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Alterations in peripheral joint muscle force control in adults with musculoskeletal disease, injury, surgery, or arthroplasty: A systematic review and meta-analysis

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ABSTRACT

Purpose: To systematically review and analyse whether musculoskeletal conditions affect peripheral joint muscle force control (i.e. magnitude and/or complexity of force fluctuations).

Methods: A literature search was conducted using MEDLINE, CINAHL and SPORTDiscus databases (from inception-8th April 2021) for studies involving: 1) participants with musculoskeletal disease, injury, surgery, or arthroplasty in the peripheral joints of the upper/lower limb; 2) comparison with an unaffected control group or unaffected contralateral limb; and 3) measures of the magnitude and/or complexity of force fluctuations during targeted isometric contractions. The methodological quality of studies was evaluated using a modified Downs and Black Quality Index. Studies were combined using the standardized mean difference (SMD) in a random-effects model.

Results: 14 studies (investigating 694 participants) were included in the *meta*-analysis. There was a significant effect of musculoskeletal conditions on peripheral joint muscle force coefficient of variation (CV; SMD = 0.19 [95 % CI 0.06, 0.32]), whereby individuals with musculoskeletal conditions exhibited greater CV than controls. Subgroup analyses revealed that CV was only greater: 1) when comparison was made between symptomatic and asymptomatic individuals (rather than between affected and contralateral limbs; SMD = 0.22 [95 % CI 0.07, 0.38]); 2) for conditions of the knee (SMD = 0.29 [95 % CI 0.14, 0.44]); and 3) for ACL injury post-surgery (SMD = 0.56 [95 % CI 0.36, 0.75]).

Conclusion: Musculoskeletal conditions result in an increase in peripheral joint muscle force CV, with this effect dependent on study design, peripheral joint, and surgical status. The greater force CV is indicative of decreased force steadiness and could have implications for long-term tissue health/day-to-day function.

1. Introduction

Musculoskeletal conditions affect the bones, joints, and muscles of the locomotor system in a way that results in impairments, functional limitations, and disability (WHO, 2021). Musculoskeletal conditions have a variety of aetiologies including disease, injury (trauma, gradual-onset), and surgery (WHO, 2021). For example, musculoskeletal conditions such as osteoarthritis (OA) (Kim et al., 2014; Oh et al., 2011) and anterior cruciate ligament (ACL) rupture (Granan et al., 2009) are highly prevalent conditions that contribute significantly to the global burden of musculoskeletal conditions (Chen et al., 2005; Hootman et al., 2007). Peripheral joint musculoskeletal conditions (henceforth termed peripheral musculoskeletal conditions) have a significant impact on motor function (Clynes et al., 2019), mental health (Mason et al., 2002), quality of life (Woolf, 2015), social independence (Ciolac and Rodrigues-da-Silva, 2016), and incur significant healthcare costs (Salmon et al., 2016). Some peripheral musculoskeletal conditions may be self-limiting, while others may require surgery to reduce pain and restore function (Gossec et al., 2005; Hovelius and Rahme, 2016; Nielsen et al., 2017; Reijman et al., 2021). Although surgeries such as joint arthroplasty and ligament reconstruction may reduce pain and improve a joint's mechanical function, not all aspects of neuromuscular function are fully restored. Residual suboptimal neuromuscular function is postulated to lead to altered local and remote tissue loading (Smith et al., 2019), with potential long-term consequences including symptomatic relapse, disease progression, and/or re-injury (Fulton et al.,

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2014). An understanding of how peripheral musculoskeletal conditions affect neuromuscular function could inform the design of better rehabilitation programmes to optimize long-term outcomes.

Both maximal and submaximal neuromuscular functions are negatively altered in peripheral musculoskeletal conditions. Persistently impaired peripheral joint maximal force-generating capacity and/or rate of force development have been observed after the onset of OA (Friesenbichler et al., 2018), shoulder dislocation (Edouard et al., 2011), ACL reconstruction (Piussi et al., 2020), and arthroplasty (Frost et al., 2006). In addition, muscle force control, which is quantified according to the inherent fluctuations in muscle force output when attempting to maintain forces at a submaximal target (Enoka et al., 2003; Oomen and van Dieen, 2017), has been reported to be affected by the onset of OA (Hortobágyi et al., 2004), shoulder instability (Saccol et al., 2014), and ACL reconstruction (Goetschius and Hart, 2016). Originally regarded as unwanted noise, the fluctuations in submaximal muscle force output are now of special interest to researchers and clinicians because they are regarded as providing a unique insight into the neural mechanisms underlying peripheral joint motor control strategies (Nagamori et al., 2021), and have been demonstrated to explain significant variance in the performance of activities of daily living (Davis et al., 2020; Feeney et al., 2018; Mani et al., 2018). Given that most activities of daily living do not routinely require maximal force, the ability to control submaximal force may be more reflective of an individual's day-to-day mechanical requirement than maximal neuromuscular measures (Kern et al., 2001).

Muscle force control is typically assessed during submaximal isometric contractions at an imposed target (Enoka et al., 2003; Oomen and van Dieen, 2017). Fluctuations in muscle force are most frequently quantified using traditional linear, magnitude-based measures, such as the standard deviation (SD) and coefficient of variation (CV) (Enoka et al., 2003; Oomen and van Dieen, 2017). These linear measures quantify the degree of deviation from a fixed point within a time-series (Slifkin and Newell, 1999) and provide an index of force steadiness, with greater values indicating decreased steadiness. The CV (representing the SD normalised to the mean force) is strongly associated with the variance in common synaptic input to motor neurons, which has been postulated to be the main determinant of muscle force control (Farina and Negro, 2015). Advances in non-linear analytical techniques have led to the recognition that fluctuations in muscle force also possess a statistically irregular temporal structure, or *complexity* (Slifkin and Newell, 1999). Complexity measures are derived from the field of non-linear dynamics and quantify the apparent regularity or randomness of a time-series (e.g. entropy statistics) (Pincus, 1991; Richman and Moorman, 2000) and the long-range fractal correlations present in a time-series (e.g. detrended fluctuation analysis) (Peng et al., 1994). Importantly, these are properties that linear, magnitude-based measures cannot quantify (Goldberger et al., 2002). Complexity reflects the ability to adapt force output rapidly and accurately in response to task demands (Vaillancourt and Newell, 2003). Due to the different information provided by linear (i.e. force steadiness) and non-linear (i.e. force complexity/adaptability) measures, it is recommended that the use of *both* types of measure is necessary to fully evaluate and characterise muscle force control (Goldberger et al., 2002; Pethick et al., 2021a; Clark and Pethick, 2022).

The causes of impaired muscle force control in peripheral musculoskeletal conditions may be attributed to alterations at multiple levels of the sensorimotor system – from disruption of mechanoreceptors (proprioceptors) in ligament ruptures and reconstructive surgery (Bonfim et al., 2003; Ingersoll et al., 2008), to reorganisation in the motor cortex and other cortical areas (Ward et al., 2015), to alterations in efferent outputs such as motor unit discharge rate (Ling et al., 2007). Regardless of the cause, any impairment in muscle force control induced by peripheral musculoskeletal conditions could have important implications for tissue health and day-to-day function. From a tissue health perspective, the inability to 'fine-tune' muscle force control is thought to contribute to excessive tissue loading (Wakeling et al., 2001), which may contribute to the onset and progression of injury. From a functional perspective, impairments in muscle force control have important implications for the performance of activities of daily living (Enoka and Farina, 2021). For example, poor force control may reduce the capacity to counteract a mechanical perturbation (Hepple and Rice, 2016; Peng et al., 2009) and, in healthy adults, is correlated with poorer performance in tasks of manual dexterity (Feeney et al., 2018), balance (Davis et al., 2020), and locomotion (Mani et al., 2018).

Impaired muscle force steadiness has been reported in different peripheral joints and as a result of different conditions. For example, increased CV during maximal knee extension in ACL injury (Goetschius and Hart, 2016), increased SD during knee extension at targets of 50 and 100 N in knee osteoarthritis (Hortobágyi et al., 2004) and increased CV during internal and external shoulder rotation at a target of 35 % maximal voluntary contraction (MVC) in superior labrum anterior-posterior (SLAP) lesions (Saccol et al., 2014) have all been observed in comparison to healthy controls. There is, however, conflicting evidence with several studies investigating the knee and shoulder finding no difference in force control as a result of peripheral musculoskeletal conditions. Several factors may account for differences in outcomes between studies, including whether comparison was made with an unaffected control group or the unaffected contralateral limb, and the peripheral joint and condition tested. No studies to date have systematically synthesized the literature on the effect of peripheral musculoskeletal conditions on muscle force control measures (i.e. force steadiness and complexity). Hence, this *meta*-analysis aimed to determine whether musculoskeletal disease, injury, surgery, and arthroplasty affect peripheral joint muscle force control. In doing this, we addressed the following research questions using the patient (P), intervention (I), comparison (C), and outcome (O) framework (Amir-Behghadami and Janati, 2020). In the present review, intervention (I) was defined as the muscle force control measurement procedure (rather than treatment procedure), and comparison (C) was the control unaffected person or limb:

Primary analysis:

1. Do adults with musculoskeletal disease, injury, surgery, and arthroplasty (P), when compared with an asymptomatic person or limb (C), demonstrate significantly different muscle force control (O)?

Secondary (subgroup) analysis:

2. Does comparison of the symptomatic limb with the unaffected contralateral limb or an unaffected control group influence results?

3. Are musculoskeletal disease, injury, surgery, and arthroplasty-related changes in muscle force control peripheral joint/condition specific?

4. Does surgical status (i.e. pre- vs post-surgery) influence peripheral joint muscle force control?

2. Methods

This systematic review and *meta*-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and meta-analyses (PRISMA) guidelines (PRISMA, 2020). The protocol was prospectively registered on PROSPERO (CRD42021246393).

2.1. Search strategy-

A systematic search of the MEDLINE, CINAHL, and SPORTDiscus databases was performed from inception to 8th April 2021. The search strategy used combinations of pre-defined key terms: (muscle force OR torque) AND (control OR variab* OR steadiness OR modulat* OR fluctuat* OR complexity OR entropy OR fractal) AND (standard deviation OR coefficient of variation OR approximate entropy OR sample entropy OR detrended fluctuation analysis) AND (injury OR musculoskeletal injury OR trauma OR surgery OR arthroplasty OR joint replacement) AND (wrist OR forearm OR elbow OR upper arm OR shoulder OR hip OR

thigh OR knee OR ankle OR foot). Grey literature sources (e.g. conference proceedings) were also considered if a full-text was available.

Titles and abstracts identified in the database search were downloaded into EndNote X9 (Clarivate Analytics, Philadelphia, USA). All titles and abstracts were screened independently by two of the research team members (JP and BL). Full texts were obtained for those meeting the inclusion criteria (see below). The reference lists of included papers were also manually searched for additional studies not retrieved by the database search.

2.2. Eligibility criteria

Criteria for studies to be included were based in part on the PICO criteria (Amir-Behghadami and Janati, 2020): 1) involving participants with clinically diagnosed musculoskeletal disease, injury, surgery, or arthroplasty in the peripheral joints of the upper or lower limb (P and I); 2) involving comparison with an unaffected control group or unaffected contralateral limb (C); 3) featuring a measure of the magnitude of force variability (e.g. SD, CV) and/or the complexity of force output (e.g. entropic or fractal scaling measures) during a targeted isometric muscle contraction (O); 4) published in English as a full-text article in a peer-reviewed journal. All types of observational studies using quantitative methods were eligible for inclusion (i.e. cohort, case-control, cross-sectional, longitudinal). Exclusion criteria were: 1) studies with individuals under the age of 18; 2) studies which focused on disease, injury, surgery, or arthroplasty and force control in the spine; 3) case studies of individuals.

2.3. Data extraction

Data were extracted by one member of the research team (JP) from selected articles and entered into a custom Microsoft Excel spreadsheet. Extracted data included: 1) authors; 2) year of publication; 3) musculoskeletal disease, injury, surgery, or arthroplasty condition investigated; 4) whether comparison was made with an unaffected control group or unaffected contralateral limb; 5) task performed (e.g. joint, joint angle, muscle group, movement [extension, flexion, abduction, adduction, internal rotation, external rotation] and contraction intensity); 6) experimental and control group sample size; 7) force control measure used as a study outcome (e.g. SD, CV, entropy statistics, detrended fluctuation analysis); 8) mean and SD of the force control measure. See Table 1 for further details of the extracted data. Where data were not clearly or completely reported, article corresponding authors were contacted (with further co-authors contacted if there was no response), and additional data requested. In cases in which authors did not respond, their data was not considered for the *meta*-analysis.

2.4. Quality assessment

The methodological quality of the included studies was assessed using a modified Downs and Black Quality Index (Downs and Black, 1998; Hall et al., 2013). The modified version of the Downs and Black Quality Index is scored out of 16 (Hall et al., 2013), with higher scores indicating higher quality studies. There are 15 questions, 14 of which can either be scored 0 (indicating no) or 1 (indicating yes). The remaining question (5) can be answered 0 (no), 1 (partially), or 2 (yes). Studies with scores ≥ 10 were considered to be high quality and studies with scores < 10 were considered to be low quality. All studies were assessed independently by two of the research team members (JP and BL). Any disagreements were resolved by a consensus discussion between these two reviewers. The third member of the research team (NC) was available if needed but was not required. Inter-rater agreement in the scoring of 15 questions was calculated using the Gwet AC1 coefficient (Gwet, 2008).

2.5. Statistical analysis

Data pooling was performed irrespective of the risk of bias score (Hall et al., 2013) to increase the number of studies eligible for data pooling. The following subgroup analyses were undertaken: 1) study designs – between- (comparing symptomatic limb against a healthy unaffected control group) and within-subject designs (comparing symptomatic limb against an unaffected contralateral limb); 2) anatomical region – shoulder, knee, others; and 3) surgical status – pre-surgery vs post-surgery.

The *meta*-analysis was performed using the *"meta"* package (v. 4.15–1) (Balduzzi et al., 2019) within R software (v 4.0.3). Data pooling was performed in Cochrane Review Manager (v. 5.3), using the standardized mean difference (SMD) in a random-effects model. Reported SMD (95 % CI) were categorised as small (<0.60), medium (0.60 to < 1.20) or large (≥1.20) (Hall et al., 2013), with statistical significance set at $p < 0.05$. Heterogeneity between studies was assessed using the I^2 test. Thresholds for the interpretation of I^2 were determined as follows: 1) not important (<40 %), 2) moderate heterogeneity (30 % to 60 %), 3) substantial heterogeneity (50 % to 90 %), 4) considerable heterogeneity (75 % to 100 %) (Higgins, 2011). Parameters that were not pooled were qualitatively synthesised.

3. Results

3.1. Search results

The initial search yielded 18,613 results. The PRISMA flow diagram illustrating the number of studies excluded at each stage is shown in Fig. 1. In total, 16 studies met the inclusion criteria, though two of these did not contain sufficient data to be included in the quantitative analysis (with the necessary data not available in either the original paper or from the authors). Thus, 14 studies were included in the *meta*-analysis.

3.2. Characteristics of included studies

The 14 included studies involved a total of 694 participants (382 male, 312 female), 358 (195 male, 163 female) of whom were patients (i.e. experiencing peripheral musculoskeletal conditions). Of the 14 included studies, eight studies investigated peripheral musculoskeletal conditions and force control in the knee (n = 217 patients) (Goetschius and Hart, 2016; Goetschius et al., 2015; Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017), five investigated the shoulder (n = 122 patients) (Camargo et al., 2009; Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013), and one investigated the elbow (n = 19 patients) (Mista et al., 2018). Of the studies on the knee, six investigated ACL injuries (n = 177 patients) (Goetschius and Hart, 2016; Goetschius et al., 2015; Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017) and two investigated OA (n = 40 patients), tibiofemoral in one case (Hortobágyi et al., 2004) and unspecified in the other (Mau-Moeller et al., 2017);. In the studies investigating ACL injury, four examined patients after ACL reconstruction (n = 132 patients) (Goetschius and Hart, 2016; Goetschius et al., 2015; Niederer et al., 2020; Spencer et al. 2020) and two examined patients pre-surgery (n = 45 patients) (Skurvydas et al., 2011; Zult et al., 2017). Of the studies on the shoulder, four investigated shoulder impingement (n = 102 patients) (Camargo et al., 2009; Overbeek et al., 2020; Zanca et al., 2010; Zanca et al., 2013) and one investigated SLAP lesions (n = 20 patients) (Saccol et al., 2014). The study on the elbow investigated chronic elbow pain (n = 19 patients) (Mista et al., 2018). All of the studies investigating surgical status focused on ACL injury (Goetschius and Hart, 2016; Goetschius et al., 2015; Niederer et al., 2020; Spencer et al., 2020; Zult et al., 2017). The studies on other anatomical regions either failed to report the surgical status of participants (Hortobágyi et al., 2004; Mista et al., 2018) or reported that prior

Table 1
Details of included studies. MVC = maximal voluntary contractions; SD = standard deviation; CV = coefficient of variation; ACL = anterior cruciate ligament; SLAP = superior labrum anterior-posterior lesions.

Study	Patient population	Control population	Study design	Peripheral joint and condition	Force control task and contraction intensity	Force control measure	Results
Camargo et al. (2009)	27 subjects (18 M, 9F; 33.5 ± 9.9 years, 77.5 ± 14.8 kg, 1.74 ± 0.10 m)	23 healthy, active subjects (15 M, 8F, 32.3 ± 9.0 years, 75.5 ± 13.0 kg, 1.73 ± 0.08 m)	Between groups	Shoulder, unilateral impingement syndrome	Isometric shoulder abduction (scapular plane, neutral rotation, 80° abduction with elbow in full extension); 35 % MVC	SD	No significant difference between patients and controls for SD and CV ($P > 0.05$)
Goetschius and Hart (2016)	53 subjects (27 M, 26F, 23.4 ± 4.9 years, 74.6 ± 14.8 kg, 1.7 ± 0.1 m)	50 healthy subjects (28 M, 22F, 23.3 ± 4.4 years, 67.4 ± 13.2 kg, 1.7 ± 0.1 m)	Between groups	Knee; anterior cruciate ligament (ACL) reconstruction (graft type not specified; surgery>6 months prior to testing)	Isometric knee extension (85° hip flexion, 90° knee flexion); 100 % MVC	CV	Significantly greater CV in ACL reconstruction patients compared to controls ($P = 0.001$)
Goetschius et al. (2015)	32 subjects (18 M, 14F, 24.1 ± 4.9 years, 73.3 ± 14.8 kg, 1.72 ± 0.12 m)	32 healthy subjects (17 M, 15F, 243 ± 4.0 years, 70.4 ± 13.6 kg, 1.72 ± 0.10 m)	Between groups	Knee; ACL reconstruction (graft type not specified; surgery>6 months prior to testing)	Isometric knee extension (85° hip flexion, 90° knee flexion); 100 % MVC before and after fatiguing protocol (inclined treadmill walking and lateral hopping)	CV	Significantly greater CV in ACL reconstruction patients compared to controls both before ($P = 0.03$) and after ($P = 0.001$) fatiguing protocol
Hortobagyi et al. (2004)	20 subjects (5 M, 15F, 57.5 ± 7.3 years, 86.8 ± 18.3 kg, 1.64 ± 0.09 m)	20 healthy subjects (5 M, 15F, 56.8 ± 5.0 years, 81.2 ± 12.5 kg, 1.67 ± 0.07 m)	Between groups	Knee; osteoarthritis	Isometric knee extension (90° hip flexion, 90° knee flexion); 50 and 100 N	SD	No significant difference between patients and controls for SD ($P > 0.05$). However, significantly greater SD in patients during eccentric and concentric contractions (not analysed in present *meta*-analysis)
Mau-Moeller et al. (2017)	20 subjects (7 M, 13F, 66.7 ± 8.8 years, 91.3 ± 17.4 kg, 1.68 ± 0.10 m)	20 healthy subjects (5 M, 15F, 62.1 ± 6.2 years, 71.5 ± 14.3 kg, 1.67 ± 0.10 m)	Between groups	Knee; osteoarthritis	Isometric knee extension (90° hip flexion, 60-70° knee flexion); 20, 40 and 60 % MVC	SD, CV	Significantly lower SD in patients compared to controls at all contraction intensities (20 %, $P = 0.04$); 40 %, $P = 0.002$; 60 %, $P = 0.005$). No significant difference between patients and controls for CV at any contraction intensity ($P > 0.05$)
Mista et al. (2018)	19 subjects (9 M, 10F, 41 ± 11 years, 70.0 ± 16.4 kg, 1.66 ± 0.02 m)	21 healthy subjects (10 M, 11F, 37 ± 13 years, 68.9 ± 12.5 kg, 1.62 ± 0.08 m)	Between groups	Elbow; chronic pain	Isometric wrist extension (90° shoulder flexion, elbow fully extended); 5, 30, 50 and 70 % MVC	SD	No significant difference between patients and control for SD at any contraction intensity ($P > 0.05$)
Niederer et al. (2020)	19 subjects (9 M, 10F, 25.7 ± 4.2 years, 1.77 ± 0.10 m)	19 healthy subjects (9 M, 10F, 24.8 ± 1.6 years, 1.75 ± 0.09 m)	Between and within groups	Knee; ACL reconstruction with ipsilateral hamstring tendon autograft	Isometric knee extension (60° knee flexion); 100 % MVC before and after fatiguing protocol (10 s contractions at 100 % MVC followed by 5 s rest, until 70 % MVC could no longer be reached)	CV	Significantly lower CV in ACL reconstructed leg compared to contralateral leg ($P < 0.05$)
Overbeek et al. (2020)	40 subjects (17 M, 23F, 50 ± 6.4 years)	30 healthy subjects (13 M, 17F, 51 ± 5.7 years)	Between groups	Shoulder; subacromial pain syndrome	Isometric shoulder abduction and adduction (arm at side in external rotation); 60 % MVC	SD, CV, approximate entropy	Significantly lower SD ($P = 0.013$) and CV ($P = 0.016$) in patients compared to controls during abduction task. Significantly lower approximate entropy in patients compared to controls during both abduction ($P = 0.048$) and adduction ($P = 0.024$) tasks
						SD, CV	

(*continued on next page*)

Table 1 (*continued*)

Study	Patient population	Control population	Study design	Peripheral joint and condition	Force control task and contraction intensity	Force control measure	Results
Saccol et al. (2014)	10 subjects with shoulder instability (all M, 22.3 ± 3.4 years, 83.8 ± 7.7 kg, 1.8 0.05 m); 10 subjects with superior labral anterior posterior (SLAP) lesions (all M, 26.9 ± 4.7 years, 77.4 ± 14.9 kg, 1.7 ± 0.05 m)	10 subjects matched with instability group (all M, 22.0 ± 3.4 years, 82.0 ± 9.2 kg, 1.8 ± 0.08 m); 10 male subjects matched with SLAP group (all M, 26.4 ± 4.5 years, 78.1 ± 8.5 kg, 1.7 ± 0.04 m)	Between groups	Shoulder; instability and SLAP lesions	Isometric shoulder internal and external rotation (90° shoulder abduction, 90° elbow flexion, 90° external rotation); 35 % MVC		Significantly greater CV in SLAP patients compared to controls during internal rotation task ($P = 0.003$). No other significant differences in SD or CV between groups
Skurvydas et al. (2011)	13 subjects (all M, 30.1 ± 9.7 years, 94.4 ± 11.8 kg, 1.84 ± 0.09 m)	Unaffected contralateral leg	Within group	Knee; ACL rupture (no surgery)	Isometric knee extension (measures taken at both 60 and 90° knee flexion) and flexion (measures taken at both 40 and 90° knee flexion); 20 % MVC	CV, permutation entropy	No significant difference in CV between ACL deficient leg and contralateral leg for either knee extension or flexion ($P > 0.05$). Significantly lower permutation entropy in ACL deficient leg compared to contralateral leg during knee extension ($P < 0.05$)
Spencer et al. (2020)	28 subjects (14 M, 14F, 20 ± 5 years, 72.2 ± 10.6 kg, 1.78 ± 0.10 m)	Unaffected contralateral leg	Within group	Knee; ACL reconstruction with bone-patellar tendon-bone autograft	Isometric knee extension (90° hip flexion, 90° knee flexion); 100 % MVC	SD, CV	Significantly greater SD in ACL reconstructed leg compared to contralateral leg ($P < 0.05$). Significantly lower CV in ACL reconstructed leg compared to contralateral leg ($P < 0.01$)
Zanca et al. (2010)	14 subjects (all F, 36.6 ± 5.2 years, 62.6 ± 75 kg, 1.65 ± 0.05 m)	15 subjects (all F, 35.5 ± 5.5 years, 64.9 ± 10.7 kg, 1.65 ± 0.02 m)	Between and within groups	Shoulder; unilateral impingement syndrome	Isometric shoulder medial (scapular plane, 90° shoulder abduction, 90° elbow flexion, 45° lateral rotation) and lateral rotation (scapular plane, 90° shoulder abduction, 90° elbow flexion, 75° lateral rotation); 50 % MVC	SD, CV	No significant differences between patients and control group for any comparison ($P > 0.05$). No significant difference between affected and unaffected limb in patient group ($P > 0.05$)
Zanca et al. (2013)	21 athletes (all M, 22.1 ± 2.7 years, 73.2 ± 12.2 kg, 1.77 ± 0.08 m)	25 asymptomatic athletes (all M, 21.0 ± 2.1 years, 72.7 ± 11.3 kg, 1.76 ± 0.09 m) and 21 non-athletes (all M, 22.2 ± 2.4 years, 78.6 ± 11.8 kg, 1.76 ± 0.06 m)	Between groups	Shoulder; unilateral impingement syndrome	Isometric shoulder internal and external rotation (90° shoulder abduction, 90° external rotation, 90° elbow flexion); 35 % MVC	SD, CV	No significant differences between patients and control groups for any comparison ($P > 0.05$)
Zult et al. (2017)	32 subjects (16 M, 16F, 23 ± 4 years, 77 ± 12 kg, 1.78 ± 0.09 m)	40 subjects (20 M, 20F) subdivided into active (10 M, 10F, 22 ± 2 years, 72 ± 12 kg, 1.78 ± 0.11 m) and less active (10 M, 10F, 22 ± 1 years, 73 ± 17 kg, 1.76 ± 0.10 m) groups	Between and within groups	Knee; unilateral ACL tear	Isometric knee extension (65° knee flexion); 20 % MVC	CV	No significant difference between patients and control groups ($P > 0.05$). No significant difference between ACL deficient leg and contralateral leg ($P > 0.05$)

surgery was one of the exclusion criteria (Camargo et al., 2009; Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013). Seven studies performed a comparison only of a symptomatic group with an unaffected control group, five studies performed a comparison between both a symptomatic group and unaffected control group and also between a symptomatic limb and unaffected contralateral limb, and two studies performed a comparison of only the symptomatic limb with the unaffected contralateral limb. Details of the included studies can be found in Table 1.

3.3. Quality assessment

Inter-rater agreement ranged from 0.53 to 1.00 (Table 2). Quality scores ranged from five to 13. Out of the 14 studies included in the *meta*-analytic component, nine were rated as high-quality (score ≥ 10) (Camargo et al., 2009; Goetschius and Hart, 2016; Goetschius et al., 2015; Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Mista et al., 2018; Niederer et al., 2020; Overbeek et al., 2020; Zult et al., 2017) and five were rated as low-quality (score < 10) (Saccol et al., 2014; Skurvydas et al., 2011; Spencer et al., 2020; Zanca et al., 2010; Zanca et al.,

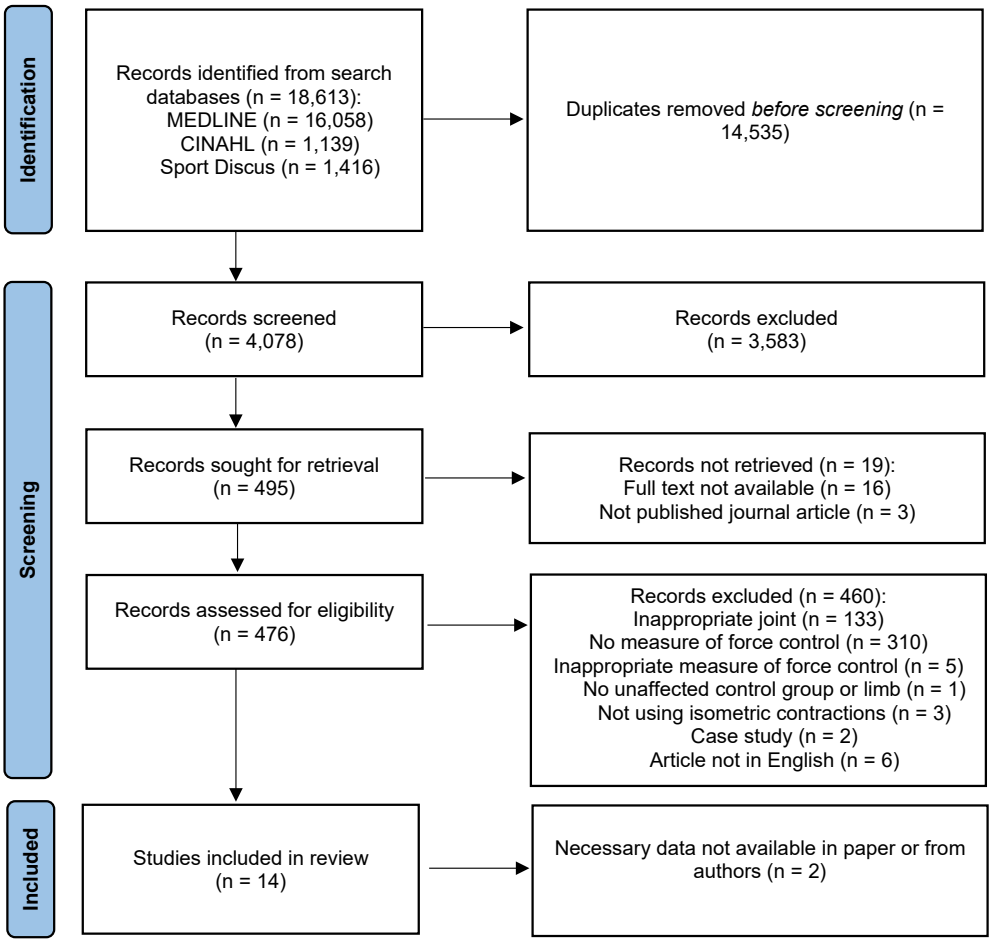

Fig. 1. PRISMA flow diagram illustrating stages of search.

2013). In all low-quality studies, there was a lack of description or consideration of confounding variables.

3.4. Muscle force standard deviation

The results of the *meta*-analysis demonstrated that there was no significant overall effect of peripheral musculoskeletal conditions on the SD of muscle force (SMD = -0.01 [95 % CI −0.26 to 0.24], $I^2 = 74$ %; P < 0.01) (Fig. 2). Nine studies contributed to the first subgroup analysis, investigating the effect of study design (Camargo et al., 2009; Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Mista et al., 2018; Overbeek et al., 2020; Saccol et al., 2014; Spencer et al., 2020; Zanca et al., 2010; Zanca et al., 2013) Eight of those studies compared a symptomatic group and unaffected control group (Camargo et al., 2009; Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Mista et al., 2018; Overbeek et al., 2020; Saccol et al., 2014; Spencer et al., 2020; Zanca et al., 2010; Zanca et al., 2013), while two studies compared a symptomatic limb and unaffected contralateral limb (Spencer et al., 2020; Zanca et al., 2010). There was no significant effect of study design on the effect of peripheral musculoskeletal conditions on the SD of muscle force (Fig. 2). For the second subgroup analysis investigating the effect of peripheral joint, nine studies were included (shoulder: Camargo et al., 2009; Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013; knee: Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Spencer et al., 2020; elbow: Mista et al. 2018). There was no effect of peripheral musculoskeletal conditions on the SD of muscle force in the shoulder region (SMD = 0.03 [95 % CI −0.18 to 0.23], $I^2 = 40$ %; P = 0.03), knee region (SMD = 0.24 [95 % CI −0.47 to 0.94], $I^2 = 87$ %; P < 0.01) or elbow region (SMD = 0.04 [95 % CI −1.27 to 0.35], $I^2 = 92$ %; P < 0.01) (Fig. 3). Only one study utilising the SD was conducted on a peripheral musculoskeletal conditions necessitating surgery and measurements were only taken 6 months after surgery (Spencer et al., 2020). As such, there was insufficient data for the third subgroup analysis investigating surgical status to be conducted.

3.5. Muscle force coefficient of variation

There was a significant overall effect of peripheral musculoskeletal conditions on the CV of muscle force (SMD = 0.19 [95 % CI 0.06 to 0.32], $I^2 = 33$ %; P = 0.02) (Fig. 4), whereby individuals with peripheral musculoskeletal conditions exhibited greater force CV than controls. Twelve studies were included in the first subgroup analysis (between group design; Camargo et al., 2009; Goetschius and Hart, 2016; Goetschius et al., 2015; Mau-Moeller et al., 2017; Niederer et al., 2020; Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013; Zult et al., 2017; within group design: Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zanca et al., 2010; Zult et al., 2017), which revealed a significant effect of study design. Only studies which adopted a between-group design reported a significantly greater force CV in individuals with peripheral musculoskeletal conditions compared to controls (SMD = 0.22 [95 % CI 0.07 to 0.38], $I^2 = 44$ %; P < 0.01) (Fig. 4).

Twelve studies were included in the second subgroup analysis, with all investigating either shoulder conditions (Camargo et al., 2009; Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013) or knee problems (Goetschius and Hart, 2016; Goetschius et al., 2015; Mau-Moeller et al., 2017; Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017). Only conditions in the knee

Table 2
Modified Downs and Black Quality Index results.

Study	1	2	3	5	6	7	10	11	12	15	16	18	20	21	25	Total
Camargo et al. (2009)	1	1	1	1	1	1	0	0	0	0	1	1	1	1	1	11
Goetschius and Hart (2016)	1	1	1	1	1	1	1	0	0	0	1	1	1	1	1	12
Goetschius et al. (2015)	1	1	1	1	1	0	1	0	0	0	1	1	1	1	1	11
Hortobagyi et al. (2004)	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	13
Mau-Moeller et al. (2017)	1	1	1	1	1	1	1	0	0	0	1	1	1	0	0	10
Mista et al. (2018)	1	1	1	1	1	0	1	0	0	0	1	1	1	1	1	11
Niederer et al. (2020)	1	1	1	1	1	0	0	0	0	0	1	1	1	1	1	10
Overbeek et al. (2020)	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	13
Saccol et al. (2014)	1	1	1	0	1	0	1	0	0	0	1	1	1	1	0	9
Skurvydas et al. (2011)	1	1	0	0	1	0	0	0	0	0	1	1	1	0	0	6
Spencer et al. (2020)	1	1	0	0	1	1	0	0	0	0	1	1	1	0	0	7
Zanca et al. (2010)	1	1	0	0	0	0	0	0	0	0	1	0	1	1	0	5
Zanca et al. (2013)	1	1	1	0	1	0	1	0	0	0	1	1	1	1	0	9
Zult et al., (2017)	1	1	1	1	1	1	1	0	0	0	1	1	1	1	1	12
Agreement	1	1	0.765	0.824	0.941	0.647	1	0.529	0.529	1	0.941	0.941	1	0.941	0.706	–

Quality appraisal items:
(1) Clear aim/hypothesis.
(2) Outcome measures clearly described.
(3) Patient characteristics clearly described.
(5) Confounding variables clearly described.
(6) Main findings clearly described.
(7) Measures of random variability described.
(10) Actual probability values described.
(11) Participants asked to participate representative of population.
(12) Participants prepared to participate representative of population.
(15) Blinding of outcome measures.
(16) Analysis completed was planned.
(18) Appropriate statistics.
(20) Valid and reliable outcome measures.
(21) Appropriate case-control matching.
(25) Adjustment made for confounding variables.

region resulted in greater muscle force CV than controls (SMD = 0.29 [95 % CI 0.14 to 0.44], I^2 = 19 %; P = 0.22) (Fig. 5). No difference was observed between individuals with conditions in the shoulder region compared to controls.

Six studies were included in the third subgroup analysis investigating surgical status (pre-surgery: Skurvydas et al., 2011; Zult et al., 2017; post-surgery: Goetschius and Hart, 2016; Goetschius et al., 2015; Niederer et al., 2020; Spencer et al., 2020) with all studies in this subgroup analysis investigating ACL injury. Force CV was greater in the ACL group compared to controls post-surgically (SMD = 0.38 [95 % CI 0.11 to 0.66], I^2 = 0 %; P = 0.85), but not pre-surgically (SMD = 0.08 [95 % CI −0.13 to 0.29], I^2 = 0 %; P = 0.83) (Fig. 6).

3.6. Complexity measures

There was insufficient data for the *meta*-analysis to be conducted on studies involving complexity measures. Only two studies utilising complexity measures met our inclusion criteria, with each using a different metric: one study utilised approximate entropy (Overbeek et al., 2020), while the other utilised permutation entropy (Skurvydas et al., 2011). Overbeek et al. (2020) observed significantly reduced approximate entropy during shoulder abduction and adduction in patients with subacromial pain syndrome compared to healthy controls. Skurvydas et al. (2011) observed significantly reduced permutation entropy in the ACL deficient leg compared to the uninjured contralateral leg during knee extension, but not knee flexion.

4. Discussion

This is the first review to investigate the effect of peripheral musculoskeletal conditions on peripheral joint muscle force control. Pooled data indicate that peripheral musculoskeletal conditions were associated with increased force CV. Subgroup analysis, however, demonstrated that this greater force CV was only evident in studies that compared symptomatic patients with an unaffected control group, in studies that examined the knee, and, with regards to surgical status, patients who had undergone ACL reconstruction. It must be noted, though, that the studies included in this analysis were all of an observational, cross-sectional design and, as such, no direct causal relationship can be established between musculoskeletal conditions and force control.

4.1. Peripheral musculoskeletal conditions and muscle force control

Pooled data analysis indicated that peripheral musculoskeletal conditions had no effect on muscle force SD, a measure of the absolute magnitude of force fluctuations. In contrast, there was an effect on muscle force CV, which provides a measure of the magnitude of force fluctuations normalised to the mean force output. The CV is regarded as the more robust of the two linear (i.e. magnitude-based) measures, as it facilitates comparison between groups of individuals with large differences in strength (Enoka et al., 2003). Importantly, large differences in strength are often evident in patients with peripheral musculoskeletal conditions compared to healthy controls (Edouard et al., 2011; Friesenbichler et al., 2018; Frost et al., 2006; Piussi et al., 2020). Moreover, 10 (Goetschius and Hart, 2016; Goetschius et al., 2015; Hortobágyi et al., 2004; Mau-Moeller et al., 2017; Mista et al., 2018; Niederer et al., 2020; Saccol et al., 2014; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017) of the 14 studies included in the quantitative analysis reported significant differences in maximal force-generating capacity between the symptomatic group and unaffected control group, or between the symptomatic limb and unaffected contralateral limb.

There was a small overall effect of peripheral musculoskeletal conditions on muscle force CV, indicating that peripheral musculoskeletal conditions are associated with poorer force steadiness. The association between peripheral musculoskeletal conditions and force CV is similar

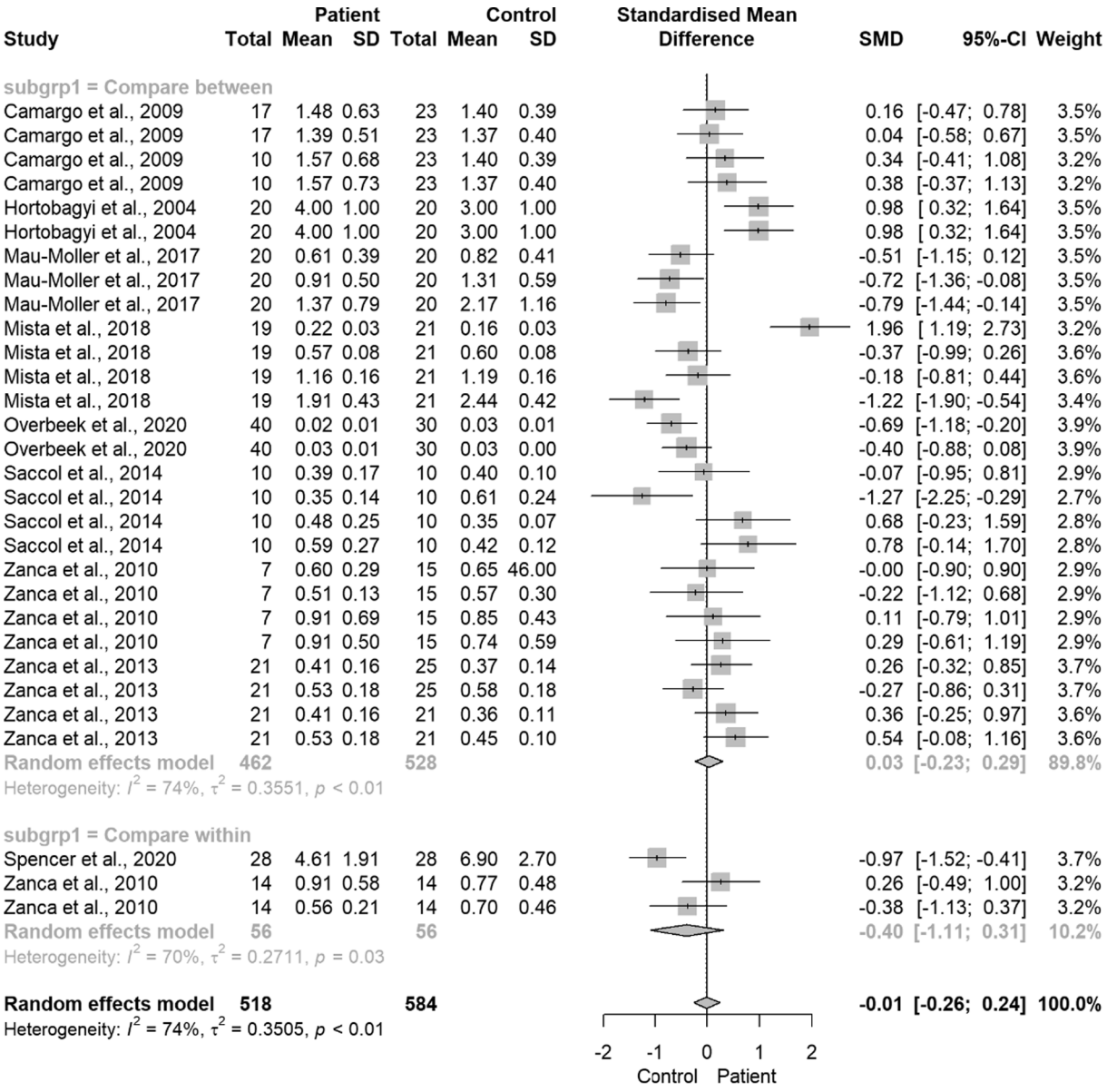

Fig. 2. The overall effect of peripheral musculoskeletal conditions on muscle force SD and the first subgroup analysis investigating the effect of study design on muscle force SD. Standard mean differences (SMD) with 95% confidence intervals. Multiple comparisons within the same study are reflective of either multiple contraction intensities or movements having been performed.

to the effects of aging (Enoka et al., 2003; Oomen and van Dieen, 2017) and neuromuscular fatigue (Castronovo et al., 2015), which are both characterized by decreased force steadiness. A greater magnitude of force fluctuations in healthy adults is indicative of a decreased ability to correct targeting errors and could reduce motor task performance in individuals free from musculoskeletal conditions (e.g. falling over, dropping an object) (Pethick et al., 2021c). Few studies have correlated poorer force control in peripheral musculoskeletal conditions patients with functional performance and more research is warranted. It has been demonstrated, though, that quadriceps and hamstring force steadiness (measured using wavelet-derived mean instantaneous torque frequency) are related to hop velocity and hop distance in ACL patients (Pua et al., 2014.

The qualitative analysis of studies using non-linear measures indicated reduced complexity as a result of peripheral musculoskeletal conditions. It must be stressed, however, that only two studies utilising non-linear measures met our inclusion criteria and quantitative analysis could not be conducted as each study utilised a different complexity metric. Overbeek et al. (2020) observed significantly reduced approximate entropy during shoulder abduction and adduction in patients with subacromial pain syndrome, whilst Skurvydas et al. (2011) observed significantly reduced permutation entropy during knee extension in patients with ACL deficiency. These findings of reduced entropy indicate outputs that are smoother and more regular, suggesting that peripheral musculoskeletal conditions mediate a decreased ability to adapt motor output in response to task demands (Vaillancourt and Newell, 2003). Given that linear and non-linear measures of force fluctuations provide different (and complementary) information and have different functional significance (Goldberger et al., 2002; Slifkin and Newell, 1999), it could be argued that the lack of studies utilising complexity measures represents a limitation to our understanding of how musculoskeletal conditions influence force control.

Any alteration in muscle force control must be a consequence of a change in the ensemble behaviour of the motor unit pool (either motor unit recruitment, firing rates, or both). Previous studies on peripheral musculoskeletal conditions using either intramuscular or high-density

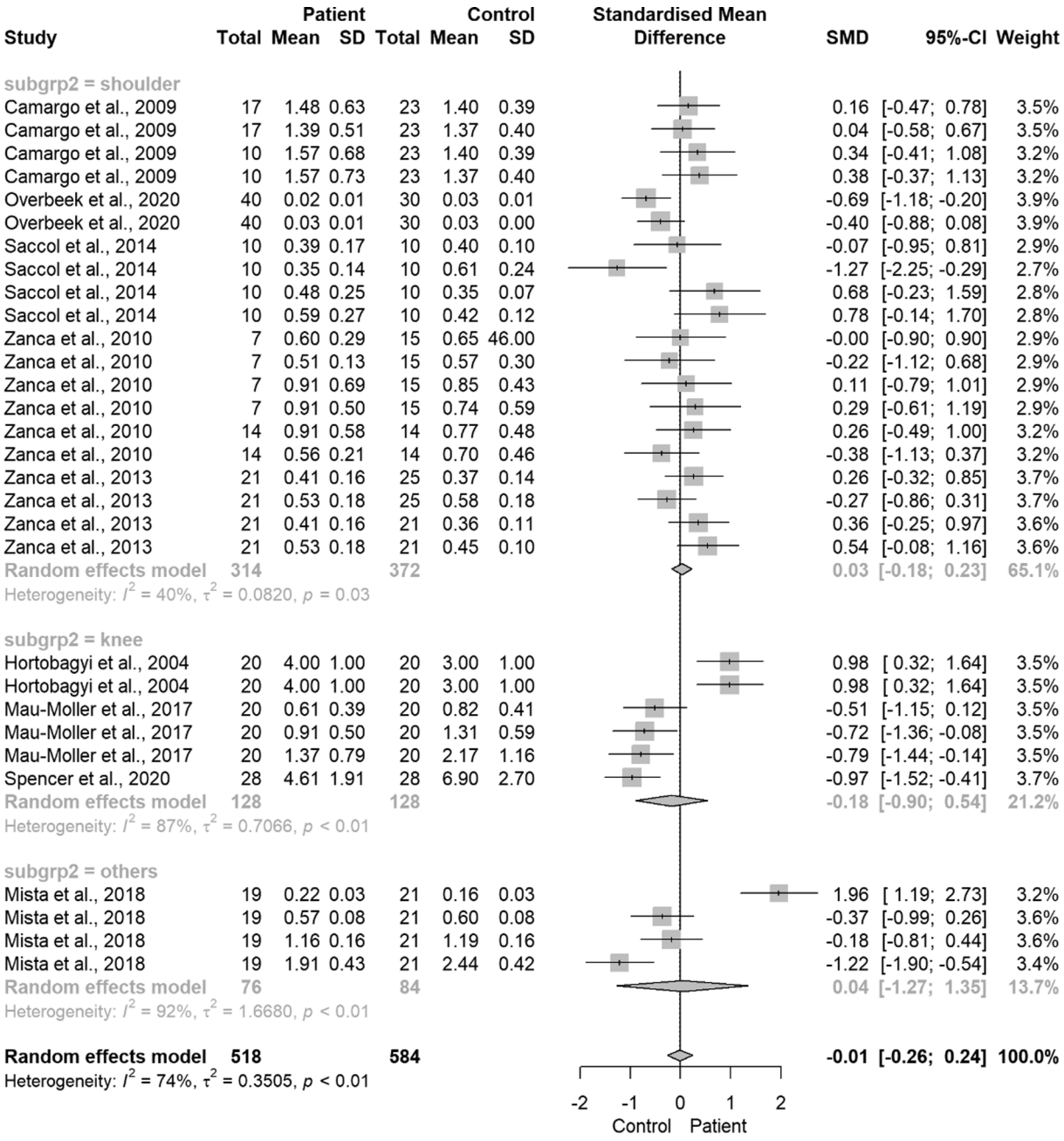

Fig. 3. The second subgroup analysis investigating the effect of peripheral joint on muscle force SD. Standard mean differences (SMD) with 95% confidence intervals. Multiple comparisons within the same study are reflective of either multiple contraction intensities or movements having been performed.

EMG have demonstrated both reduced (Nuccio et al., 2021) and increased (Gallina et al., 2018; Ling et al., 2007) neural drive to muscle compared to healthy controls, with the direction of change dependent on the condition investigated. For example, during submaximal isometric contractions, osteoarthritis has been demonstrated to result in greater motor unit recruitment (Ling et al., 2007) and patellofemoral pain is associated with greater motor unit firing rates (Gallina et al., 2018). In contrast, ACL reconstruction has recently been shown to result in lower motor unit recruitment thresholds and discharge rates compared to controls (Nuccio et al., 2021). Furthermore, the CV of force fluctuations has been demonstrated to be highly coherent with the common component of the cumulative motor unit spike train (Negro et al., 2009), indicating that force control is determined by variance in common noise transmitted to motor neurons (Farina and Negro, 2015). Our observation of an increase in the CV of force fluctuations with musculoskeletal conditions suggests that such conditions may be associated with an increase in the variability of common synaptic input that motor neurons receive. It must be emphasised, though, that the design (i.e. observational, cross-sectional) of the studies included in the *meta*-analysis precludes any attempts to assess causal relationships between musculoskeletal conditions and increasing force CV. Indeed, other factors that accompany the presence of an injury (*inter alia* reduced level of activity and pain) could account for some, or all, of the observed increase in force CV.

Changes in the ensemble behaviour of the motor unit pool are responsible for the increased magnitude of force fluctuations. Motor neurons receive synaptic input from afferent feedback from peripheral joint mechanoreceptors (Conway et al., 1995), descending pathways from the motor cortex (Negro and Farina, 2011), and descending pathways from the reticular formation (Baker, 2011). Motor neuron inputs

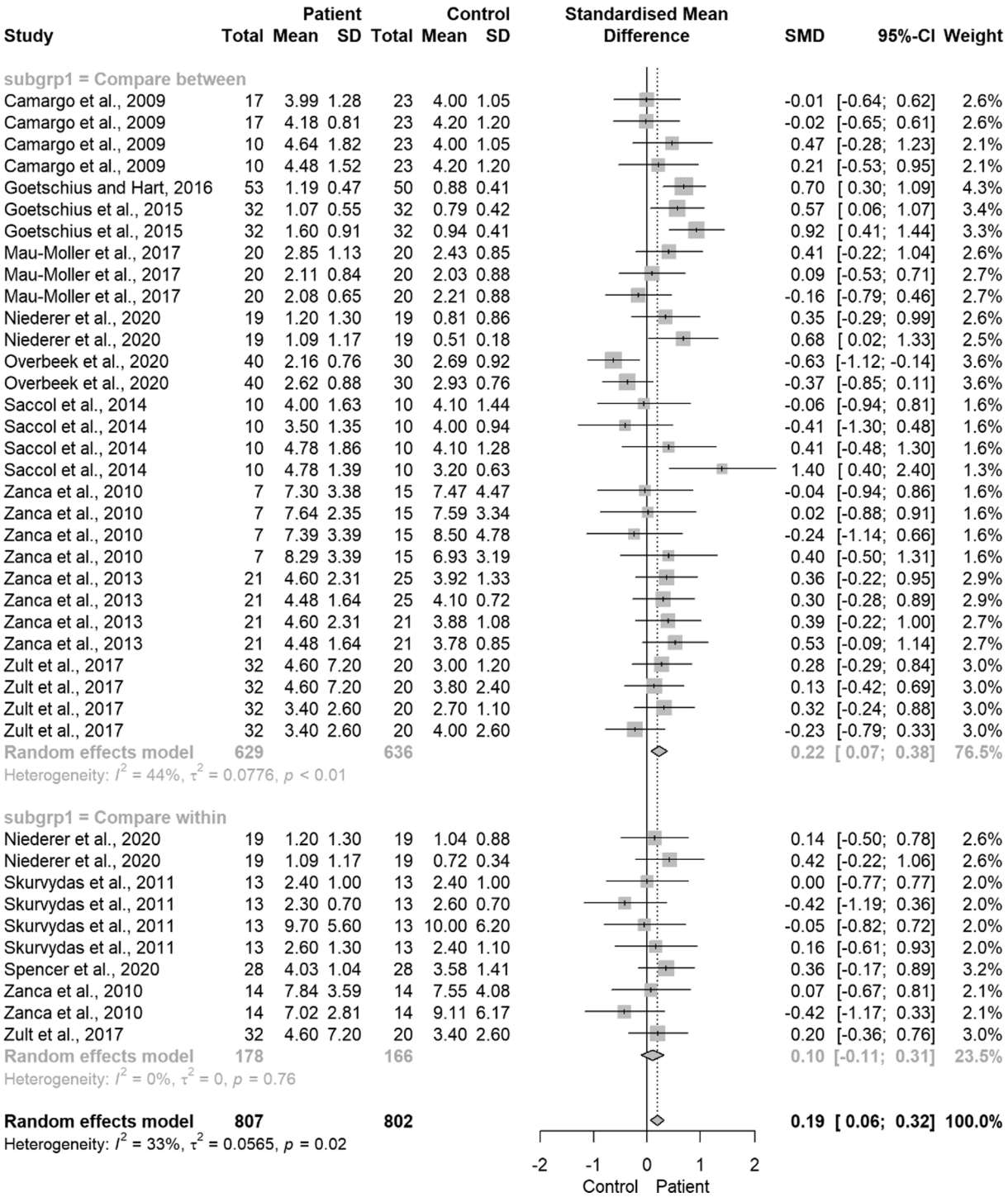

Fig. 4. The overall effect of peripheral musculoskeletal conditions on muscle force CV and the first subgroup analysis investigating the effect of study design on muscle force CV. Standard mean differences (SMD) with 95% confidence intervals. Multiple comparisons within the same study are reflective of either multiple contraction intensities or movements having been performed.

are also modulated by pre-synaptic excitatory and inhibitory spinal interneurons (Brownstone and Bui, 2010) and a variety of neuromodulators (Johnson and Heckman, 2014). Motor units are, therefore, the "final common pathway" by which multiple excitatory and inhibitory inputs are filtered to then activate skeletal muscle (Enoka and Farina, 2021). Subsequently, multiple mechanisms are potentially responsible for altering common synaptic input and, in turn, motor unit behaviour and skeletal muscle force control. Therefore, the exact physiological mechanism by which peripheral musculoskeletal conditions affect force control may vary between conditions.

4.2. Study design

Subgroup analysis demonstrated that peripheral musculoskeletal conditions only had a significant effect on muscle force CV when comparison was made between symptomatic patients and an unaffected control group (Camargo et al., 2009; Goetschius and Hart, 2016; Goetschius et al., 2015; Mau-Moeller et al., 2017; Niederer et al., 2020;

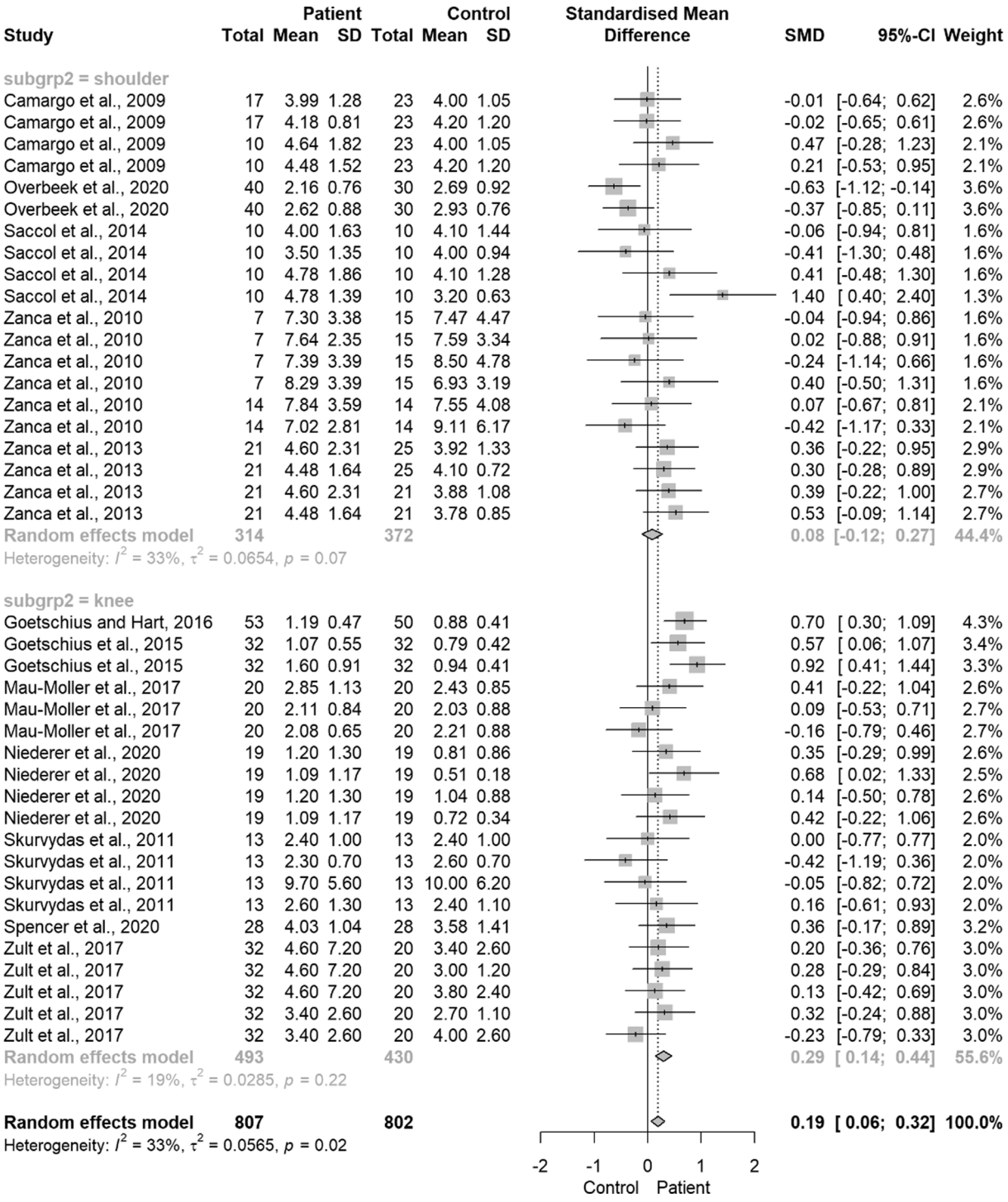

Fig. 5. The second subgroup analysis investigating the effect of peripheral joint on muscle force CV. Standard mean differences (SMD) with 95% confidence intervals. Multiple comparisons within the same study are reflective of either multiple contraction intensities or movements having been performed.

Overbeek et al., 2020; Saccol et al., 2014; Zanca et al., 2010; Zanca et al., 2013; Zult et al., 2017), and not when comparison was between the symptomatic limb and unaffected contralateral limb (Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zanca et al., 2010; Zult et al., 2017). Four of the five studies comparing the symptomatic limb with the unaffected contralateral limb were conducted in patients with an ACL injury. This finding adds to previous literature demonstrating that proprioception (Arockiaraj et al., 2013), maximal force-generating capacity (Chung et al., 2015), and dynamic balance (Culvenor et al., 2016) are all reduced in the unaffected contralateral limb of patients with an ACL injury compared to healthy controls. Thus, these findings add further support to the view that the unaffected contralateral limb should not be used as a reference standard for rehabilitation decision-making for people with ACL-injury (Hiemstra et al., 2007).

The decreased force steadiness observed in the unaffected contralateral limb (or, indeed, the affected limb) may simply be due to an enforced period of reduced activity (i.e. detraining) rather than the musculoskeletal condition itself. Previous research has demonstrated an increase in the CV of knee extensor and ankle plantarflexor fluctuations after four weeks of an experimentally-induced reduction in physical

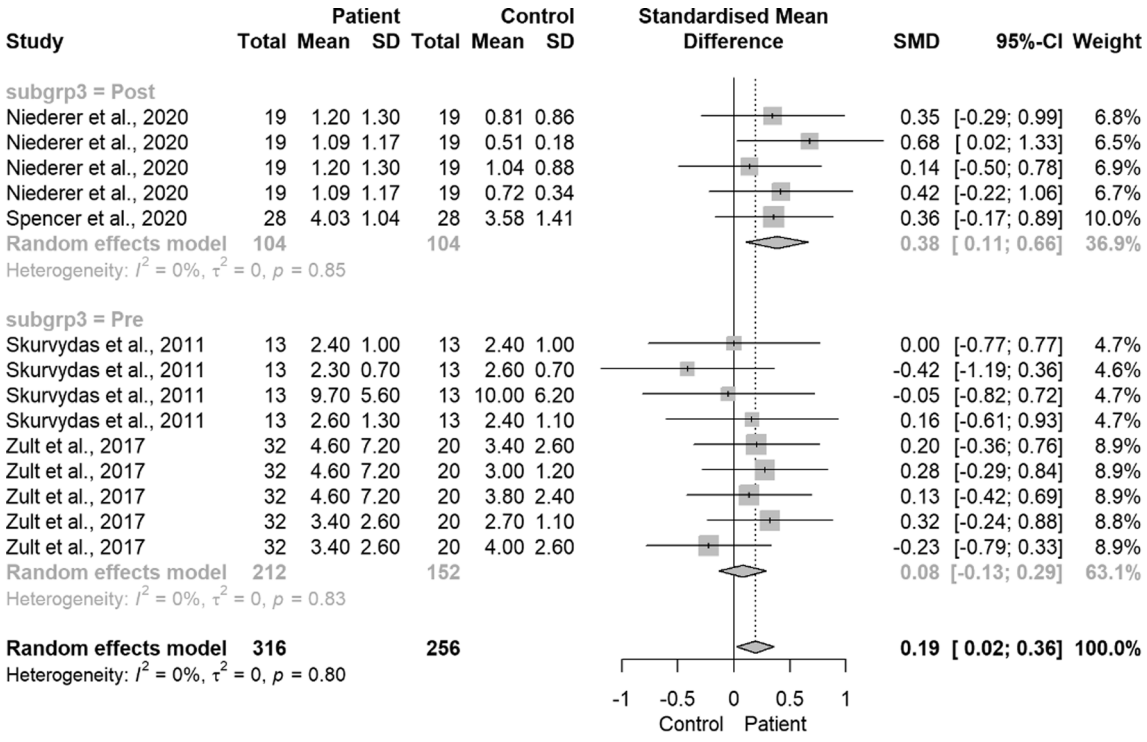

Fig. 6. The third subgroup analysis investigating the effect of surgical status on muscle force CV. Standard mean differences (SMD) with 95% confidence intervals. Multiple comparisons within the same study are reflective of either multiple contraction intensities or movements having been performed.

activity (unilateral limb suspension) (Clark et al., 2007). Alternatively, it could relate to a crossover of neural effects. Neural inhibition, measured using the twitch interpolation technique, has been observed in both the injured and contralateral legs following knee arthroscopy compared to uninjured controls (Suter et al., 1998). Such changes may be reflective of alterations in motor unit recruitment in the contralateral leg, which could then influence muscle force control in that limb.

4.3. Anatomical regions

Subgroup analysis demonstrated that only peripheral musculoskeletal conditions in the knee (Goetschius and Hart, 2016; Goetschius et al., 2015; Mau-Moeller et al., 2017; Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017), and not in the shoulder (Camargo et al., 2009; Overbeek et al., 2020; Saccol et al., 2014, Zanca et al., 2010; Zanca et al., 2013) had a significant effect on muscle force CV. From a physiological perspective, there may be intrinsic differences in the way upper and lower limb muscles are controlled. It has been demonstrated that there are significant differences in the number of muscle spindles found in the leg and shoulder (Banks, 2006), which could relate to differences in muscle fibre type composition (Kokkorogiannis, 2004). The lack of significant effect in the shoulder could have also been due to the conditions investigated and differences in pathoaetiology. Four of the five studies on the shoulder investigated impingement syndrome (Camargo et al., 2009; Overbeek et al., 2020; Zanca et al., 2010; Zanca et al., 2013), with three reporting no effect on muscle force control (Camargo et al., 2009; Zanca et al., 2010; Zanca et al., 2013) and the fourth reporting a lower CV of force fluctuations (i.e. increased steadiness) in patients (Overbeek et al., 2020). The other study on the shoulder investigated glenohumeral joint SLAP lesions, finding a greater CV in patients (Saccol et al., 2014). Historically, impingement syndrome is a diagnostic term representing a musculoskeletal condition occurring at the sub-acromial joint (Koester et al., 2005). The sub-acromial joint, however, is not a synovial joint and, therefore, does not contain any capsuloligamentous or intracapsular accessory structure mechanoreceptors that feedback to motor unit cell bodies in the spinal cord (Constant, 1989). In contrast, the glenoid labrum is a synovial joint intracapsular accessory structure that does contain afferent nerve endings which transmit sensory information to the spinal cord (Bresch and Nuber, 1995; Tibone et al., 1997). Therefore, differences in the findings of shoulder studies may be due to fundamental differences in neuroanatomy and afferent neurocircuitry that inputs to motor units.

The observed regional differences in force control could be confounded by methodological differences, such as joint angle and contraction intensity tested. Joint angle has been demonstrated to significantly affect proprioceptive acuity and pain (Anderson and Wee, 2011) and muscle force control (Pethick et al., 2021b). Contraction intensity has been demonstrated to have a significant effect on the age-related loss of force control, with increased CV typically observed only at low- to moderate-intensity contractions (Enoka et al., 2003). The studies included in the present *meta*-analysis used a wide range of target intensities, though typically only one intensity per study and with a tendency towards higher intensities in the knee (knee: range 20–100% MVC, average 62% MVC; shoulder: range 35–60% MVC, average 43%). This could indicate that peripheral musculoskeletal conditions-induced impairments in force control are more evident at higher contraction intensities. As the mechanical requirement of many day-to-day tasks typically does not exceed 20% MVC (Kern et al., 2001), this could indicate a limited role for the peripheral musculoskeletal condition-induced decrease in force control in poorer performance of functional tasks.

4.4. Surgical status

The studies forming this sub-group analysis all studied ACL reconstruction as a surgical intervention (Goetschius and Hart, 2016; Goetschius et al., 2015; Niederer et al., 2020; Skurvydas et al., 2011; Spencer et al., 2020; Zult et al., 2017). Interestingly, subgroup analysis revealed that muscle force CV was greater post-surgery compared to pre-surgery. Not only did ACL reconstruction fail to restore normal force control, it also worsened it. Moreover, a negative effect on force control was

reported in participants six (Spencer et al., 2020) and 38 months post-surgery (Niederer et al., 2020), indicating that the effects of surgery on force control are prolonged.

The studies investigating the effect of surgery used a bone-patellar tendon-bone autograft (Spencer et al., 2020) and an ipsilateral hamstring tendon autograft (Niederer et al., 2020). It has been speculated that the mechanistic basis for this prolonged decrement in force control follows a loss of mechanoreceptors from the harvested patellar tendon and ACL, with such a loss thought to affect the ability to effectively monitor and maintain a consistent force output (Spenceret al., 2020). Furthermore, the onset of anterior knee pain can also follow ACL reconstruction (Dai et al., 2021) and itself may contribute to muscle force control exhibited by ACL patients. Indeed, individuals with patellofemoral pain have been demonstrated to exhibit greater force CV during knee extension and hip abduction tasks (Ferreira et al., 2019), with such changes associated with greater motor unit firing rates (Gallina et al., 2018). Future mechanistic studies are required to understand the benefit/harm of surgical interventions across a spectrum of neuromuscular measures.

4.5. Recommendations for future research

The results of this review have served to highlight several limitations of previous studies. Consequently, there are several recommendations for future research to increase our understanding of how peripheral musculoskeletal conditions influence muscle force control. These can be divided into those relating to the measures of muscle force control and those related to study design. With regards to measures of muscle force control, it is recommended that future studies use the CV as their linear-(magnitude) based measurement of force control. The SD increases in direct proportion to the force exerted (Enoka et al., 2003; Slifkin and Newell, 1999), meaning stronger individuals will exhibit a greater absolute magnitude of fluctuations. The CV, on the other hand, normalises fluctuations to the mean force output and allows more appropriate comparison between groups differing in strength, as is often the case when comparing individuals with peripheral musculoskeletal conditions to healthy individuals (Edouard et al., 2011; Friesenbichler et al., 2018; Frost et al., 2006; Piussi et al., 2020). Secondly, in addition to traditional linear measures of force control, studies should also make use of non-linear (complexity) based measures. This is because the current dearth of studies utilising non-linear based measures limits our understanding of how peripheral musculoskeletal conditions affect muscle force control.

With regards to study design, a range of contraction intensities, to examine force control over the spectrum of voluntary forces, should be investigated. Secondly, the mechanistic basis of the peripheral musculoskeletal condition-induced loss of force control needs to be established. The majority of studies included in this *meta*-analysis were purely descriptive and, while such research has been useful in demonstrating peripheral musculoskeletal condition-induced changes in muscle force control, the lack of mechanistic focus is a limitation. Future research should utilise techniques such as intramuscular or high-density EMG, in order to assess changes in motor unit firing rates and recruitment, and transcranial magnetic stimulation in order to assess potential spinal and corticospinal adaptations. Finally, current research simply provides a snapshot of force control at a single instance in time, thus limiting our understanding of the evolution of changes in force control with either disease progression or recovery. Future studies should monitor muscle force control longitudinally, in order to assess the longevity and recovery profile of the observed decrement.

4.6. Limitations

Our study was conducted following international (PRISMA) guidelines for systematic reviews and *meta*-analyses. However, some limitations should be acknowledged. Firstly, the studies included in this *meta*-analysis were observational, cross-sectional studies and, as such, no causal relationship between musculoskeletal conditions and force control can be determined. However, it must be acknowledged that experimental models which involve the types of musculoskeletal conditions included in this review do not exist in humans. Secondly, the inclusion criteria were studies that featured a measure of force control during a targeted isometric contraction. Whilst force fluctuations during isometric contractions are predictive of performance in dynamic activities (Enoka and Farina, 2021), studies investigating sinusoidal, concentric and eccentric contractions may provide additional useful information. Thirdly, the 14 studies included in the *meta*-analysis featured 12 different target contraction intensities. Given the sensitivity of force control to contraction intensity (Enoka et al., 2003; Nagamori et al., 2021; Slifkin and Newell, 1999), such disparate targets could explain some of the heterogeneity observed between studies.

4.7. Conclusion

In conclusion, this review is the first to provide a synthesis of evidence describing the influence of selected peripheral musculoskeletal conditions on muscle force control. There was a small overall effect of peripheral musculoskeletal conditions on the CV of muscle force, though this effect is dependent on study design, peripheral joint tested, and surgical status. The effect on force control is likely mediated by alterations in common synaptic input to motor neurons, though the exact mechanism by which peripheral musculoskeletal conditions modulate synaptic input is still to be established. Further research using, amongst other things, both linear and non-linear measures of force control, a wide range of target contraction intensities, and more mechanistic methodologies are required to fully elucidate the influence of peripheral musculoskeletal conditions on muscle force control.

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Authors' contributions.

All authors were involved in the conception and design of the review. JP performed the literature search. JP and BL analysed the data. All authors contributed to the writing and critical revision of the manuscript. All authors approved of the final submitted version of the manuscript.

Data sharing.

Data are available from the authors on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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