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REVIEW ARTICLE

PRE-SURGERY EXERCISE AND POST-OPERATIVE PHYSICAL FUNCTION OF PEOPLE UNDERGOING KNEE REPLACEMENT SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Objective: **To summarize the evidence regarding the effectiveness and dose-response characteristics of pre-operative exercise programmes on post-operative physical function following total knee arthroplasty.**
Data sources: **CINAHL, Cochrane Library, PubMed, SPORTDiscus and EMBASE.**
Study selection: **Randomized controlled trials were eligible if they provided full description of physiological stress (i.e. mode, frequency, intensity and duration).**
Data extraction: **Data extraction and evaluation were performed by one reviewer. Methodological quality of the selected studies was assessed using the Physiotherapy Evidence Database scale.**
Data synthesis: **Twelve candidate studies were identified, but only 3 papers satisfied all inclusion criteria: 2 studies evaluated the effect of resistance training and 1 trial investigated proprioceptive training. The latter study elicited significantly enhanced post-operative gains in function for indices of standing balance (overall stability index: Hedges' $g = -1$; anteroposterior stability index: Hedges' $g = -1.15$; 6 weeks post-surgery). Results of meta-analysis based on the findings of 2 studies showed that, compared with controls, prehabilitative exercise involving resistance training offered no additional gains in isometric quadriceps muscle strength at 6 and 12 weeks post-operatively.**
Conclusion: **Despite a potential for efficacy of exercise-based conditioning, this review highlights the scarcity of robust dose-response evidence to guide the formulation of total knee arthroplasty prehabilitation effectively.**

Key words: arthroplasty, exercise, knee osteoarthritis, prehabilitation.

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Total knee arthroplasty (TKA) is an elective surgical procedure, which is performed when normal function of the knee is limited by disease (1, 2). This orthopaedic operation is a cost-effective intervention for patients with advanced knee osteoarthritis (OA) (3), with a cost-effectiveness ratio ranging from €1,276 to USD 18,300 per quality-adjusted life year gained (4, 5). However, the costs of surgery and subsequent rehabilitation generate a growing economic burden on healthcare systems globally (6, 7).

Patients experience reduced pain symptoms, and improved perceived function and health-related quality of life (QoL) following TKA surgery (7, 8). Nevertheless, they often have considerably impaired muscle strength (8–13), postural stability (14), and knee joint proprioception (9, 15, 16). Full recovery of muscle strength and physical function to a normal level is rare (10, 12) and impairments may persist several years after surgery (17–20). In addition, these impairments can lead to reduced balance and movement control (21, 22) and a greater risk of falling (22, 23). Neuromuscular performance capabilities are altered significantly in people with arthritis, and impairments are evident pre-operatively (24). Alterations in neuromuscular performance may take the form of inhibition (25–27) or aberrant facilitation (26) of the unaffected musculature surrounding an injured joint, and have been particularly observed as weakness of the quadriceps muscles (27).

The beneficial effects of exercise are well documented, and international guidelines recommend exercise as a treatment to reduce pain and improve physical function in patients with OA (28–31). However, specific guidelines regarding optimal dosage of exercise mode, frequency, duration and intensity remain elusive (30, 32). Preoperative physical function (including muscular function indices) has been identified as the strongest determinant of postoperative pain and functioning (33–35). Consequently, beneficial exercise-mediated effects on pain and function in patients with OA have provoked interest in pre-operative exercise intervention programmes. Reducing clinical impairments that are apparent prior to surgery might facilitate the ultimate goal of improving post-surgical function and accelerating recovery.

Recent systematic reviews and meta-analyses agree there is no definitive evidence as to whether a pre-operative exercise programme accelerates post-surgical recovery of physical function (36–40). These reviews focused on the effect of certain types of strengthe-

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ning, flexibility, aerobic or balance exercise; however, precise exercise prescription information pertaining to physiological stress and dosage within the included studies was either missing or inconsistently reported. Incomplete information about dosage inevitably hinders understanding of response characteristics. The literature suggests that the intervention exercise programmes are likely to have varied substantially in the type of exercise, intensity, frequency, duration and verification of its delivery.

The aim of this systematic review and meta-analysis was to evaluate post-operative effectiveness and dose-response characteristics (as appropriate, depending on the availability of evidence) of specific pre-operative exercise programmes, which detailed the applied physiological stress (i.e. mode, frequency, intensity and duration) in people undergoing TKA. The review addresses a knowledge gap regarding optimal exercises types and dosages, as previous reviews have not explicitly evaluated dosage-response (36–40). Evidence from this review will facilitate understanding of the benefit and hierarchy of importance of particular pre-operative exercise modalities in this patient population.

METHODS

Data sources

A comprehensive review of the existing literature was undertaken using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Five bibliographic databases were searched for results published before January 2015: CINAHL; Cochrane Library; PubMed; SPORTDiscus; and EMBASE. For each database, individual and comprehensive search strategies were constructed using subject-heading mapping. The literature search included search terms such as: knee, joint, arthroplasty, replacement, exercise, physiotherapy, prehabilitation, rehabilitation, neuromuscular, sensorimotor, pre-operative and postoperative. All terms were searched as keywords (MeSH) and/or text words. In order to identify randomized controlled trials (RCTs), the following search terms were used: randomized controlled trials, clinical trials, placebo, control* and random*. One of the authors (MP) identified and screened relevant titles and abstracts following the systematic literature search. Consensus on inclusion of the study by Gstöttner et al. (41) was reached by discussion between 2 authors (MP and NG).

Study selection

Publications were eligible if: (*i*) the post-operative effect of an exercise-based prehabilitation programme was assessed; (*ii*) the study provided full description of physiological stress applied during the intervention; (*iii*) physical function was evaluated (self-reported and performance-based); (*iv*) all participants were diagnosed with OA (in one or both knees) and awaiting TKA (trials including people with knee and hip OA, separate data on the knee were available); (*v*) the study was written in English or German; and (*vi*) an RCT compared an exercise intervention with no-intervention or standard treatment. The exercise-based rehabilitation programme was defined as a specific, land-based, lower extremity activity that was applied for more than one session including strengthening, flexibility, neuromuscular, proprioception and/or aerobic activities.

Data extraction

Data extraction from published data was performed (by MP) and if required, authors were contacted for further information. Customized data extraction forms were used to systematically collect information on the exercise type; duration; intensity; frequency; number of supervised sessions and programme compliance.

Assessment of risk of bias

Methodological quality of the included articles was assessed using the original 11-item criteria of the Physiotherapy Evidence Database (PEDro) scale (42). Based on previous reviews (43, 44), the methodological quality rating system was interpreted as follows: a PEDro score of 9 or more indicated "excellent" quality, 6–8 "good" quality, 4–5 "fair", and less than 4 indicated "poor" quality.

Quantitative data synthesis

Meta-analysis was completed for studies with similar physical function outcomes and involving interventions with comparable conditioning dosage. The meta-analysis was conducted using the "metan" procedure in Stata (Stata Statistical Software 2013, College Station, TX, USA: StataCorp LP). Raw mean post-intervention inter-group differences were employed, as the outcome measures were the same. Statistical significance level was set at $p<0.05$. The study effect size was calculated from the raw mean difference between groups and the associated pooled standard deviation using Hedges' *g* (*g*) (0.20, 0.50, >0.80 for small, moderate and large changes, respectively (45)). From the study pooled standard deviation, the inverse of the variance provided the study weight (and thus the percentage study weight). A qualitative review of studies was performed when evidence could not be pooled.

RESULTS

Study selection

The literature search yielded 6,799 references, of which 67 were unique trials. Twelve studies were identified as potential candidates, but only 3 papers satisfied all criteria including description of exercise mode and physiological stress: Gstöttner et al. (41) ($n=38$), McKay et al. (46) ($n=22$), and van Leeuwen et al. (47) ($n=22$). Although 9 candidate studies (48–56) included information on intervention duration and frequency the intensity applied was either not stated at all or not in sufficient detail, which is necessary to replicate an intervention programme (57). Most of the information from these 9 excluded articles has been described in previously conducted reviews (37–40,

43) and their results are therefore not reported here. As such, these studies will only be used to contextualize the findings of this review. In addition, the Villadsen et al. (58) study was excluded as it included patients with knee and hip OA, but did not provide separate hip and knee raw data. Fig. 1 schematically illustrates the search strategy used to identify trials for inclusion.

Risk of bias within studies

PEDro scores ranged between 5 and 7 out of a possible maximum total of 10 points. Two of the 3 studies have "good" methodological quality, with PEDro scores of 6 (41) to 7 (46). As it was not possible to blind the participants or the therapist from the intervention programme, all studies scored 0 for these criteria. Table I provides detailed information on the methodological quality of the studies.

Table I. Methodological quality of included randomized controlled trials

	PEDro criterion											
Author, year	1	2	3	4	5	6	7	8	9	10	11	Total
Gstöttner et al. (41)	✓	✓	✓	×	×	×	×	✓	✓	✓	✓	6
McKay et al. (46)	✓	✓	✓	✓	×	×	×	✓	✓	✓	✓	7
van Leeuwen et al. (47)	✓	×	×	✓	×	×	✓	✓	×	✓	✓	5

Note: PEDro Scale:
1. Eligibility criteria were specified
2. Subjects were randomly allocated to groups
3. Allocation was concealed
4. The groups were similar at baseline
5. There was blinding of all subjects
6. There was blinding of all therapists
7. There was blinding of all assessors
8. Measures of at least 1 key outcome were obtained from more than 85% of the subjects
9. Subjects for whom outcome measures were available received the treatment or control condition
10. Results of between-group statistical comparisons are reported
11. The study provides both point measures and measures of variability

Criterion 1 is not included in the total score

Key*:* ✓ yes × no.

Participant characteristics

The mean age of participants in the included studies was 67.5 years (range 60.6–72.8 years) and the mean body mass index (BMI) was 30.0 (range 27.4–35.0). In addition, a mean of 59.2% were women (range 30.0%–88.8%). All studies included participants diagnosed with severe knee OA, except the trial conducted by McKay et al. (46), which does not indicate the degree of severity of OA.

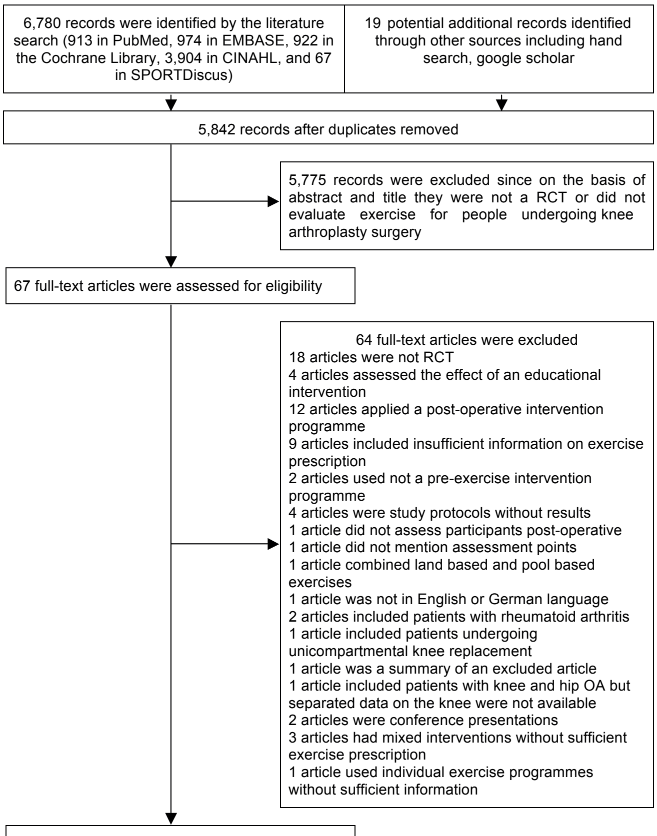

Fig. 1. Identification of trials for inclusion in the meta-analysis. RCT: randomized controlled trial; OA: osteoarthritis.

Content and design of interventions

Pre-operative intervention exercise programmes were based on isotonic resistance and proprioception training. Table II summarizes the exercise modalities and outcome measurements employed. McKay et al. (46) and van Leeuwen et al. (47) based their intervention programme on bilateral quadriceps strength exercises. Both studies started their exercise programmes 6 weeks prior to surgery. McKay et al. (46) delivered the programme 3 days/week using 2 sets of 8 repetitions, whereas participants in the study by van Leeuwen et al. (47) performed the programme 2–3 days/week, starting with 3 sets of 15 repetitions. van Leeuwen et al. (47) commenced their programme by systematically adjusting participants' exercise load according to their ability to perform 3 sets of 15 repetitions with a selected weight. If participants performed more or less than 15 repetitions then the weight for the next set was modified by ~3% per repetition. This study avoided 1 repetition maximum (1 RM) testing, due to potentially adverse pain responses, which could have led to early withdrawal from training. Over time, the training programme ensured a progressive overload by decreasing repetition and increasing weight intensity. However, the study by van Leeuwen

Table II. Content and design of interventions

Study	Participant characteristics (n, age (years) mean (SD); BMI (kg/m^2) Mean (SD)	Programme type	Supervised sessions: group (*n*) or individual	Supervised sessions conducted by:	Intervention period	Frequency of supervised classes	Unsupervised home exercise programme	Exercises group content (including intensity if available)	Control group content	Compliance with exercise programme	Outcome measurements
Gstöttner et al. (41)	*n* = 38 TG: *n* = 18, age: 72.8 (range 65–78 years); BMI: mean 27.4. CG: *n* = 20, age: 66.9 (range 61–75 years); BMI: mean 28.2	Proprioceptive training	Not described by author	PT	6 weeks	2–3 days/ week	Daily (exercise group content)	Warm up: 5–10 min heel, toe and fast-paced walking; stretches of the gastrocnemius muscles, quadriceps femoris muscles, biceps femoris muscles, gluteal muscles & abductor muscles, each side 3 × for 20 s. Proprioceptive training (barefoot) bilateral exercises starting with eyes opened and repeated by eyes closed: forward/back slide, step forward/back 10–15 × – with gradually increasing speed and ROM, single leg stand – maintain for 10 s, squats – maintain for 10 s. Progression: hard floor to different mats of varying heights and compliance characteristics	Not described by author	Not described by author	Biodex Stability System (Balance) 60 m walk test Stair climb test (ascend/descend) WOMAC KSS
McKay et al. (46)	*n* = 22 TG: *n* = 10, age: 63.5 (4.9); BMI: 35.0 (6.1) CG: *n* = 12, age: 60.6 (8.1); BMI: 33.8 (7.1)	Resistance training	Not described by author	Trained kinesiologist	3 days/week for 6 weeks	3 days/ week of approximately 30 min	Not described by author	Lower-body resistance training Warm up: 10 min aerobic exercises on either treadmill, stationary exercise bike, rowing ergometer or recumbent stepper. Bilateral resistance exercises: standing calf raise (only with body weight), seated leg press, leg curl, knee extension. 2 × 8 reps Intensity: Starting at 60% of their 1 RM Progression: from 60% of their 1 RM increase by 1–2 kg/week	Upper-body resistance training Warm-up: 10 min aerobic exercises on either treadmill, stationary exercise bike, rowing ergometer or recumbent stepper. Bilateral resistance exercises: seated latissimus dorsi [lat] pull, chest press, elbow flexion, elbow extension. 2 × 8 reps Intensity: Starting at 60% of their 1 RM Progression: from 60% of their 1 RM increase by 1–2 kg/ week	TG: 98% CG: 93%	Dynamometer (maximal isometric extensor strength) 50 feet walking test Stair climb test (ascent/ descendent) WOMAC SF-36 Arthritis self-efficacy scale
van Leeuwen et al. (47)	*n* = 22 TG: *n* = 11, age: 71.8±7.5; BMI: 27.9 (4.6) CG: *n* = 11, age: 69.5 (7.1); BMI: 27.9 (3.1)	High intensity resistance training plus standard training (CG)	Not described by the author	PT	2–3 days/ week for 6 weeks 12±2 sessions	Not described by the author	2–3 days/ week Step-up and squat exercises (only TG)	Standard training plus bilateral high intensive resistance training (leg press 1-leg, step up 1-leg, squat and leg extension 1-leg) Intensity: not 1 RM, weights were adjusted to the patients' abilities in relation to the number of repetition. First training (3 × 15 reps), if either more or less than 15 reps were performed, the weight for the next set was adjusted with ~3% per repetition. Progression: Week 1: 3 × 15 reps Week 2: 3 × 12 reps Week 3: 4 × 12 reps Week 4: 3 × 10 reps Week 5: 4 × 10 reps Week 6: 4 × 8 reps	Standard training: information and advice, exercise of ADLs, training on how to use walking aids, maintenance of mobility, aerobic training (cycling, walking), no resistance training 11 ± 4 sessions	Exercises log (including adherence, alteration and intensity of the exercise programme)	Dynamometer (maximal voluntary torque -extensor and flexor muscles, voluntary activation-electrical stimulation) 5 × sit to stand 6-min walk test Stair climb test (ascent/ descendent) WOMAC

n: number of participants randomized to each group. SD: standard deviation; TG: treatment group; CG: control group; PT: physiotherapist, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, KSS: Knee Society Score; SF-36: Medical Outcomes Study Short Form 36.

et al. (47) did not report participants' exact intensity level upon completion of the training regime. In total, the resistance-training group completed 12±2 training sessions (range 11–17) and finished the programme with 4 sets of 8 repetitions. Three participants out of 11 participants in the intervention group required small changes to their intensity level due to pain, but detailed information regarding these changes was not reported. The study by McKay et al. (46) started the training regime at 60% of participants' 1 RM and progressed intensity by 1–2 kg/week. All participants demonstrated training progression from baseline to follow-up, with mean increases in maximum training load of 33% (range 17%–67%) for leg press, 49% (range 0%–113%) for leg curl, and 86% (range 0%–167%) for leg extension. Similar to the study by van Leeuwen et al. (47) the research by McKay et al. (46) did not provide the exact level of participants' training intensity when completing the intervention.

Gstöttner et al. (41) based their intervention programme on bilateral proprioception training 6 weeks prior to surgery. Each exercise was performed 10–15 times and the programme progressed from performances on the hard floor to different mats of varying height and material compliance characteristics. In addition, the exercises started with eyes open and were repeated with eyes closed. However, the trial by Gstöttner et al. (41) does not report further details on how many people were able to progress and to what level.

In addition to their supervised interventions, 2 of the trials also encouraged their participants to perform exercises at home (41, 47). Participants in the van Leeuwen et al. (47) study completed step-up and squat exercises 2–3 days/week; however, the number of repetitions and participant adherence were not reported. The study by Gstöttner et al. (41) engaged participants in daily home-based proprioception training.

Synthesis of results

The primary outcome of isometric quadriceps strength, as an established performance-based measure, offered by McKay et al. (46) and van Leeuwen et al. (47) facilitated limited scrutiny by meta-analysis of the influence of pre-surgery conditioning on post-operative outcome. However, the secondary outcome measures from the studies included in this review proved too varied to permit pooling of results and quantitative analysis by meta-analysis. Table III summarizes Hedges' *g* and confidence interval results for each self-reported outcome measurement used for assessing the relative effect between groups at pre-determined study' end-points. Similarly, Tables IV shows values of the objective instruments of each individual study.

Table III. Relative effect sizes (Hedges' g) on resistance and proprioception training: self-reported measures[a]

Study type	Study	Outcome measure	Item	Group	Baseline Mean (SD)	6-week post-operative Mean (SD)	12-week post-operative Mean (SD)	Hedges' *g* 6 week	95% CI 6 week	Hedges' *g* 12 week	95% CI 12 week
Resistance training	van Leeuwen et al. (47)	WOMAC	Total score[b,c]	TG	64 (11)	70 (16)	83 (15)				
				CG	67 (11)	79 (11)	93 (4)	−0.63	−23.9, 5.9	−0.86	−22.6, 2.6
Resistance training	McKay et al. (46)	WOMAC	Pain[d]	TG	10.80 (2.20)	5.60 (2.72)	4.40 (3.20)				
				CG	11.92 (3.58)	4.92 (4.50)	3.58 (4.40)	0.18	−2.9, 4.3	0.21	−3.3, 4.9
		WOMAC	Function[d]	TG	33.70 (11.80)	18.10 (11.85)	13.10 (11.56)				
				CG	40.25 (4.99)	19.17 (15.01)	14.33 (15.42)	−0.08	−14.3, 12.1	−0.09	−15.9, 13.5
		SF-36[e,g]	PCS[c]	TG	26.85 (7.01)	31.79 (8.25)	41.25 (10.06)				
				CG	24.24 (4.52)	29.80 (6.71)	34.83 (9.78)	0.27	−5.3, 9.2	0.65	−3.9, 16.8
Proprioception training	Gstöttner et al. (41)	WOMAC	Pain[f]	TG	2.98 (1.6)	1.3 (1.1)					
				CG	4.4 (1.9)	0.98 (0.99)		0.31	−0.4, 1.04		
		WOMAC	Stiffness[f]	TG	3.1 (2.4)	1.5 (1.5)					
				CG	4.7 (1.6)	1.1 (1.5)		0.26	−0.6, 1.4		
		WOMAC	Function[f]	TG	2.0 (1.4)	1.2 (1.2)					
				CG	3.7 (1.8)	1.9 (1.0)		−0.64	−1.5, 0.1		
		KSS[c]		TG	55.5 (17.2)	82.5 (19.2)					
				CG	47.4 (6.9)	80.6 (17.5)		0.10	−10.8, 14.6		
		KSS	Function[c]	TG	72.7 (15.1)	74.3 (14.6)					
				CG	70.6 (17.8)	73.9 (15.9)		0.03	−10.3, 11.1		

[a]These figures are calculated on the assumption of sample independence without consideration of inflation and deflation. Values are represented as mean and standard deviation (SD).
[b]WOMAC total score: pain, stiffness and function subscale.
[c]Scores were transformed to a 0–100 scale, where a 100 score indicates the best quality of life.
[d]Items were rated using a 5-point Likert scale (0–4), with lower scores expressing lower symptom or disability level.
[e]SF-36 PCS: 36-item Short Form Health Survey – physical component summary.
[f]Items were rated using a 11-point scale, with 0 indicating no symptoms or disability and 11 extreme symptoms or disability.
[g]Study included the Arthritis Self-efficacy scale and Short Form-36 mental component summary. The results of these measurements will not be mentioned, as this is not within the scope of this review.
CI: confidence interval.

Table IV. Relative effect sizes (Hedges' g) on resistance and proprioception training – objective measures[a]

Study type	Study	Outcome measure	Side	Group	Baseline Mean (SD)	6-week post-operative Mean (SD)	12-week post-operative Mean (SD)	Hedges' *g* 6-week	95% CI 6-week	Hedges' *g* 12-week	95% CI 12-week
Resistance training	van Leeuwen et al. (47)	Double torque, Nm[b]									
			Affected side	TG	49 (13)	34 (10)	39 (12)	−0.09	−12.9, 10.9	0	−13.9, 13. 9
				CG	51 (19)	35 (13)	39 (14)				
			Unaffected side	TG	53 (12)	50 (14)	51 (16)	0	−16.04, 16.04	0.07	−14.9, 16.9
				CG	50 (15)	50 (17)	50 (13)				
		Voluntary activation, %[b]	Affected side	TG	79 (13)	79 (9)	80 (10)	−0.67	−12.8, 2.8	−1.09	−19.9, −0.1
				CG	80 (13)	84 (4)	90 (8)				
			Unaffected side	TG	75 (19)	80 (13)	83 (11)	−0.74	−19.3, 3.3	−0.87	−17.9, 1.9
				CG	84 (12)	88 (6)	91 (6)				
		Maximum voluntary torque flexion, Nm[b]	Affected side	TG	40 (22)	37 (18)	42 (17)	0.06	−17.1, 19.1	−0.40	−29.4, 13.4
				CG	46 (25)	36 (16)	50 (23)				
		Maximum voluntary torque flexion, Nm[b]	Unaffected side	TG	43 (29)	47 (27	47 (26)	– 0.28	−37.7, 21.7	−0.31	−36.1, 20.1
				CG	57 (33)	55 (30)	55 (26)				
		5×sit to stand test, s[c]		TG	12.6 (2.6)	13.3 (3.4)	11.8 (1.8)	0.26	−2.4, 4.03	0.60	−0.8, 2.8
				CG	12.3 (2.7)	12.5 (2.5)	10.8 (1.5)				
		Stair climb test, s[c]		TG	12.4 (3.1)	20.9 (10.8)	12.8 (3.4)	0.34	−6.8, 13.4	−0.50	−4.1, 1.5
				CG	12.9 (3.8)	17.6 (7.5)	14.1 (0)				
		6-min walk test, m[b]		TG	453 (81)	380 (109)	456 (62)	−0.60	−165.9, 45.9	−0.72	−142.3, 28.3
				CG	460 (52)	440 (87)	513 (97)				
Resistance training	McKay et al. (46)										
		50 foot walk, s[c]		TG	16.88 (16.14)	14.23 (7.55)	11.80 (5.66)	0.20	−4.4, 6.7	−0.005	−4.5, 4.4
				CG	14.21 (5.36)	13.11 (3.30)	11.82 (2.97)				
		Stair climb test, s[c]		TG	34.53 (29.51)	30.53 (24.85)	26.99 (26.73)	0.20	−14.8, 22.4	0.25	−15.1, 24.7
				CG	33.31 (27.42)	26.72 (12.05)	22.18 (10.98)				
Propriception training	Gstöttner et al. (41)	60 m, s[c]									
				TG	53.5 (18.2)	56.8 (17.7)		0.36	−4.6, 14.6		
				CG	50.5 (11.8)	51.8 (9.9)					
		Stairs climb test – ascend, s[c]		TG	29.0 (11.6)	33.8 (13.8)		0.34	−3.9, 11.5		
				CG	28.3 (5.3)	30.0 (8.4)					
		Stairs climb test – descend, s[c]		TG	25.1 (9.1)	34.6 (17.4)		0.31	−5.3, 13.7		
				CG	24 (7.8)	30.4 (10.2)					
		OSI[c]		TG	3.1 (1.4)	2.2 (0.7)		−1	−1.2, −0.2		
				CG	3.4 (0.93)	2.9 (0.7)					
		APSI[c]		TG	2.5 (1.0)	1.7 (0.4)		−1.15	−0.9, −0.2		
				CG	2.6 (0.7)	2.3 (0.6)					
		MLSI[c]		TG	2.1 (1.1)	1.6 (0.7)		−0.47	−0.7, 0.1		
				CG	2.3 (0.8)	1.9 (0.6)					

[a]These figures are calculated on the assumption of sample independence without consideration of inflation and deflation. Values are represented as mean and standard deviation (SD).
[b]Higher score indicates better results.
[c]Lower score indicates better results.
OSI: overall stability index; APSI: anteroposterior stability index; MLSI: mediolateral stability index; CI: confidence interval.

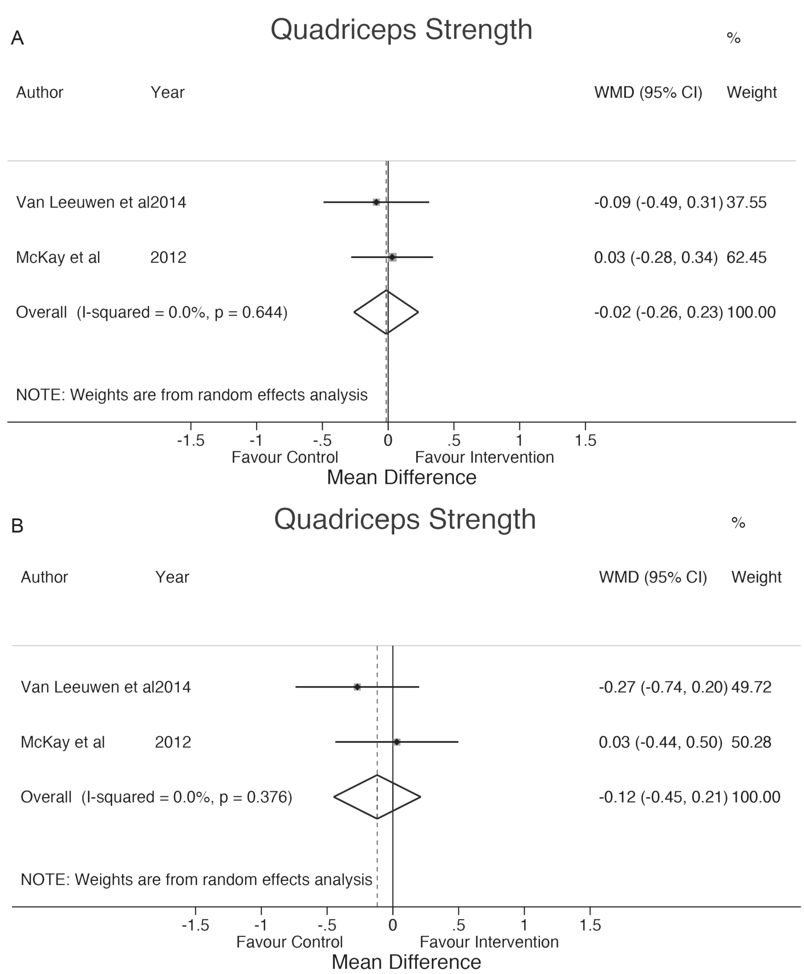

Fig. 2. Forest plot of the effect of pre-surgery resistance training on isometric quadriceps muscle strength (A) 6 weeks and (B) 12 weeks post-operatively. Weights are from a random-effects analysis. Effects are shown with 95% confidence interval (95% CI). WMD: weighted mean difference.

Results of the meta-analysis of the primary outcome (Fig. 2) revealed that, compared with controls, prehabilitative exercise involving resistance training offered no additional gains in isometric quadriceps muscle strength at 6 and 12 weeks post-operatively. Effect size calculations (g) for secondary outcomes presented in Table III demonstrate that resistance training had small to moderate effects on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (pain, function, total score) and Medical Outcomes Study Short Form 36 (SF-36) outcomes at 6 weeks and small to large effects at 12 weeks post-operatively. Table IV shows that effect sizes for physiological measures (double torque, voluntary muscle activation, maximal voluntary torque) and physical performance measures of function (5 times sit to stand test, stair climb test, 60 m walk test, 6 min walk test) illustrated small to moderate effects at week 6 and small to large effects at week 12 post-operatively.

Proprioceptive exercise training elicited significantly enhanced post-operative gains in function for indices of standing balance (overall and antero-posterior stability index) 6 weeks after surgery (Table IV). Moderate effect sizes for physical performance measure of function were observed (Table IV). Similarly, moderate effects were observed for pain, function and stiffness subscales of the WOMAC, while small effects were seen for the Knee Society Score (KSS) at 6 weeks (Table III).

DISCUSSION

This systematic review located 3 RCTs focusing on the effect of pre-operative exercise (which described the applied physiological stress sufficiently) on post-operative TKA function. Pooling of studies' data indicate that the trials presented expected patterns for perceived functional recovery following TKA. Physiological measures and physical performance measures of function demonstrated anticipated functional decline 6 weeks post-surgery and tendency of improvement at week 12. However, prehabilitative exercise involving resistance training offered no additional gains in isometric quadriceps muscle strength at 6 and 12 weeks post-operatively, but prehabilitative exercise involving proprioceptive training elicited significantly enhanced post-operative gains in function for indices of standing balance.

Overall, the included studies demonstrated "good" methodological quality according to the PEDro scale, with the main limitation being lack of blinding of participants and therapists. In addition, 2 of the studies were not able to blind the assessors; potentially presenting a source of bias, which may have influenced study findings. However, the sample sizes of the included studies were relatively small, indicating that they may have insufficient statistical power to prevent occurrence of a type II error and identify subtle changes in physical function. A further factor that may have influenced the results in the studies on resistance training is that both studies (46, 47) allowed their control group to perform exercises. Even though a placebo intervention would have been ideal, a study design involving a credible non-exercise control group was deemed unrealistic by the authors. This option may have potentially prevented functional decline in the control group during the pre-operative period as observed in previous studies (54, 59, 60). Another methodological limitation of the included studies was that although the papers detailed the applied physiological stress (i.e. mode, frequency, intensity and duration) of pre-operative exercise programmes, heterogeneity of exercise type and intensity, as well as lack of information regarding verification of exercise delivery hindered further analysis that might delineate a possible dose-response relationship.

Resistance training

Quadriceps strength is one of the largest contributing factors to physical function of people with knee OA (35, 46, 61); however, the pre-operative resistance training applied in the studies reviewed here failed to demonstrate beneficial effects in increasing isometric quadriceps strength, reducing functional limitations, and accelerating post-operative recovery. Nevertheless, several aspects need to be considered with respect to the conclusion that can be drawn from the included studies (46, 47).

The study conducted by McKay et al. (46) followed the recommendations of the ACSM's guidelines (57) for older adults and highly deconditioned persons, wherein an exercise regime of ≥1 set of 10–15 repetitions of moderate intensity (i.e. 60%–70% 1 RM) should be applied. However, it appears that the overall exercise conditioning dosage had not been sufficiently potent (57, 62). Results of a previous study indicate that 8 weeks of resistance exercise are required to produce large improvements (effect sizes ranging between 0.64–3.13) in self-reported pain and function, and objective measures including walking time and muscle torque of patients with knee OA (14). Therefore, the 6-week resistance training protocols of the studies included for review may not have been long enough to achieve improvements in physical function, which can be maintained through the post-operative period. In addition, to improve muscle strength, muscle mass and (to an extent) endurance, programmes of conditioning focusing on regular exposure to stimuli for adaptation involving a resistance of ~ 60% to 80% of the individual's 1 RM and titratable progression are required (57, 62). The exercise stimulus of 60% of 1 RM prescribed by McKay et al. (46) was at the lower end of this intensity range, which may still potentially confer beneficial physiological effects, but could be below the threshold necessary to elicit functional improvements.

Similar findings were reported in the systematic review of Hoogeboom et al. (37). Hoogeboom et al. (37) estimated the exercise intensity of the included studies by calculating the metabolic equivalents (METs) using the Compendium of Physical Activities (63) and multiplying the intensity in METs by time spent exercising. The review found that only one study out of 9, focusing on participants undergoing TKA, reported a supervised exercise dose greater than the recommended weekly amount of physical activity (10 METs/h/week).

Furthermore, even though there is evidence that people with arthritis appear to have negative alterations in their neuromuscular performance capabilities, the level of deconditioning prior to TKA surgery is still not known. People with severe OA demonstrate cardiorespiratory deconditioning with reduced peak oxygen consumption levels (12.8 ± 3.7 ml/kg/min) (64). Although cardiorespiratory fitness of asymptomatic controls in the knee sub-population of the study was generally low, VO_2 peak of individuals with knee OA was, in mean, a worrying 27% lower (65). As cardiorespiratory function declines, it is plausible that neuromuscular deconditioning occurs in tandem or shortly thereafter. Given that the level of deconditioning in people awaiting TKA is not known, and cannot be ascertained with certainty from the current evidence in the literature, it is plausible that protocols of conditioning involving relatively intensive exercise (>75% RM (66)) would be required to potentially elicit physiological gains, maintain functional capacity in the "lead-up" to surgery and counter the stressor of TKA surgery.

Exercise programme compliance in the prehabilitation study of McKay et al. (46) was very good (98%) with all participants able to increase their workload over time. This result is comparable to research that showed that progressive explosive-type resistance training is feasible in people awaiting hip replacement surgery, with a high (93%) level of adherence and acceptable exercise-related pain (67). Similar adherence has been reported for high-intensity resistance training in patients with medial compartment knee OA and malalignment (68). Therefore, it is speculated that higher intensity training could potentially be tolerated by this clinical population. Monitoring intervention dosage is essential to achieve and maintain ideal exercise dosage (69). McKay et al. (46) increased the intensity by 1–2 kg/week, as tolerated by the participant, but this study did not perform weekly measures of 1 RM for accurately titrated progression to ensure sufficient workload dosage. The study conducted by van Leeuwen et al. (47) fails to report the exact information concerning participants' compliance, intensity progression, adjustments and verification of dosage delivery, and hence, judgment on optimal exercise stress is not possible.

A further aspect that could have influenced the reduced effects illustrated in the studies is arthrogenic muscle inhibition (AMI), which is a presynaptic reflex inhibition affecting the musculature surrounding a joint following damage to the structure (70). Quadriceps AMI contributes to muscle atrophy, and can delay or even prevent effective strengthening (27). Notably, more than half of quadriceps strength loss can be explained by an increase in AMI 3–4 weeks following TKA surgery (71). Furthermore, researchers have observed higher quadriceps activation deficits in women (64, 72) and in people with moderate (stage II) OA, compared with those with greater (stage IV) deterioration (73). In addition, swelling is identified as a significant factor influencing quadriceps AMI (26, 27, 74), and is often perennial in arthritic conditions (27). Swelling can also increase the intra-articular pressure (IAP) and can increase the discharge of neurones with large, myelinated axons (group II afferents) (27). Therefore, the degree of AMI is regulated according to the joint angle and the amount of swelling that is present; the greater the swelling, the stronger the relationship between joint angle and inhibition (27). Studies point out that a knee angle of 30–50° has a low IAP, and subsequently, this position is recommended to allow more effective quadriceps strengthening (75–77). However, some studies argue that although exercising the quadriceps in an inner range may indeed reduce the IAP, it may also result in ineffective training due to the knee not being maximally contracted (78, 79). Nevertheless, considering the length-tension relationship (80), it is likely that a more favourable degree of myofilament and contractile protein overlap occurs at 45° rather than 25° (81), hence an increase in muscle specificity may take place. The studies included in this proposed review do not report information pertaining to the amount of swelling exhibited, and the knee angles, which have been used during the exercise intervention programmes. Nonetheless, the aforementioned aspects may be important to consider when designing an adequately dosed exercise protocol, which aims to overcome neuromuscular alterations in patients undergoing TKA and improve physical function post-operatively.

Proprioceptive training

The application of 6 weeks' pre-operative proprioceptive training conducted by Gstöttner et al. (41) led to improvements in standing balance. However, the results of this study should be interpreted with caution because participants in the control group were, in mean, 5.9 years younger than those in the treatment group. This is important because muscle strength declines, in mean, by 4.5%–5% every 5 years after the age of 65 years (82, 83). Crucially, impairments in muscle strength correlate with balance (84) and risk of falls (85). It is possible that a group in which age-related declines in muscle function and balance might be more apparent may demonstrate a greater response to proprioceptive training.

The proposed review illustrates that the hierarchy of importance with regards to pre-operative exercise content is still not known. Interventions other than resistance and proprioceptive training, such as neuromuscular training, which aims to improve joint stability and sensorimotor/neuromuscular control (86), may improve post-surgical physical function. The study by Villadsen et al. (58) was excluded from this review as raw data for the knee OA subgroup were not accessible. However, the authors' neuromuscular intervention programme offers a functional task-oriented approach that includes strength, coordination, balance and proprioceptive exercises that may also be beneficial. Nevertheless, the present review is unable to comment on verification of dosage delivery and efficacy of exercise stress in this trial.

Limitations of the systematic review

The present review adds to the current literature the most comprehensive accumulation of published evidence regarding the post-operative effectiveness and dose-response characteristics of pre-surgical exercise programmes (detailing applied physiological stimulus) in people undergoing TKA. The strength of this systematic review is that it followed the PRISMA guidelines and included only RCTs, which should increase confidence in the results as findings are expected to be less subject to bias.

Several factors must be considered with respect to the conclusions that can be drawn from this systematic review. Although a wide-ranging literature search for eligible studies was conducted, other studies may exist. Study selection was based on predetermined inclusion criteria, and only the main author assessed full-text articles for eligibility, potentially introducing bias in study selection, which may have been alleviated with a second assessor. This review includes patients receiving TKA with diagnosed knee OA. Therefore, it is not clear the extent to which these findings are generalizable with regard to pre-operative intervention exercises for patients undergoing surgery due to other knee joint pathologies. In addition, while pain and functionality outcomes were evaluated, no study formally assessed other important aspects, such as medication requirements.

Conclusion

Despite a potential for efficacy of exercise-based conditioning, this systematic review with meta-analysis highlights the scarcity of robust dose-response evidence to guide the formulation of TKA prehabilitation.

In accordance with existing studies reporting that the potential waiting time for surgery not only represents a significant burden for patients (87, 88), but also results in deterioration regarding pain, functional limitations and QoL (which in turn affect post-operative outcomes) (89–91), an optimally dosed pre-operative intervention programme may reduce physiological de-conditioning and deterioration of physical function prior to surgery and potentially accelerate post-operative recovery. While this idea is plausible, lack of published evidence about prehabilitation "composition", tolerance by patients, individually-optimized dosing, potency of physiological stress-related stimulus and responsiveness, means that these aspirations are currently untested. Future adequately powered research with appropriately dosed and completely described interventions needs to address these aspects before clinical recommendations can be made with regard to the mode and delivery of TKA prehabilitation.

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