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UP-TO DATE REVIEW AND CASE REPORT

Effects of amino acid supplementation on muscle mass, muscle performance and functional capacity in subjects undergoing total knee arthroplasty: a systematic review of randomized clinical trials

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Abstract

The aim of the present study was to summarize the effectiveness of amino acid supplementation on muscle strength, muscle volume, and functional capacity in patients undergoing total knee arthroplasty. For this, in November 2022, a search was carried out in the PubMed, Cochrane Library, and EMBASE databases, identifying a total of 2182 documents, of which only 4 were included in the present review. The included studies had 148 participants (47 men and 101 women), with a minimum age of 53 and a maximum of 92 years, and supplementation times of 13 to 30 days (1 to 3 times a day). For the results, in relation to muscle performance, when comparing the control and experimental groups, greater muscle atrophy was observed in the pre- and post-moments of the control group, in relation to the experimental group. In addition, studies suggest a good tendency for muscle mass gain, and improvement in the functional capacities of patients who used supplementation. Therefore, the use of amino acids after TKA surgery reduces muscle atrophy, which preserves muscle mass and leads to better performance in tests of strength and functional capacity, when compared to the use of a placebo.

Keywords Isokinetic · TUG · Muscle volume · Quadriceps · Knee extension

Introduction

The number of total knee arthroplasty (TKA) procedures has been rising steadily for many decades in Europe and the USA [1]. The pace of increase varies between countries, with a gradual increase in the incidence in northern and central Europe, and with a trend toward a slowdown in the USA and an exponential increase in the UK [1]. In Brazil, data on the prevalence and incidence of this surgery in impact articles are militated.

One of the main indications for performing TKA is knee osteoarthritis, and several factors may be related to its development, such as genetic predisposition, sex, age, meniscal injuries, misalignment of the lower limbs, injuries to the articular cartilage, and increased practice of sports [2]. Considering the degree of evolution of this health condition, TKA can become an elective surgery [3]. Unfortunately, TKA is accompanied by acute postoperative joint pain, which is considered more severe than other arthroplasties performed on other joints [4].

Recently, a study has shown that patients who have increased pain in the operated knee, decreased quadriceps muscle strength, and decreased functional status of the lower limb are associated with the presence of kinesiophobia [5]. Regardless of the fear of moving the operated knee, quadriceps muscle strength is considered one of the major determinants of overall physical function, and its deficit associated with TKA can last for months after surgery [6]. The literature also emphasizes the role of alterations in the structural components of the neuromotor system as determinants of extensor muscle weakness after TKA [7]. TKA patients also present large deficits in functional capacity compared to age-matched healthy controls [8]. Asymmetry of limb weight bearing is associated with decreased performance and mobility in everyday life [8].

Although there are effective physical–functional rehabilitation resources for the recovery of quadriceps muscle

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mass and strength after TKA [8–10], a recent systematic review [11] investigated the role of supplementary nutritional therapies, such as the use of amino acids, as adjuvants or for isolated use to reduce the muscle mass and strength of the lower limbs after TKA, thus accelerating the recovery of functional capacity. Although nutritional optimization there are some positive effects of its use reported during the preoperative period, the authors attest that there is limited evidence to support the use of nutritional supplementation in patients undergoing TKA. As the systematic review completed its electronic search in November 2017, there is a 5-year gap during which new randomized clinical trials could have emerged to clarify the role of amino acids in the treatment of TKA. Essential amino acids, the focus of the present study, are reported to be able to increase the body's ability to synthesize proteins and repair muscle tissue, which can thus develop greater functional reserve to withstand surgical trauma [12]. From the month of November 2017 [11], to date, systematic reviews have associated the use of antifibrinolytic amino acids to reduce excessive blood loss and the need for blood transfusions during the perioperative period of TKA [13–15].

In view of the above, the objective of this systematic review is to comprehensively summarize the effectiveness of the use of amino acids in outcomes considered critical for the patient, because good recovery of the structure and muscular strength of the lower limbs and recovery of the functional capacity of patients submitted to TKA may be essential to guarantee the functional independence of the individuals.

Materials and methods

Type of study and guidelines for writing

This is a systematic review study [16]. For the description of the items in this systematic review, the recommendations contained in the PRISMA 2020 *statement* were used [17].

Eligibility criteria

Randomized clinical trials [18] published in indexed journals in the investigated databases were included. The eligibility criteria were structured using the components of the PICOS acronym. Population: individuals undergoing TKA without restriction of sex, age, and the presence of comorbidities. Intervention: administration of nutritional supplementation of amino acids in the pre- and/or postoperative period, without restriction regarding the classification of the types of investigated amino acids. Comparator: groups receiving placebo therapy. Outcomes: muscle mass, muscle performance, and functional capacity. Time-points: not restricted. Time points referred to pre- and post-surgical intervention moments and all follow-ups (follow-up time without intervention).

Information sources

Electronic searches performed directly in the *PubMed*, *Cochrane Library,* and *EMBASE* databases [19] were conducted during the month of November 2022. No publication dates were restricted for the materials collected in any of the databases. Studies contained in the gray literature (e.g., theses, conference abstracts), studies not published in the English language, and studies developed with animals were excluded from the searches. Expert researchers and organizations related to the research topic were not contacted to further search for original articles. The reference lists of included articles were manually scanned to identify additional studies.

Search strategy

For the search strategy, controlled vocabularies were used. Controlled vocabularies were identified using the English language medical metadata system, denominated *Medical Subject Headings* (MeSH). The sequence of Boolean descriptors and operators described below were used as a search engine in the databases:

PubMed: ((amino acids) OR (amino acid)) AND ((knee replacement) OR (knee arthroplasty) OR (total knee replacement) OR (total knee arthroplasty)); *Cochrane Library:* ((amino acids) OR (amino acid) AND ((knee replacement) OR (knee arthroplasty) OR (total knee replacement) OR (total knee arthroplasty)); *EMBASE*: ((amino acids) OR (amino acid)) AND ((knee replacement) OR (knee arthroplasty) OR (total knee replacement) OR (total knee arthroplasty)).

As the above descriptors are consolidated in the literature, searches using *text words* (free terms) were not necessary. When appropriate, *MeSH* descriptors were exploded so as not to miss relevant articles (e.g., use of double quotes around compound terms). Only searches in the *PubMed* and *EMBASE* databases used filters for the type of study, such as a *randomized controlled trial*. The choice of health descriptors and search strategies was reviewed and consolidated by a specialist librarian with 13 years of experience in electronic searches in health sciences databases [19].

Selection process

The selection process of titles and abstracts was carried out by a single researcher. This initial screening approach (judgment of titles and abstracts by a researcher) has already been shown to be adequate [19]. However, at the complete reading stage of the potential articles to be included, two researchers independently applied the eligibility criteria to generate a final list of included articles. Disagreements between authors regarding the final articles included were resolved by a third researcher. The researchers involved in all stages of the selection process strictly used the pre-established eligibility criteria for screening the articles (item 2.2).

Data collection process and data extracted

The basic characteristics of each included study are detailed in Table 1, considering: (a) name and year of the study; (b) number of participants and sex per group; (c) description of the age groups; (d) interventions: description of the administered supplementation dosage; (e) comparators: description of the administered placebo dosage; and (f) time-points and outcomes.

The outcome domains were defined a priori as follows: (1) muscular performance measured in muscles of the operated lower limb using different techniques and measuring instruments; (2) muscle mass of any body segment measured by any techniques and instruments for measuring the volume of a muscle of the lower limb of the operated limb using; (3) functional capacity measured by performance tests of the lower limbs in different functional tasks.

The outcomes of the present study were chosen as critical and important for patients undergoing TKA according to the systematic reviews by Reynaud et al. and Gagnier et al. [20], [21]. With the aim of comparing between the studies, the outcomes/assessment instruments and study results (by time-point and follow-ups) are presented in Table 2(Muscle Performance), 3(Muscle Volume), 4(Functional Capacity).

The data highlighted above were extracted independently by two authors. Disagreements between the authors were resolved by a third researcher. An electronic form on *Google Forms* was structured to facilitate data collection. The advantages of this form of data extraction are that it allows the storage, sharing, and grouping of data, with the possibility of editing as needed [19].

Risk of bias of the studies

To assess the risk of bias in the studies, the *Physiotherapy Evidence Database* (PEDro) scale was used. This scale aims to identify the risk of bias of randomized clinical trials, through a final score (maximum of 10 points; scores ≥ 6 points indicate the study is of high quality) [22, 23]. The scale assesses 11 items: eligibility criteria, random allocation into groups, blinded allocation of subjects, subjects similar in terms of prognostic indicators, blinded subjects, blinded therapists, blinded outcome raters, at least one outcome obtained in over 85% of subjects, analysis by intention to treat, intergroup statistical comparisons, precision measures presented. Each item is evaluated with "yes" or "no," and the total score is the number of items considered yes (excluding the analysis of criterion 1, which does not score). The evaluation of the clinimetric properties of the PEDro scale reveals acceptable levels of validity and reliability [24, 25]. The information for judging the items can be obtained from the *Physiotherapy Evidence Database* (website: https://pedro.org.au/english/resources/pedro-scale/). If the risk of bias was analyzed by study and not by the result of the aforementioned database, it was analyzed by an independent researcher, unrelated to the objectives of the study, who at the time of the study had 10 years of experience in this type of research.

Measure of the effects

The summary of each outcome will be described in the results section through tables. For each synthesis, studies with the same outcome domain may be included, but measured and resulting in different units of measurement through the use of different measuring instruments (e.g., muscle strength can be measured in units of measurement such as Newton, Newton-meter, kilogram, among others).

Due to the methodological heterogeneity of the studies (e.g., comparison of different body segments evaluated between studies), it was not possible to perform the meta-analysis.

Results

Flowchart and included studies

The electronic searches initially located 2182 documents. Of these, the following were excluded: 78 articles duplicated between the databases, 49 articles on animal experimentation, 85 because they were only abstracts, 555 review articles, 2 conference abstracts, 377 articles that did not perform supplementation in patients undergoing TKA, 447 articles not classified as randomized clinical trials, and 577 articles for not using dietary supplements. Thus, after reading the titles and abstracts, 12 studies were analyzed by reading the full text. Of these, 2 articles were excluded because they did not use amino acid supplementation, 1 because it was only a biomechanical assessment of the knee, and 5 because they did not present the desired outcomes in the inclusion criteria. Thus, 4 studies were included in this systematic review [26–29]. Figure 1 presents the flowchart of electronic searches and the number of articles included.

Table 1 Characterization of the included studies

Author, year	Participants	Age (years)	Intervention group
Dreyer et al. [29]	28 patients underwent total knee arthroplasty (9 men, 19 women) Intervention ($n=16$) Control ($n=12$)	Intervention: 68 ± 5 Control: 70 ± 5	20 g of essential amino acids Composition: 2.2 g of histidine, 2 g of isoleucine, 3.6 g of leucine, 3.2 g of lysine, 0.6 g of methionine, 3.2 g of phenylalanine, 2.8 g of threonine, and 2.4 g of valine Ingestion: 2 times a day between meals, 1 week before and 2 weeks after total knee replacement surgery
Nishizaki et al. [28]	23 patients with knee osteoarthritis (11 men, 12 women) Intervention ($n=13$) Control ($n=10$)	Intervention: 69.8 Control: 71.1	HMB/Arg/Gln supplementation dissolved in 240–300 ml of water Composition: 2400 mg of HMB, 14,000 mg of L-glutamine, 14,000 mg of L-arginine, 158 kcal of energy, and 0 mg of protein Ingestion: 5 days before surgery and 28 days from the day after surgery, twice daily after meals
Roy et al. [27]	37 adults with osteoarthritis undergoing total knee arthroplasty (17 men, 20 women) Intervention ($n=18$) Control ($n=19$)	Intervention: 63.7 ± 10.0 Control: 63.3 ± 0.2	10 g creatine monohydrate supplement Composition: 5 g of creatine monohydrate + 4 g of dextrose + flavoring Ingestion: 2 sachets for 10 days before surgery + Postoperative 1 sachet for 30 days
Ueyama et al. [26]	60 patients who underwent unilateral total knee arthroplasty for primary knee osteoarthritis (10 men, 50 women) Intervention ($n=30$) Control ($n=30$)	Intervention: 75.9 (58 to 92) Control: 75.8 (65 to 87)	3 g of essential amino acids Composition: isoleucine, 603 mg; leucine, 684 mg; lysine, 756 mg; methionine, 603 mg; phenylalanine, 405 mg; threonine, 405 mg; tryptophan, 207 mg; valine, 603 mg; arginine, 630 mg; histidine, 315 mg; and starch 1089 mg Ingestion: three times a day after each meal, from one week before to two weeks after TKA

Author, year	Control group	Outcome measures
Dreyer et al. [29]	20 g of non-essential amino acids Composition: 20 g of alanine Intake: 2 times a day between meals, 1 week before and 2 weeks after total knee arthroplasty	Measurements: 1 week before surgery, 2 and 6 weeks after surgery Muscle volume: MRI Isometric strength: Biodex Functional mobility: 6-min walk, TUG, timed ascent and descent of stairs
Nishizaki et al. [28]	Placebo Composition: The orange juice contained 226 kcal of energy and 280 mg of protein Ingestion: 5 days before surgery and 28 days from the day after surgery, twice daily after meals	Measurements: before surgery and postoperatively 2 weeks, 4 weeks, and 6 weeks Knee extension strength test: BIODEX Total amount of exercise: lifestyle recorder Cross-sectional area of the rectus femoris: computed tomography
Roy et al. [27]	10 g Placebo Composition: 7 g dextrose + flavoring Ingestion: 2 sachets for 10 days before surgery + Postoperatively 1 sachet for 30 days	Measurements: 1 week before surgery and 4 weeks after total knee replacement Body composition: bioelectrical impedance Muscle function: knee isometry, ankle dorsiflexion and handgrip strengths, 30-ft timed walk, and 4-step timed climb Blood, urine and muscle collection
Ueyama et al. [26]	9 g Placebo Composition: lactose powder Ingestion: daily from one week before to two weeks after TKA	Measurements: Twice > 4 weeks apart Femoral muscle area and quadriceps muscle diameter: ultrasound Serum albumin level: blood samples Knee pain: visual analogue scale Mobility: 6-m walk Femoral-tibial angle: digital pull-type handheld dynamometer Prosthetic alignment: radiography

g, gram; mg, milligram; ml, milliliter; HMB, beta-hydroxy-beta-methylbutyric acid; Arg, arginine; Gln, glutamine; TUG, timed up and go test; kcal, kilocalorie

Table 2 Results of the studies included for the muscle performance outcome

Author, year	Muscle group	Time	Assessment instrument	Muscle performance														
				Control group						Intervention group						Mean difference		
				n	Pre	SD	Post	SD	ES	*n*	Pre	SD	Post	SD	ES	Control	Intervention	*p*
Dreyer, [29]†	Quadriceps 45° (operated side)	7 days before and 14 days after surgery	Dynamometer (N)	12	87	15	36	7	–	16	87	9	45	6	–	− 49 ± 16	− 32 ± 11	0.85
	Quadriceps 45° (non-operated side)				112	16	100	12	–		100	7	100	10	–	− 14 ± 6	9 ± 5	0.14
	Hamstrings 45° (operated side)				39	6	22	5	–		41	4	27	4	–	− 19 ± 4	− 12 ± 3	0.27
	Hamstrings 45° (non-operated side)				45	6	42	6	–		54	11	42	5	–	− 4 ± 2	− 14 ± 14	0.42
	Quadriceps 60° (operated side)				97	16	33	8	–		89	9	41	6	–	− 67 ± 19	− 42 ± 10	0.65
	Quadriceps 60° (non-operated side)				126	18	105	12	–		109	9	109	10	–	− 29 ± 9	7 ± 6	0.01
	Hamstrings 60° (operated side)				36	5	19	6	–		35	3	24	5	–	− 16 ± 5	− 11 ± 3	0.7
	Hamstrings 60° (non-operated side)				42	5	42	5	–		41	4	40	4	–	− 1 ± 2	1 ± 2	0.75
Nishizaki et al. [28] Knee Extension (operated side)		Day 14	Biodex (Nm/Kg)	10	1.1	0.62	0.7	± 0.9	–	12	1.1	0.3	0.9	0.4	–	–	–	0.02
		Day 28			1.1	0.62	1.0	± 0.9	–		1.1	0.3	1.0	0.4	–	–	–	NR
		Day 42			1.1	0.62	0.9	± 0.6	–		1.1	0.3	1.0	0.4	–	–	–	NR

Table 2 (continued)

Author, year	Muscle group	Time	Assessment instrument	Muscle performance: Control group *n*	Pre	SD	Post	SD	ES	Intervention group *n*	Pre	SD	Post	SD	ES	Mean difference: Control	Intervention	*p*
Roy et al. [27]	Knee extension	7 days to 30 days	Isometric dynamometer (Nm)	19	93.0	52.3	46.0	±21.1	–	18	102.0	43	48.1	27	–	−54.3 ± 47.3	−53.9 ± 35.3	< 0.05
	Ankle dorsiflexion		Isokinetic dynamometer (Nm)		41.2	17.3	32.4	±14	–		44.0	14.7	33.9	12.5	–	−8.8 ± 8.8	−10.0 ± 7.1	< 0.05
	Handgrip strength		Hand dynamometer (Kg)		35.2	10.7	33.4	±9.6	–		37.6	9.7	38.2	10.4	–	−1.8 ± 3.8	0.6 ± 4.1	< 0.07
Ueyama et al. [26]	Quadriceps	> 4 weeks	Digital handheld dynamometer (N)	30	130	36 to 287	95	29 to 245	Pre: 0.573 Post: 0.687	30	140	31 to 310	90	34 to 193	Pre: 0.573 Post: 0.687	84 (15 to 248)	78 (22 to 257)	0.687

SD, standard deviation; ES, effect size; Nm, Newton-meter; kg, kilogram; N, Newton; NR, not reported by the authors

†"Because of some missing data, the meandifference score and percentage change values are not exact reproductions of differences in the means at the two time points" Dreyer et al. [29]

Characterization of the included studies

The included studies have a total of 148 participants (47 men and 101 women), with a minimum age of 53 and a maximum of 92 years. The sample considering all groups, experimental and control, ranging from 10 to 30 individuals. Supplementation time ranged from 13 to 30 days. The frequency of supplementation varies from 1 to 3 times a day. All control groups ingested a placebo, with the same frequency as the respective experimental groups. (Table 1).

Results by outcome

Muscle performance

In Table 2, it is possible to observe that when comparing the control and experimental groups, there was greater muscle atrophy in the pre- and post-moments of the control group, in relation to the experimental group. Similar results were also noticed in the non-operated limb. In addition, another study showed significant improvement in isometric knee extension strength 14 ($p = 0.02$) and 30 ($p < 0.05$) days after TKA. Similarly, there were also significant results in ankle dorsiflexion ($p < 0.05$). With regard to handgrip ($p < 0.07$) and quadriceps strength gains, the included studies only suggest a trend in these aspects.

Muscle mass

One of the studies demonstrated that the use of amino acid supplementation showed a good tendency to gain muscle mass on the operated side ($p = 0.06$). This result is in line with another study, which had a larger number of participants than the former, which reported a significant effect on quadriceps muscle mass gains ($p = 0.029$). Regarding the rectus femoris, the results present divergent data, in that one study shows statistically significant muscle mass gains ($p = 0.026$), while another study, despite showing gains, reported that these were not statistically significant ($p = 0.15$). The study by Roy et al. [27], despite not presenting intergroup statistical data, demonstrates a decrease in body weight (97 kg ± 16.7 to 94.8 kg ± 16.2; $p < 0.05$) and fat-free mass (60.6 kg ± 15.3 to 60.3 kg ± 15.9), and increase in type 1 muscle fibers (32% ± 12.2% to 38.8% ± 11.8%) in the experimental group (Table 3). Furthermore, according to the results of Dreyer et al. [29], the intervention group, when compared to the control group, also presented attenuated atrophy in the non-operated limb.

Functional capacity

The first study in Table 4 shows a statistically significant result for the TUG ($p = 0.019$) and climbing and descending

Table 3 Results of the studies included for the muscle volume outcome

Author, year	Muscle group	Assessment instrument	Volume muscular														
			Control group						Intervention group						Mean difference		
			n	Pre	SD	Post	SD	ES	*n*	Pre	SD	Post	SD	ES	Control	Intervention	*p*
Dreyer, [29]†	Quadriceps (operated side)	MRI (cm^2)	12	133	13	114	13	–	16	120	11	120	12	–	− 20 ± 4	− 4 ± 5	0.06
	Quadriceps (non-operated side)			150	16	136	15	–		140	12	136	13	–	− 15 ± 3	− 6 ± 3	0.13
	Hamstrings (operated side))			154	17	129	14	–		142	13	128	11	–	− 25 ± 5	− 17 ± 4	0.5
	Hamstrings (non-operated side)			150	15	135	15	–		147	13	134	14	–	− 15 ± 4	− 13 ± 6	0.77
	Intermuscular adipose tissue (operated side)			46	7	44	6	–		66	7	64	7	–	− 2 ± 2	− 1 ± 1	0.74
	Intermuscular adipose tissue (non-operated side)			40	5	37	4	–		62	8	61	8	–	− 1 ± 2	0 ± 1	0.49
Nishizaki et al. [28]	Rectus femoris	Computed tomography (cm^2)	10	542	164	506	164	–	13	528	164	572	171	–	4.3 ± 26.2%	10.0 ± 20.5%	0.15
Roy et al. [27]	Body mass	Bio-electrical impedance (kg)	19	88.7	15.1	86.5	13.9	< 0.05	18	97.0	16.7	94.8	16.2	< 0.05	–	–	–
	Fat-free mass			55.9	13.6	56.1	13.2	–		60.6	15.3	60.3	15.9	–	–	–	–
	Muscle fiber area			–	–	–	–	–		32.0% type 1 68.0% type 2	12.2% 12.2%	38.8% type 1 61.2% type 2	11.8% 11.8%	–	–	–	–

Table 3 (continued)

Author, year	Muscle group	Assessment instrument	Volume muscular: Control group *n*	Pre	SD	Post	SD	ES	Intervention group *n*	Pre	SD	Post	SD	ES	Mean difference: Control	Intervention	*p*
Ueyama et al. [26]	Rectus femoris	Ultrasound (mm^2)	30	301	159 to 467	291	108 to 479	Pre: 0.073 Post: 0.457	30	256	126 to 409	276	141 to 418	Pre: 0.073 Post: 0.457	97 (68 to 155)	116(71 to 206)	0.02
	Quadriceps	Ultrasound (mm)		19.7	11.0 to 29.5	21.1	10.9 to 32.4	Pre: 0.231 Post: 0.861		17.9	10.2 to 29.7	21.3	12.3 to 35.8	Pre: 0.231 Post: 0.861	109 (84 to 163)	123 (86 to 171)	0.02

SD, standard deviation; ES, effect size; cm^2, square centimeter; kg, kilogram; mm, millimeter; mm^2, square millimeter

†"Because of some missing data, the mean difference score and percentage change values are not exact reproductions of differences in the means at the two time points" Dreyer et al. [29]

stairs ($p=0.015$ and $p=0.011$, respectively). In contrast, the other studies did not show statistically significant improvements, and in one of the studies a statistically significant decline ($p<0.01$) was found intergroup in the Timed 4-step climb and Timed 30-ft Walk tests, 30 days after surgery (there was no statistical difference between groups). The other study, conducted by Ueyama et al. [26], reports only a reduction in the execution time of the 6-min walk test (CG: 7.6 s to 6.9; EG: 7.9 s to 6.8), and an evolution of some participants in the intervention group (walking with a cane to walking without a cane), while in the control group the result was the opposite, and intensified (participants not only started to walk with a cane, they also started to use a walker).

Risk of bias in the studies

The PEDro scale (Table 5) ranged from 5–8 points, and only 3 studies were classified as having a high methodological quality (PEDro ≥ 6). All studies scored on items 2, 4, 10, and 11 (random assignment, baseline comparison, group comparison, and measures of precision and variability). In contrast, none of the studies received a score on items 6 and 9 (blinded therapists and intention -to treat). Item 3 (blinded allocation) was covered by 2 studies, item 5 (blinded subjects) by 3 studies, item 7 (blinded assessors) by 2 studies, and item 8 (< 15% dropouts) by 3 studies. Thus, the final average of the PEDro scale was 6.5.

Discussion

The objective of the present study is to comprehensively summarize the effectiveness of the use of amino acids in outcomes considered critical for the patient, as good recovery of the structure and muscle strength of the lower limbs and recovery of the functional capacity of patients undergoing TKA can be essential to ensure the functional independence of the individuals. Thus, after applying the eligibility criteria in the studies found, our qualitative analysis showed that supplementation with amino acids brings benefits in performance and muscle mass after TKA.

Physical inactivity can reduce the amount of muscle mass present in the human body, therefore, increasing protein consumption can help maintain muscle mass [30]. However, the constant use of high doses of proteins does not necessarily lead to an increase in muscle mass, this occurs due to the efficiency of protein use, the change in the level of physical activity, the energy balance, and the amount of protein ingested [31]. Thus, it is believed that due to the post-surgical need, the body can increase its ability to use supplemented amino acids, which could generate positive

Table 4 Results of the studies included for the functional capacity outcome

Author, year	Assessment instrument	Functional capacity														
		Control group						Intervention group						Mean difference		
		n	Pre	SD	Post	SD	ES	*n*	Pre	SD	Post	SD	ES	Control	Intervention	*p*
Dreyer et al. [29]†	TUG (s)	12	–	–	–	–	–	16	–	–	–	–	–	31.9 ± 10.2%	−4 ± 9.5%	0.019
	Timed stair climb (s)		–	–	–	–	–		–	–	–	–	–	205.9 ± 32.8%	94.6 27.2%	0.015
	Timed stair descent(s)		–	–	–	–	–		–	–	–	–	–	53.9 ± 13.5%	0.05 ± 13.5%	0.011
Roy et al. [27]	Timed 4-step climb (s)	19	–	–	–	–	–	18	–	–	–	–	–	–	–	‡
	Timed 30–ft walk (s)		–	–	–	–	–		–	–	–	–	–	–	–	‡
Ueyama et al. [26]	6 min walk (s)	30	7.6	3.9 to 12	6.9	4.5 to 11	Pre: 0.530 Post: 0.821	30	7.9	4.5 to 20	6.8	4.0 to 12	Pre: 0.530 Post: 0.821	103 (66 to 154)	97 (43 to 143)	0.287
	Walking without a cane		23	–	22	–	Pre: 1.000 Post: 0.532		22	–	25	–	Pre: 1.000 Post: 0.532	–	–	–
	Walking with a cane		5	–	4	–	Pre: 0.748 Post: 1.000		7	–	4	–	Pre: 0.748 Post: 1.000	–	–	–
	Walking with a walker		2	–	4	–	Pre: 1.000 Post: 0.203		1	–	1	–	Pre: 1.000 Post: 0.203	–	–	–
	Wheelchair		0	–	0	–	Pre: 1.000 Post: 1.000		0	–	0	–	Pre: 1.000 Post: 1.000	–	–	–

SD, standard deviation; ES, effect size; s, second

†"Because of some missing data, the mean difference score and percentage change values are not exact reproductions of differences in the means at the two time points" Dreyer et al. [29]

‡No statistical difference between groups

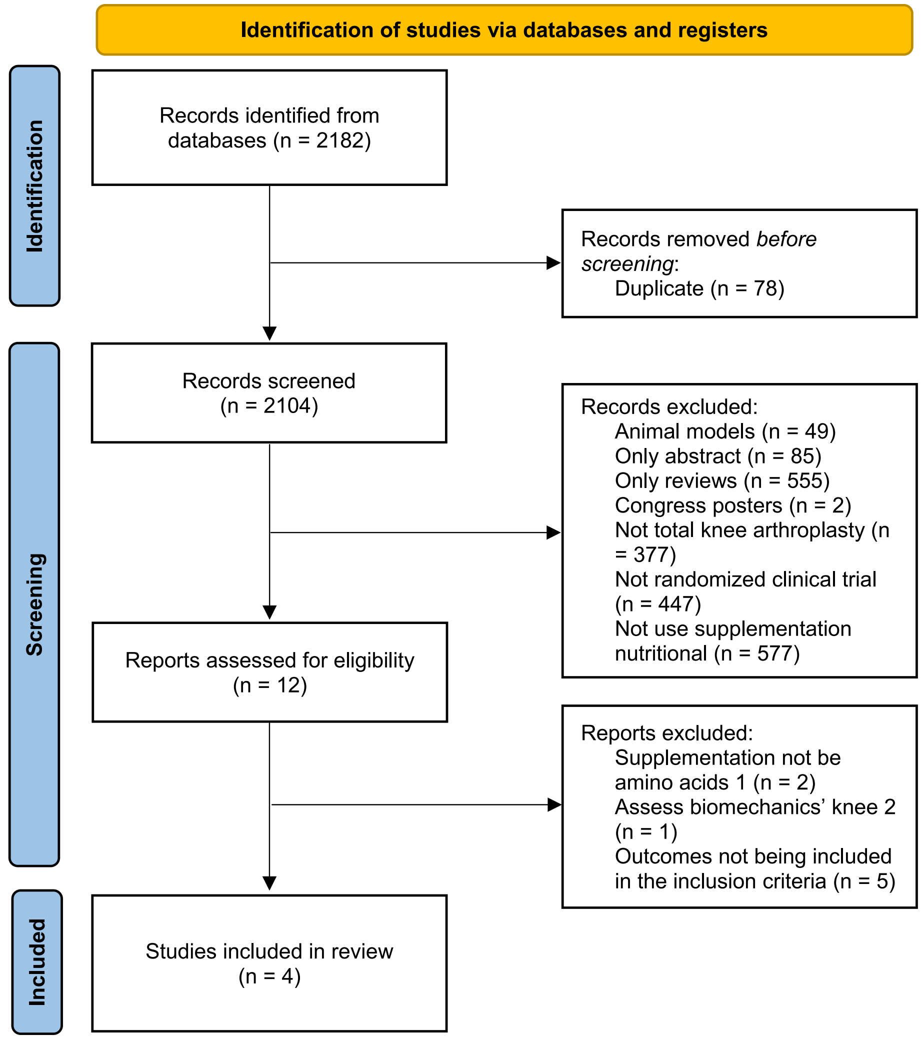

Fig. 1 Fluxograma das buscas eletrônicas

results, such as those found by Ueyama et al. [26] in the group that used supplementation. On the other hand, this same principle may also explain the fact that only a trend toward a positive result was found by Nishizaki et al. [28], and maintenance of muscle mass was evidenced by Dreyer et al. [29] and Roy et al. [27].

In view of the above, and knowing that the greater the muscle mass, the greater the probability of the subject having a superior performance in physical and functional tests, due to the greater possibility of the amount of work that a muscle can exert, the significant increases in strength found in knee extension [27, 28], ankle dorsiflexion [27], handgrip strength [27], and quadriceps [26, 29] were already expected. It is believed that this occurs because with a more preserved muscle mass, the subjects would achieve a better performance in strength tests, as a larger sarcomere can exert greater work on muscle action. Therefore, the decrease in muscle atrophy may also be associated with functional capacity, as demonstrated in the study by Dreyer et al. [29], who showed an association between functional mobility and quadriceps muscle atrophy ($F=5.78$; $p=0.021$).

Although amino acid supplementation is safe and reduced muscle wasting [32], being shown in the present study to be able to generate strength maintenance and gains, these results were not expressed in significant improvements in the clinical framework when considering the patient's functional capacity. This may have occurred because the post-TKA follow-up period was short (i.e., up to 30 days), and the patient could have been analyzed before their full recovery, during which time they may still be afraid of moving the knee (i.e., kinesiophobia) and asymmetry between operated and non-operated limbs. Another point to be considered is the post-operative functional capabilities, which are associated with preoperative capabilities [33]. However, it should be noted that when comparing the experimental and control groups, the groups that ingested amino acids performed better in the pre- and post-surgery follow-up in all the tests performed by Dreyer et al. [29], Roy et al. [27], and Ueyama et al. [26].

Table 5 PEDro scale

Author, year	1 eligibility criteria*	2 Random allocation	3 Concealed allocation	4 Initial comparison	5 Blinded subjects	6 Blinded therapists	7 Blinded assessors	8 <15% of dropouts	9 Intention to treat	10 Comparison between groups	11 Measures of precision and variability	Total
Dreyer et al. [29]	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	6
Nishizaki et al. [28]	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Roy et al. [27]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	7
Ueyama et al. [26]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	8

*This item should not be counted toward the total point count

Thus, a longer follow-up period should be performed to analyze the effects of supplementation on functional capacity.

The present study has the following limitations: lack of quantitative analysis of the findings (i.e., meta-analysis), which could not be performed due to the small number of included studies, and their heterogeneity; the inclusion of a study with low methodological quality; and studies with a short post-surgical follow-up period. Therefore, for future studies, it is suggested that randomized clinical trials be performed with a *follow-up* period according to the total recovery period after TKA. However, as a practical application, since the use of amino acid supplementation is safe after TKA surgery [32] and is able to attenuate the reduction in muscle atrophy, aiding recovery, the use of essential amino acids is recommended after TKA surgery.

As patient-reported outcome measures (PROMS) are commonly used to asses quality and outcomes (i.e., limb function, general activities, and physical health) after knee TKA, future randomized controlled trials investigations need to employ knee biomechanical assessments (i.e., biomechanical analysis in walking, running, and squatting) to growing interest in identifying the relationship between the effects of amino acid supplementation and post-surgery TKA arthroplasty.

Conclusion

According with the literature evidence about the improvements of intake protein supplements for increases muscle mass, strength, and function due to the physiological reduced rate of muscle protein syntheses after TKA, our study is supporting evidence that the association between the effects of amino acid supplementation and post-surgery TKA arthroplasty are safe and able to increase muscle health conditions. So, the present finding extends our understanding of the potential improvements to the use of amino acids on muscle mass, muscle performance and functional capacity recovery after total knee arthroplasty.

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Declarations

Conflict of interest Authors declare that they have no conflict of interest.

Ethical approval As this is a systematic review, an Ethics Committee was not required for this type of study. We are carrying out an ECR on the subject, this one with an approved Ethics Committee.

Informed consent As this is a systematic review, an Informed Consent was not required for this type of study.

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