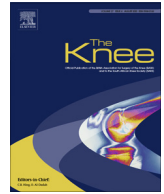




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# The Knee

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## Review

# Changes in co-contraction magnitude during functional tasks following anterior cruciate ligament reconstruction: A systematic review



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## ABSTRACT

**Background:** Anterior cruciate ligament reconstruction (ACLR) is a common orthopedic surgery procedure whose incidence has increased over the past few decades. Nevertheless, it is believed that neuromuscular control remains altered from the early stages after ACLR to later years. Therefore, the aim of this study was to systematically evaluate the magnitude of co-contraction during functional tasks in subjects with unilateral ACLR.

**Methods:** A systematic review design was followed. The search strategy was conducted in PubMed, Scopus, EBSCO, PEDro, Cochrane Library, and Web of Science databases from inception to March 2024. The inclusion criteria involved studies using electromyography (EMG) data to calculate muscle pair activation via the co-contraction index (CCI) in ACLR individuals during functional tasks. The Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed, and study quality was evaluated using National Institutes of Health (NIH) Study Quality Assessment Tools.

**Results:** The search strategy found a total of 792 studies, of which 15 were included in this systematic review after reviewing the eligibility criteria. The magnitude of co-contraction was assessed in a total of 433 ACLR individuals and 206 controls during functional tasks such as hop, drop-land, step-up/step-down, and gait. Overall, approximately 79.6% of individuals who had undergone ACLR exhibited increased levels of co-contraction magnitude in the ACLR limb, while 8.5% showed low co-contraction levels.

**Conclusions:** The findings of the review suggest that, during functional tasks, most individuals who have undergone ACLR exhibit changes of co-contraction magnitude in the involved limb.

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## 1. Introduction

Anterior cruciate ligament (ACL) tear is a prevalent sports-related injury, resulting in a variety of immediate and lasting consequences, including pain, gait impairment, decreased involvement in sporting activities, and articular degeneration [1]. Following ACL tears, reconstructive surgery is commonly suggested to reestablish knee stability [2,3]. Anterior cruciate ligament reconstruction (ACLR) is among the most common orthopedic surgical procedures performed in the United States [4], and its incidence is increasing. In a descriptive epidemiological study, Buller et al. [5] observed that the overall ACLR procedures conducted in the United States surged from 33.0 in 1994 to 45.1 per 100,000 individuals in 2006. This increase in the number of surgeries was also verified in the Italian population between 2001 and 2015, in which the incidence increased from 21.7 to 33.6 per 100,000 individuals [6], and within the Australian population, where the occurrence of primary ACLR surgeries surged 43% between 2000 and 2015, increasing from 54.0 to 77.4 per 100,000 individuals, accounting for the world's greatest normalized rate [7].

Nevertheless, despite ACLR and the rehabilitation process, neuromuscular control remains altered upon returning to activity [8–15] and in the years following surgery [1,8]. Neuromuscular control involves the unconscious development of mechanisms necessary to maintain and restore joint stability, during the preparation and response to movement and loading. However, when stability is impaired, compensatory motor strategies can be triggered to provide the necessary additional stability [16].

Concurrent activation between agonist and antagonist muscles, commonly known as co-contraction, represents an efficient mechanism in providing joint stability [17], and is suggested to be significantly controlled by supraspinal functions related to movement control [18]. Although co-contraction is acknowledged as an appropriate motor control function for both joint protection and dynamic stability [19], increased co-contraction can impact the distribution of joint loading and accelerate the progression of pathological conditions [20]. It is suggested that increased co-contraction during gait, stair ascent, and landing tasks results in higher knee compressive loadings at the articular surface [20–24], and abnormal loading patterns can expose cartilage areas to stresses that are not typically experienced in healthy knees, eventually leading to the development of osteoarthritis (OA) [25,26]. Interestingly, in a meta-analysis that included 4,108 ACLR patients, Cinque et al. [27] reported that the probability of developing post-traumatic osteoarthritis (PTOA) was 11.3% at 5 years, 20.6% at 10 years, and 51.6% at 20 years post-surgery.

Accordingly, the purpose of this systematic review was to assess the magnitude of co-contraction in ACLR limbs during functional tasks such as hopping, landing, stair ascent/descent, and gait, compared to either contralateral limbs or healthy controls.

## 2. Methods

### 2.1. Registration

The systematic review was performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations [28]. The review protocol was registered in PROSPERO database in October 2022 (registration number: CRD42022359354). No protocol had been pre-registered for this systematic review.

### 2.2. Search strategy

The search was carried out in PubMed, Scopus, EBSCO, PEDro, Cochrane Library, and Web of Science databases from inception to March 2024 (Supplementary Table S1), using the following keywords: (“Anterior cruciate ligament reconstruction”) OR (“anterior cruciate ligament surgery”) AND (“co-contraction”) OR (“co-activation”). In addition, electronic search was complemented by searching the reference list of retrieved research. The search was conducted without any restrictions regarding publication year.

### 2.3. Eligibility criteria and study selection

The inclusion criteria for studies in this systematic review were case-control, cross-sectional, and cohort studies related to ACLR, in which normalized electromyography (EMG) data were used to calculate the magnitude of a muscle pair activation through co-contraction index (CCI) during functional tasks and compared between limbs (injured/uninjured) or healthy controls. In addition, only studies published in English were included.

Abstracts, posters, unpublished trials, uncontrolled trials, articles unrelated to ACLR, systematic reviews, meta-analyses, case series with <5 participants, book chapters, conference articles, and thesis were excluded. Moreover, studies were excluded if they involved: (1) post-mortem individuals or animals; (2) revision surgery; and (3) co-contraction assessments based on the temporal duration required for task completion or on the relative activation of a muscle pair using the co-contraction ratio (CCR).

All studies identified by the search strategy were exported to Mendeley Reference Manager 2.76.0 © 2022 by a reviewer (RP), who then cross-referenced the results and removed duplicates. After removing duplicates, two independent reviewers (RP and CC) assessed all titles and abstracts to determine their eligibility for the review. Excluded studies were discussed by both authors and any disagreements were settled during a collaborative meeting, where a third reviewer (AMM) was available if needed.

### 2.4. Outcome

The outcome assessed was the magnitude of activation, between antagonist muscles pairs, measured via CCI during functional tasks.

### 2.5. Data extraction

Two independent reviewers (RP and CC) used Microsoft Excel® to extract and compare data from each eligible study. Discrepancies were discussed and resolved through reviewer collaboration. The following data were extracted from all included studies: (1) Study characteristics: first author's name, publication year, study design, and sample size; (2) Participants characteristics: age, sex, type of graft, associated injuries, time since surgery; (3) Testing protocol: number of participants, task performed, muscles tested, comparison of affected limb (uninvolved limb or healthy controls), and EMG normalization method; (4) Outcome measures: magnitude of co-contraction activation between antagonistic muscle pairs expressed as co-contraction indices (CCIs).

### 2.6. Quality assessment of the included studies

Two independent reviewers (RP and CC) evaluated the quality of the included studies using the National Institutes of Health (NIH) Study Quality Assessment Tools. Any disagreements were addressed during a collaborative meeting, where a third reviewer (JLA-B) was present. These Quality Assessment Tools provide guidelines for assessing the internal validity of studies, covering aspects such as population, sample size, statistical analysis, and outcome measures. Quality questions can be addressed with ‘Yes’, ‘No’, ‘Cannot Determine’, ‘Not Applicable’, and ‘Not Reported’. Studies are categorized as ‘Good’, ‘Fair’, or ‘Poor’ based on the quality assessed.

### 3. Results

#### 3.1. Study selection

The search strategy identified 792 studies, of which 677 were selected after duplicate removal. The initially selected studies underwent title screening, leading to the identification of 52 studies eligible for a comprehensive abstract assessment. Fifteen studies were excluded, resulting in 37 for full-text assessment. Among these, 13 studies met the inclusion criteria. Additionally, two studies were included after manually searching the references of selected studies. Therefore, a total of 15 studies were included in this systematic review after applying the selective criteria and were grouped according to the task investigated (i.e., hop, drop-land, step-up/step-down, and gait). The comprehensive study selection process and explanations for excluded articles are provided in the PRISMA flow chart (Figure 1).

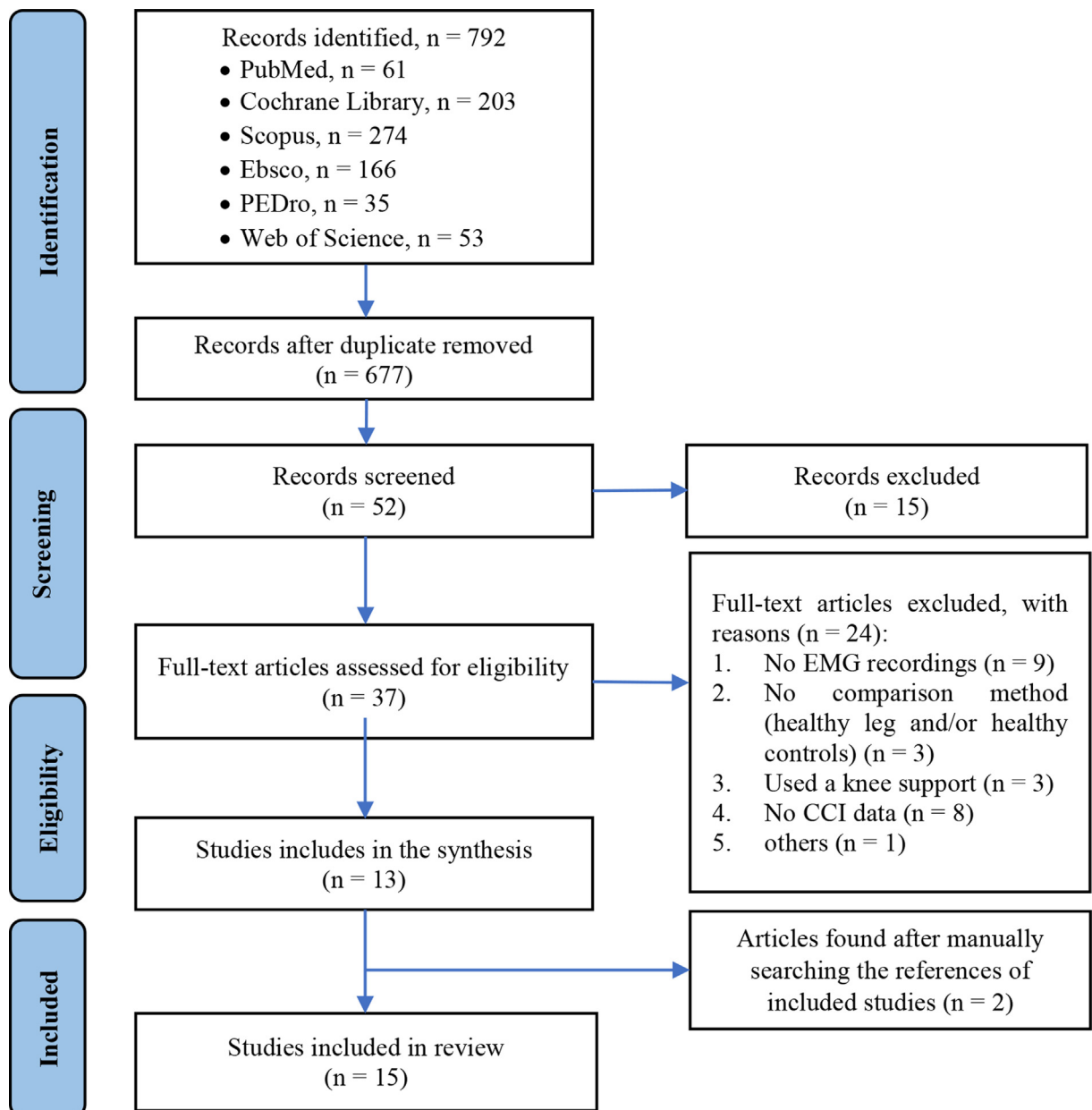


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) flow chart.

### 3.2. Study characteristics

The 15 selected studies included a total of 639 participants (55.2% females and 37.9% males, 6.9% not reported) with an average age between 20 and 34.5 years.

Four hundred and thirty-three individuals underwent ACLR (50.6% females and 41.6% males, 7.8% not reported), while 206 were healthy controls (65% females and 30.1% males, 4.8% not reported). The sample size ranged from 19 to 80 participants in the included studies. Table 1 provides a summary of the participant characteristics.

Time between surgery and study participation varied among studies, with a range from 3 months to 18 years, and ACLR individuals with concomitant injuries were allowed to participate in five studies [29–33], while three excluded associated injuries within the study population [34–36]. Seven studies did not describe or control additional injuries of the included participants [22,37–42].

Hamstring tendon (HT) was the most frequently documented graft (36.7%), followed by patellar tendon (PT) (25.6%), bone-patellar tendon-bone (9.9%) and semitendinosus gracilis (STG) (8.3%). Furthermore, between 10% and 12% were allografts.

The most commonly assessed outcomes reported encompassed the CCI between quadriceps:hamstrings (Q:H), vastus medialis:semitendinosus (VM:ST), and vastus lateralis:biceps femoris (VL:BF).

Most studies used the equation described by Rudolph et al. [43] to calculate CCI, which involved dividing the level of activity in the less active muscle by the level of activity in the more active muscle, and then multiplying this ratio by the sum of the activity found in the two muscles:

$$CCI = \frac{EMGS}{EMGL} \times (EMGS + EMGL)$$

Nevertheless, two studies [31,42] reported measurements for CCI using the method described by Unnithan et al. [44] and Frost et al. [45] where CCI was calculated by overlaying the linear envelopes of the agonist and antagonist muscles and then dividing the overlap area by the number of data points [46]:

$$CCI = \frac{\text{Common Area}}{\text{Total Area}}$$

Out of 639 participants who were included in the selected studies, 31.6% performed hop tasks (94 ACLR and 108 controls), 8.1% performed a single-legged drop landing (26 ACLR and 26 controls), 11.7% performed a step-up or step-down (38 ACLR and 37 controls), and 48.5% performed gait (275 ACLR and 35 controls).

#### 3.2.1. Hop tasks

Jumping tasks were reported in four studies and consisted of a hop for distance followed by a cutting maneuver [29,39], drop jump [22], or side-hop [30]. Nevertheless, studies examining the hop for distance followed by a cutting maneuver demonstrated certain methodological variations. In one study, the task involved a single-legged forward hop followed by an immediate cutting maneuver at a 45° angle to either the medial or lateral direction over a predetermined distance (25% of body height) in an unanticipated manner. The cutting maneuver was performed with hands placed behind the lower back, and data analysis was based on twelve hops (3 per direction, medial and lateral, per leg) [39]. In the alternative study, subjects were instructed to perform a double-leg forward jump over a 17 cm box, followed by a single-leg landing and an immediate lateral jump to the opposite side. The tested limb was randomly determined before takeoff, and three successful trials were analyzed [29].

The single-legged drop jump was described in one study [22], where participants positioned themselves on a 25 cm high platform and were instructed to land with the tested limb and then execute a maximal upward jump. Furthermore, the data analysis involved the use of three trial assessments.

One study evaluated the side-hop task [30], in which participants hopped single-legged with hands behind their backs in the ipsilateral direction, covering a distance of over 25% of their body height, and then quickly returned to the initial position. Five successful trials were recorded for data analysis.

Three out of four studies that evaluated hop tasks found increased Q:H CCIs in ACLR individuals when compared to healthy controls. Increased co-contraction was found during the LOAD phase (from initial contact [IC] to peak knee flexion angle), when performing single-leg side-hop ( $p = 0.001$ ) [30], and drop-landing ( $p = 0.004$ ) [22]. Furthermore, in one study, a significant interaction between groups and phases during an unanticipated medial diagonal hop was found, with VM:ST ( $p = 0.025$ ) and VL:BF ( $p = 0.030$ ) CCIs showing increased mean values in ACLR individuals compared to healthy controls, but not to healthy athletes, at 100 ms prior to IC, 50 ms after IC, and from IC to peak knee flexion [39].

Nonetheless, one study found no differences in VL:BF CCIs between ACLR individuals and healthy controls [29]. These observations were made during ground contact to 250msec post ground contact of the double-leg forward jump and land on single-leg ( $p = 0.447$ ).

#### 3.2.2. Single-legged landing task

The single-leg vertical drop landing (VDL) was similarly described in two studies, in which participants were instructed how to perform the landing task, dropping off a 30 cm high platform, and landing single-legged. Practice trials for familiar-

**Table 1**  
Characteristics of included studies.

Study	Quality Score	Participants	Age (years, mean ± SD)	Graft type	Associated injuries	Time since surgery (range, mean ± SD)	Task performed	Muscles tested	EMG normalization	Outcome measured (CCI)
Alfayyadh [32]	8	45 ACLR: 18F–27M	M: 24 ± 7; F: 22 ± 7	M: 12 BPTP, 8 HT, 7 allografts; F: 11 BPTP, 5 HT, 2 allografts	Some participants underwent meniscectomies	3 months	Gait	VM; VL; RF; SM; BF; MG; LG	MVIC	VM:ST; VL:BF; VM:MG; VM:LG; VL:LG; VL:MG;
Alfayyadh [33]	8	44 ACLR: 18F–26M	23 ± 10	20 BPTB, 14 HT, 9 allografts, 1 hybrid	Concomitant grade III injury to other ligaments and repairable meniscus tears were excluded	3 months (3.1 ± 0.5)	Gait	VM; VL; RF; SM; BF; MG; LG	MVIC	VM:ST; VL:BF; VM:MG; VM:LG; VL:LG; VL:MG;
Arumugam and Häger [39]	8	34 ACLR: 25F–9M; 24 Controls: 20F–4M; 22 Athletes: 19F–3M	ACLR: 24.5 ± 4.6; Controls: 23.4 ± 3.4; Athletes: 21.3 ± 2.9	HT	NR	7–129 months (median 18)	One-leg double hop	BF; ST; VL; VM	Peak EMG value during landing	VM:ST; VL:BF;
Blackburn [37]	8	50 ACLR: 35F–15M; 25 Controls: 19F–6M	ACLR: 20 ± 3; Controls: 20 ± 1	28 PT, 16 HT, 3 QT, 3 allografts	NR	6 months–5 years (27 ± 15)	Gait	VM; VL; BF; ST	Peak EMG value during stance	Q:H; VM:ST; VL:BF;
Blackburn [41]	7	72 ACLR: 52F–20M	21 ± 3	41 PT, 25 HT, 3 QT, 3 allografts	Concomitant meniscal injury was not controlled	6–59 months (27 ± 16)	Gait	VM; VL; BF; ST	Peak EMG value during stance	Q:H;
Hall [38]	7	18 ACLR: 10F–8M; 17 Controls: 10F–7M	ACLR: 26 ± 6; Controls: 26 ± 4 (between 18 and 35 years)	6 PT, 10 HT, 1 combination of HT and PT, 1 unknown graft	NR	1–18 years (5)	Stair ascent/ Stair descent	G; VM; VL; RF; BF; SM; GMED	MVIC	VM:ST; VL:BF; VM:VL; SM:BF
Lepley [29]	7	12 ACLR: 5F–7M; 13 Controls: 9F–4M	ACLR: 22.08 ± 4.7; Controls: 22.9 ± 4.3	7 PT, 5 STG	Grade I Injury: 4 MCL, 1 LCL, 1 both; Meniscus repair: 2 Lateral, 1 both	7–10 months (248 ± 54.6 days)	Double-leg forward jump and land on single-leg	VL; BF	MVIC	VL:BF
Leporace [42]	8	9 ACLR; 10 Controls	ACLR: 33.1 ± 11.1; Controls: 29.4 ± 3.1 (between 20 and 40 years)	9 HT	NR	8–15 months (11.2 ± 2.4)	Gait	VL; BF	Mean of three Peaks EMG	VL:BF
Lustosa [31]	7	15 ACLR full return; 10 ACLR limited return	Full return: 34.5 ± 8.85; Limited return: 33.4 ± 7.53	25 PT	19 associated meniscus lesions	≥2 years (Full return: 67.31 ± 28.52 months; Limited return group: 52.20 ± 31.33 months)	Gait	VL; BF	MVIC	VL:BF
Markström [30]	8	21 ACLR high fear: 11F–10M; 17 ACLR low fear: 9F–8M; 39 Controls: 32F–7M	ACLR HIGH-FEAR: 24.0 ± 3.9; ACLR LOW-FEAR: 25.5 ± 5.8; Controls: 22.4 ± 3.0	38 HT	No complete tear of any other ligament and no major menisci were included	ACLR HIGH-FEAR: 11.2 months; ACLR LOW-FEAR: 10.1 months;	Single-leg standardized rebound side-hop	VM; VL; ST; BF	Mean peak value	Q:H
Rostami [34]	8	12 ACLR: 12M; 12 Controls: 12M	ACLR: 23.83 ± 5.49; Controls: 24.92 ± 2.81	4 PT, 6 STG, 2 allografts	Excluded injuries to the MCL, LCL, PCL, or meniscus	18–36 months (23.75 ± 6.3)	Single-leg vertical drop landing	GMED; AL	MVIC	GMED:AL

Table 1 (continued)

Study	Quality Score	Participants	Age (years, mean $\pm$ SD)	Graft type	Associated injuries	Time since surgery (range, mean $\pm$ SD)	Task performed	Muscles tested	EMG normalization	Outcome measured (CCI)
Smeets [40]	8	20 ACLR: 6F–14M; 20 Controls: 6F–14M	ACLR: 23.7 $\pm$ 4.3; Controls: 21.4 $\pm$ 1.5	20 ST	NR	8.5 $\pm$ 1.8 (months)	Step-down	VM;VL; ST; BF; MG; LG; GMED	MVIC	Q:H; VM: ST; VL:BF;
Tsai [22]	7	10 ACLR: 10F; 10 Controls: 10F	ACLR: 25.3 $\pm$ 2.4; Controls: 24.9 $\pm$ 1.7 (Between 18 and 35 years)	BPTB or allograft	Concomitant meniscal injury was not controlled. Other ligament injuries were excluded	36.2 $\pm$ 18.5 (months)	Single-leg drop-land	VM; VL; RF; ST; BF; MG; LG	MVIC	Q:H + G
Vairo [35]	8	14 ACLR: 9F–5M; 14 Controls: 9F– 5M	ACLR: 22.5 $\pm$ 4.05; Controls: 22.8 $\pm$ 3.5	14 STG	Associated ligamentous or meniscal pathology were excluded	21.4 $\pm$ 10.7 (months)	Single-leg vertical drop landing	VM; VL; ST; BF; MG	MVIC	Q:H
Wellsandt [36]	7	30 ACLR: 11F–19M	ACLR: 30.5 $\pm$ 11.1 (Between 14 and 51 years)	11 STG, 19 allografts	Concomitant grade III injury to other ligaments and repairable meniscus injury were excluded	26.7 $\pm$ 2.8 (wks)	Gait	VM; VL; RF; ST; BF; MG; LG	MVIC	Q:H + G

ACLR (anterior cruciate ligament reconstruction); PCL (posterior cruciate ligament); MCL (medial collateral ligament); LCL (lateral collateral ligament); F (Female); M (Male); BPTB (bone patella tendon bone); HT (hamstring tendon); PT (patellar tendon); QT (quadriceps tendon); STG (semitendinosus-gracilis tendon); ST (semitendinosus tendon); Q (quadriceps); VM (vastus medialis); VL (vastus lateralis); RF (rectus femoris); H (hamstrings); ST (semitendinosus); SM (semimembranosus); BF (biceps femoris); G (gastrocnemius); MG, (medial gastrocnemius); LG (lateral gastrocnemius); GMED (gluteus medius); AL (adductor longus); EMG (electromyography); MVIC (maximum voluntary isometric contractions); CCI (co-contraction index); NR (not reported); SD (Standard Deviation).

ization were allowed, and three trials were used for analysis if participants landed properly. However, there are methodological differences between the studies. One study assessed Q:H CCI and included participants of both sexes [35], while another study exclusively included male individuals and assessed gluteus medius:adductor longus (GMED:AL) CCI [34].

Results showed that during single-leg VDL, ACLR participants exhibited significantly greater preparatory ( $p = 0.033$ ) and reactive ( $p = 0.022$ ) Q:H CCI [35], and significantly lower reactive GMED:AL CCI ( $p = 0.026$ ), with a strong effect size (1.04) [34], when compared to matched controls.

### 3.2.3. Step-up and step-down task

The step-up/step-down task was evaluated in two studies, wherein disparate step heights were reported across experiments. Specifically, one study incorporated a step height of 10 cm [40], while another study implemented a step height of 18.5 cm [38]. Also, one study utilized a three-step staircase to examine the step-up and step-down tasks. This investigation employed a self-selected step-over-step technique with step detection at 5% of body weight (BW) [38]. On the contrary, another study examined the step-down task under varied environmental challenges, in which the participants were instructed to land with 1 leg and stand for 5 s. Additionally, a warm-up consisting of five minutes running and a set of hopping tasks was provided [40]. In both studies, 3 trials performed on both the left and right leg were used for analysis.

Studies that assessed step-up and/or step-down task found that CCI were significantly higher in ACLR individuals, compared to controls [38,40] and with the uninvolved knee [40]. During step-up, ACLR individuals exhibited a significantly higher VL:BF and vastus lateralis:vastus medialis (VL:VM) CCI in 51–100% stance ( $p = 0.01$  and  $p = 0.05$ , respectively), compared to the controls [38]. During the step-down task, ACLR subjects revealed significantly higher vastus medialis:semimembranosus (VM:SM) CCI in 1–50% of the stance ( $p = 0.02$ ) [38], higher Q:H CCI ( $p < 0.001$ ; effect size = 1.20) and higher VL:BF CCI from 50 ms post IC to 250 ms post IC ( $p < 0.001$ ; effect size = 1.34) [40], compared to controls. Furthermore, from 50 ms post IC to 250 ms post IC, ACLR individuals showed higher VL:BF CCI in their injured leg compared to their uninjured leg ( $p < 0.001$ ; effect size = 0.64) [40].

### 3.2.4. Gait

All studies that assessed gait reported that subjects walked at a self-selected speed. Nonetheless, the distance walked for gait analysis varied between experiments. Of the seven studies that assessed gait, five reported the use of a 3-meter [31,37], 6-meter [32,33], or 8-meter [42] walkway, while the distance walked was not reported in the remaining two studies [36,41]. Moreover, one study used a platform capable of inducing an unexpected disturbance, tilting 20° in the medial and lateral directions by means of an electromechanical device [31]. Assessments included in data analysis varied between three to eight trials.

Most studies revealed co-contraction changes in ACLR patients during gait analysis. During heelstrike phase, two studies reported that ACLR limb showed higher Q:H CCI than the contralateral limb [ $p = 0.008$ ] [37] and [ $p = 0.026$ ] [41] and the index limb of healthy controls ( $p = 0.029$ ; effect size = 0.48) [37], and higher VM:ST co-contraction than the index limb in healthy controls ( $p = 0.007$ ) [37]. Moreover, during the preparatory phase (100 ms prior to heelstrike), one study reported that ACLR limb displayed greater Q:H CCI than the contralateral limb ( $p = 0.006$ ) and the index limb of healthy controls ( $p = 0.038$ ; effect size = 0.45) [37]. Also, during weight acceptance interval (100 ms before heel strike to peak knee flexion angle), two studies found significantly higher CCI for the VL:BF ( $p = 0.02$  [32] and  $p < 0.05$  [47]), and a tendency for higher vastus lateralis:lateral gastrocnemius (VL:LG) indices in the ACLR limb compared to the uninvolved limb, with a medium effect size (partial eta-squared = 0.07) [32]. In contrast, one study found lower VL:BF CCI, 250 ms before perturbation, in the involved limb of ACL reconstruction patients compared to the uninvolved limb ( $p = 0.049$ ), in two groups of ACLR participants, one who returned to their pre-injury functional level, and another who did not [31].

However, two studies found no differences in co-contraction between limbs of ACLR individuals and healthy controls during gait analysis. When measured at peak medial compartment contact force, during the first half of stance, one study found that Q:H CCI were not different between limbs of ACL-injured individuals (injured:  $0.13 \pm 0.06$ ; uninjured:  $0.13 \pm 0.08$ ) [36]. Also, during each gait cycle (from 0% to 100%), another study found no difference for VL:BF CCI between ACLR individuals and healthy controls ( $p = 0.236$ ; effect size = 0.56) [42].

### 3.3. Quality assessment

The studies in this systematic review had an average score of 7.5 'Fair' out of 12 points on the NIH Quality Assessment Tool for Observational Cohort and Cross-sectional Studies, and an average score of 7.6 'Fair' from a total of 11 points in the NIH Quality Assessment Tool for Case-Control Studies (Supplementary Tables S2 and S3).

According to NIH guidelines, cross-sectional studies automatically scored 'No' on criteria 6 and 7. Domains with the highest risk were specification and clear definition of the population (11/15 studies), sample size justification, power description or variance and effect estimates (5/15 studies), exposure assessment more than once during the study period (12/12 studies), measurement and statistical adjustment of potential confounding variables (4/12 studies), and confirmation that the exposure/risk occurred prior to the development of the condition or event (3/3 studies). The blinding of outcome assessors to the exposure status of participants was considered 'Not Applicable' due to the visible scar resulting from the surgical intervention, which would be easily identifiable.

#### 4. Discussion

This systematic review aimed to evaluate the magnitude of activation between antagonist muscles pairs among different functional tasks following ACLR. The findings suggest that most individuals who have undergone ACLR exhibit an increase in the magnitude of co-contraction between quadriceps and hamstrings muscles in their involved limb when compared to the uninvolved limb and healthy controls.

The management of an efficient joint stability depends on the synergistic interaction between passive and dynamic structures [16,48]. However, when passive structures are impaired, as observed in ACL injuries, the involvement of dynamic structures may become crucial [48]. In situations of delayed sensorimotor processing, the central nervous system (CNS) compensates for impaired stability by increasing muscle co-contraction [49].

In this review, increased levels of co-contraction in ACLR limbs were reported in ten studies (66.6%) [22,30,32,33,35,37–41], comprising 345 ACLR individuals (79.6%). This neuromuscular strategy is essential to ensure stability when passive structures are injured [19]. Nevertheless, increased levels of muscle co-contraction during functional tasks can adversely affect proprioception [41], motor performance [50], and elevate the metabolic cost associated with task execution [45,51]. Moreover, increased co-contraction levels have been proposed to heighten the probability of ACL injury [52] and PTOA development after ACLR [37,38].

While most investigations reported an increased magnitude of co-contraction, some studies (13.3%) including 37 ACLR individuals (8.5%) found low levels of co-contraction in the ACLR limb [31,34], whereas others (20.0%) involving 51 ACLR individuals (11.7%) observed no significant differences [29,36,42] in comparison to the uninjured limb or healthy individuals.

These inconsistent findings could be attributed to various factors, such as the method used to calculate co-contraction, specific muscle pairs analyzed, and task phase used for data analysis.

During the analysis of hop tasks, it was observed that only one study reported no differences in CCI, measured from ground contact to 250 ms post ground contact [29]. The discrepancies in the findings can be attributed to variations in the time period used during data analysis, as muscular co-contraction results can vary depending on the specific details of the task [19,53,54]. This inconsistency arises from the fact that the other studies focused on evaluating specific landing phases, such as pre-landing, IC, and deceleration, while also controlling for kinematic variables to accurately measure peak knee flexion.

Also, when assessing VDL, one study found that individuals who had undergone ACLR exhibited lower levels of co-contraction in comparison to matched controls [34]. However, it is worth noting that these authors were the only ones to evaluate the magnitude of co-contraction between the hip abductors and adductors, which may account for the disparities observed in the results. Nevertheless, while increased levels of co-contraction suggest a high activation pattern in both antagonistic muscles, low values suggest reduced activity in both antagonistic muscles or an imbalanced activation pattern [43]. The low co-contraction levels reported by these authors were associated with reduced abductor activity, while the adductor activity remained unchanged [34]. It is proposed that compensatory strategies can be developed due to dynamic limitations within the affected joint and motor adjustments in the adjacent segments [16].

During the analysis of gait, two distinct methods were identified for calculating the CCI. Studies that used the method described by Rudolph et al. [43] found that individuals who underwent ACLR display an increased magnitude of co-contraction, with exception of one study that found no differences between limbs of ACLR individuals. However, the authors evaluated the magnitude of co-contraction between knee flexors (hamstrings and gastrocnemius) and knee extensors (quadriceps) specifically at the peak medial compartment contact force [36], while the other studies reported co-contraction values between quadriceps and hamstrings during different intervals, including the preparatory phase, heel strike, load acceptance, and weight acceptance. Incorporating data collected during these time periods (preparation and loading) can lead to a more comprehensive muscle activity evaluation [37].

When the CCI was calculated according to the method described by Unnithan et al. [44] and Frost et al. [45] the studies reported different results. Nevertheless, previous investigations have indicated that differences in methods used to calculate CCI can affect the resulting co-contraction values [19,46,55–57]. This can help explain the differences observed between the two methods employed during gait analysis, as each method provides different information and interpretations of co-contraction. The co-contraction assessment method described by Unnithan et al. [44] and Frost et al. [45] focuses on a single agonist and antagonist muscle pair and uses normalized EMG that results in equal contributions from both muscles [46]. While it provides outcome measurements reflecting the magnitude of activation between antagonistic muscles, it does not provide information on the duration and timing of the co-contraction [58]. In contrast, the method described by Rudolph et al. [43] estimates the temporal and magnitude aspects of antagonistic muscle activation [43,59], can incorporate multiple agonist and antagonist muscles and has been found to be correlated with joint stiffness [56].

Although increased Q:H co-contraction levels might suggest a neuromuscular strategy aimed at minimizing the stress on the reconstructed ACL [60], they also result in heightened joint compressive forces [21]. It should be noted that in the current review, all studies that examined the composite Q:H CCI consistently reported that ACLR individuals exhibited an increased co-contraction magnitude [30,35,37,40,41]. Using data from 'in vivo' measurements of knee contact forces, Trepczynski et al. [23] observed that an increased co-contraction magnitude resulted in higher compressive forces at tibiofemoral joint surfaces. Greater loadings on articular surfaces are known to exert a catabolic effect on cartilage metabolism, leading to articular degeneration and contributing to the development of OA [61]. In a prospective cohort study, Hodges et al. [62] reported that

during gait, longer periods of VM:ST co-contraction were associated with annual reductions in the volume of medial tibial cartilage ( $p = 0.003$ ). The decrease in cartilage volume exhibited a 0.14% increase with each 1% extension in the temporal duration of VM:ST co-contraction.

In this review, the majority of studies that investigated medial co-contraction (VM:ST) reported increased magnitudes in ACLR individuals [37–39]. This strategy is believed to contribute to elevated articular compression forces, which has the potential to facilitate joint damage [63], leading to uni-compartmental or multi-compartmental OA development [24]. Interestingly, in a 22-year follow-up study after ACL reconstruction, Curado et al. [64] observed that tibiofemoral OA was more frequently observed in the medial compartment (23%) compared to the lateral compartment (9%).

Similarly, most of the studies that assessed lateral co-contraction (VL:BF) reported an increased magnitude among individuals who underwent ACLR [32,33,38–40]. This neuromuscular strategy has been associated with higher valgus moments and reduced knee flexion displacement [37]. Although ACL injuries likely have a multi-factorial etiology, reduced knee flexion displacement [65] and increased knee abduction moments are commonly reported as intrinsic risk factors for non-contact ACL injury [65,66]. Moreover, the increased magnitude of lateral muscles has been proposed as an indication of uni-compartmental OA development [24].

Indeed, all studies that investigated both medial and lateral co-contractions, reported increased magnitudes for at least one muscle pair. Although co-contraction may vary depending on the specific demands of the task [19,54], the differences reported in medial and lateral co-contraction between studies might indicate distinct strategies adopted to enhance joint stability. Nevertheless, variations in the magnitude of activation between antagonist muscle pairs could potentially result in significantly different compression forces on the articular surface [23], which, in turn, can contribute to varying rates of joint degeneration [24].

The studies included in the current review had a similar methodological quality 'Fair' with consistent flaws, such as population definition and repeated exposure assessment. However, it should be noted that while repeated within-limb co-contraction measurements on the same day are suggested to have acceptable reliability, it is suggested to avoid these assessments on different days due to their poor reliability. Therefore, co-contraction measurements are recommended for conducting group comparisons analysis and interventional studies [67].

There are some potential confounding variables that must be considered when interpreting the results of this review:

#### 4.1. Age-related co-contraction differences

Differences in muscle co-contraction have been documented between healthy young and older adults. In a systematic review, Kim and Chou [68] found that when walking with balance perturbations, older adults exhibited increased co-contraction levels in ankle and knee muscles when compared to young adults. Additionally, a recent study investigated the influence of different walking surfaces on co-contraction in both young (age:  $28.0 \pm 5.1$ ) and older adults (age:  $72.7 \pm 5.4$ ) of both sexes. This study revealed that tibialis anterior:lateral gastrocnemius co-contraction was significantly greater in older adults throughout the entire gait cycle ( $p = 0.010$ ), during the stance phase ( $p = 0.016$ ), and in the swing phase ( $p = 0.011$ ), when walking over uneven surfaces [69]. Commonly, adulthood is divided into young adulthood (20–39 years), middle adulthood (40–59 years), and old age ( $\geq 60$  years) [70]. Although older adults may exhibit greater muscle co-contraction, the participants included in this review were considered young and middle-aged adults, with the average age falling within the young adult category. Thus, we suggest that age had no impact on the outcomes presented in the included studies.

#### 4.2. Sex differences

Most of the studies included in this review (86.6%) evaluated participants of both sexes, except for one study that assessed females only [22], and another study that exclusively evaluated males [34]. Although research studies have reported conflicting results between males and females in terms of hop task performance [71,72], consistent findings regarding Q:H co-contraction indicate differences between the sexes, with females exhibiting increased levels of co-contraction during tasks such as walking [69,73], landing [74] and cutting [52,74,75], regardless of their status (healthy or injured). In this review, only one study directly compared the magnitude of co-contraction between sexes [32]. The findings reported by these authors align with previous research, indicating that females displayed higher levels of co-contraction compared to males, irrespective of the limb assessed. Thus, we strongly suggest for future studies to carefully consider sex differences in muscle co-contraction when assessing these outcomes.

#### 4.3. Associated injuries

The management of associated injuries varied among the included studies, with approximately half addressing concomitant injuries. Reconstruction of the ACL often involves concurrent meniscal procedures [76], and while minor concomitant injuries may not significantly affect functional outcomes [77], grade II and III medial collateral ligament (MCL) injuries [78] and grade II or higher chondral damage [79] may lead to poorer outcomes. However, no study has investigated the impact of concurrent injuries in muscle co-contraction. Thus, future research could explore potential grade-related differences in concomitant injuries and their effect on the simultaneous activation of antagonist muscles.

#### 4.4. Type of surgery

In this systematic review, studies included various types of grafts in their analyses, and although recent research suggests that the choice of autograft is not significantly correlated with several outcome measures, including the single-leg hop test [80–82], there is a lack of studies investigating muscle co-contraction between individual that underwent ACLR with different graft types. Therefore, future studies should explore whether there is a relationship between graft choice and co-contraction during functional tasks, as donor muscles may reduce their contribution to muscular support [83].

#### 5. Limitations

It is important to acknowledge the inherent limitations within this review. First, it is worth noting that studies reporting the magnitude of co-contraction activation between ACLR individual limbs and healthy controls are highly heterogeneous. Secondly, certain studies were excluded from the analysis due to the absence of reported EMG assessments, as they measured co-contraction solely based on the time required to perform the task. Additionally, studies that exclusively measured the CCR were also excluded, since CCR calculates the relative activation of antagonistic muscle pairs without considering the magnitude of activation. Consequently, muscles with different activation magnitudes could exhibit the same co-contraction level [63]. This needs to be considered when comparing this research with other reviews that include a different method to measure co-contraction. Thirdly, none of the studies included in this review reported pre-injury co-contraction measurements. This may be of interest, since an altered Q:H co-contraction is suggested to potentially contribute to an increased risk of ACL injury [52]. Finally, co-contraction analysis involves technical limitations in surface EMG measurements, including factors like subcutaneous tissue depth, skin movement, muscle crosstalk, and background noise [18].

#### 6. Conclusions

The findings from this systematic review suggest that most individuals who have undergone ACLR exhibit an increase in the magnitude of co-contraction between quadriceps and hamstrings muscles during functional tasks. These neuromuscular strategies adopted to enhance stability can have deleterious effects on various physiological functions and lead to an increase in joint compressive force, which, subsequently, plays a critical role in the development of joint degeneration.

Additional research is required to understand how the magnitude of co-contraction activation behaves in adjacent joints (hip and ankle) of ACLR individuals and its influence on knee biomechanics, while considering the confounding variables (potential bias) identified in this review. These findings have significant implications for researchers and clinicians involved in investigating neuromuscular strategies in ACLR patients, understanding joint degeneration progression, and optimizing rehabilitation strategies.

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#### CRediT authorship contribution statement

**Ricardo Paredes:** Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. **Carlos Crasto:** Data curation, Formal analysis, Methodology, Writing – review & editing. **Antônio Mesquita Montes:** Formal analysis, Methodology, Writing – review & editing, Data curation. **José L. Arias-Burúa:** Formal analysis, Methodology, Supervision, Writing – review & editing, Data curation.

#### 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.

#### Appendix A. Supplementary material

Supplementary material to this article can be found online at <https://doi.org/10.1016/j.knee.2024.05.005>.

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