently present in OA and correlate with pain and other clinical outcomes[13]. A recent study used clinical examination to detect and score knee effusions subsequent to acute anterior cruciate ligament (ACL) injury but found no

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association between the size of an effusion and AMI[14]. To date capsular distension on MRIs has not been assessed for this purpose.

The aim of this study was to assess the relationships between AMI, pain and structural changes of BMLs and capsular distension on MRI in persons with predominantly patellofemoral joint OA (PFJOA).

The hypothesis was that quadriceps AMI would be significantly associated with knee pain severity and structural changes. Since AMI underlies much of the weakness that affects people with knee OA, identifying factors associated with AMI may offer a glimpse into factors that may alter muscle weakness and its consequences in OA.

Methods

The study was approved by the Central Manchester Local Research Ethics Committee (LREC) and Wellcome Trust Clinical Research Facility, Scientific Advisory Board. Scans and other measures were performed at the Wellcome Trust CRF, Manchester, UK.

Subjects

Participants were recruited from local primary care centres, hospital based orthopaedic, rheumatology and physiotherapy clinics. All participants were part of a larger randomized clinical trial testing patellofemoral bracing International Standard Randomised Controlled Trial Number (ISRCTN) (50380458) with a projected sample size of 120. The present study constitutes a secondary analysis of data collected during that study.

Inclusion criteria

Subjects were included if they were aged between 40 and 70 years, had a Kellgren–Lawrence (K–L) score grade 2 or 3 in the patellofemoral joint (PFJ) greater than the K–L score for the tibiofemoral joint (TFJ) of the same knee[15]. Subjects had to have PFJ symptoms such as pain reproduced with stair climbing, kneeling, prolonged sitting or squatting and lateral or medial patellar facet tenderness on palpation or a positive patellar compression test. Pain must have been present daily for the previous 3 months and above a score of 4 on the visual analogue scale (VAS) for their nominated aggravating activity.

Exclusion criteria

Subjects were excluded if the predominant symptoms emanated clinically from the TFJ, from meniscal or ligament injury, if they had rheumatoid arthritis or other forms of inflammatory arthritis or if they had an intra-articular steroid injection into the painful knee in the previous month. Because we obtained contrast enhanced (CE) MRI during this study, patients were excluded if they had a cochlear implant, metal objects in the body including a joint prosthesis, a cardiac or neural pacemaker, a hydrocephalus shunt, an intrauterine contraceptive device or coil, if they had impaired renal dysfunction or were undergoing renal dialysis.

AMI evaluation

Quadriceps inhibition measurements were performed prior to MRIs. Isometric single joint extension torque of the lower limb was measured using an isokinetic dynamometer (Isocom, Isokinetic Technology, Bingham Industrial Estate, Nottingham, UK). For percutaneous stimulation of the quadriceps, a High Voltage Stimulator was used (DS7AH Digitimer Ltd., Hertfordshire, England). We used a single twitch with a pulse duration of 200 ms and a stimulus amplitude of 100 mA. Patients were seated with the hip and knee at 90° flexion and with torso, hip, and thigh straps applied. The tibial pad of the lever arm was placed just proximal to the lateral malleolus. Two electrodes (100 × 130 mm, Axelgaard Co Ltd., Fallbrook, CA, USA) were placed at one-third and two-thirds from the distance between the anterior superior iliac spine and the upper border of the patella over the muscle bellies of vastus lateralis and vastus medialis respectively. Prior to data collection, familiarisation of the stimulation sensation was made with several test stimuli at approximately 50% of the maximum voluntary contraction (MVC) which also confirmed correct electrode placement. After a 5 min rest period, the single twitch was triggered by the assessor manually on the relaxed muscles prior to the MVC (resting twitch torque − RTT)[16]. The subject contracted the quadriceps maximally for the MVC during which another single twitch was delivered to the muscle when voluntary force reached a plateau on the screen (interpolated twitch torque − ITT). Each MVC attempt lasted 4–5 s with a rest of 2 min between each attempt with standardised verbal encouragement and visual feedback from the monitor; they were asked to grasp the chair handles. Three trials were done and the data collected were the maximal single peak torque value with twitch interpolation and also the activation deficit (AD) levels at 100% MVC. AD was calculated from the ratio: AD = (ITT/RTT) × 100. This technique has been assessed for reliability in our facility and has an Intraclass correlation coefficient ($ICC_{2,1}$) 0.73, standard error of measurement (SEM) = 3.26% and smallest detectable difference (SDD) = 9.03%[17]. All measurements were taken by an assessor (MJC) who was blinded to the MRI results (Fig. 1).

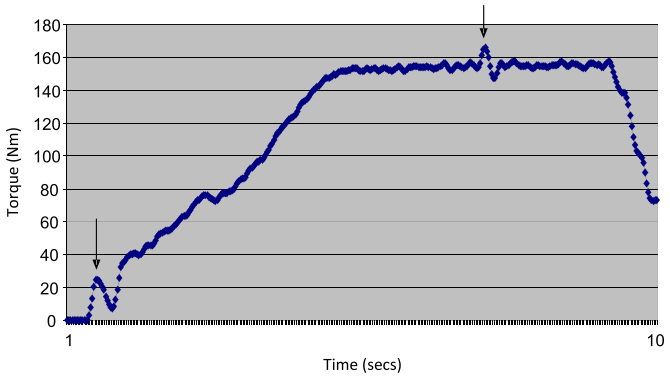

Fig. 1. Diagram of resting twitch (first arrow) and superimposed twitch (second arrow).

MRI methods for BMLs and capsular distension

Subjects had CE MRIs of their more symptomatic knee using a 1.5 T Philips Gyroscan ACS NT (Philips, Best, NL). The imaging protocol included sagittal spin-echo proton density- and T2-weighted images [repetition time (TR), 2200 ms; time to echo (TE), 20/80 ms] with a slice thickness of 3 mm, a 1 mm interslice gap, 1 excitation, a field of view (FOV) of 11–12 cm, and a matrix of 256 × 192 pixels; and coronal and axial spin-echo fat-suppressed proton density- and T2-weighted images (TR 2200 ms; TE 20/80 ms) with a slice thickness of 3 mm, a 1 mm interslice gap, 1 excitation and with the same FOV and matrix.

Intravenous gadolinium (Doteram, Gadoteric Acid, Guerbet Ltd., Solihull, UK) was administered at a dose of 0.2 ml (0.1 mmol) kg body weight. Two minutes after completing the injection of the gadolinium, sagittal sequences were obtained immediately followed by the axial sequences.

BMLs were assessed by the Whole Organ MRI score (WORMS)[18] i.e., BMLs in the subarticular marrow were defined as poorly marginated areas of increased signal intensity in the normally

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