Musculoskeletal Care

WILEY

SYSTEMATIC REVIEW OPEN ACCESS

Classification of Physical Activity Programs Based on the Kellgren & Lawrence Scale for Knee Osteoarthritis: A Systematic Review

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Received: 29 October 2024 | **Revised:** 4 November 2024 | **Accepted:** 13 November 2024

Funding: This study was funded by the European Union – NextGenerationEU - The Italian Ministry of University and Research (MUR)—(grant number PRIN 2022PZH8SX).

Keywords: arthritis | exercise | health | osteoarthritis | pain

ABSTRACT

Introduction: Knee osteoarthritis is a common orthopaedic disease, is the leading cause of disability in the elderly, and can lead to pain, loss of function, and reduced quality of life. This research aims to determine how PA programs can be effectively classified and customised to align with the stages of knee OA according to the KL classification.

Objective: The research aims to fill the gap in understanding the relationship between the type and intensity of PA and the stages of OA as defined by the KL classification.

Materials and Methods: A systematic search was performed using PubMed, Web of Science, and Scopus databases. This review included different types of studies published after January 1, 2013.

Results: Two thousand one hundred and thirty-six were picked up and only nine articles met the inclusion criteria. The beneficial effects of exercise were found in the function of the joints, pain, and quality of life. Aerobic, isometric, and resistance training showed positive effects and presented improvements in physical function, quality of life, and pain.

Conclusion: The exercise programs appear to be both safe and effective in subjects with knee osteoarthritis with regard to quality of life, pain, and knee function.

Trial Registration: PROSPERO registration number: CRD42024550463

1 | Introduction

Osteoarthritis (OA) is a chronic disease composed of both inflammatory and metabolic factors. OA primarily affects articular cartilage, which is severely degraded during the disease. Articular cartilage is the smooth part of cartilage that covers the end of long bones, provides low friction to the joint, and is capable of transferring heavy loads (Abramoff and Caldera 2020; Lespasio et al. 2017). The cartilage shows obvious changes and the entire joint is involved, including synovia, articular ligaments, and subchondral bone, leading to a reduction in joint space (Abramoff and Caldera 2020; Lespasio et al. 2017; O'Neill and Felson 2018). Inflammation plays an important role in the pathogenesis of OA within the joint (Abramoff and Caldera 2020;

Felson 2006). Degrading cartilage leads to an external body reaction in synovial cells; it stimulates the production of inflammatory cytokines, which causes the degenerative process of the cartilage. Bone remodelling leads to periarticular muscle weakness, while synovitis causes ligament laxity, contributing to the development of bone marrow lesions and subsequent bone trauma (Felson 2006; O'Neill and Felson 2018).

Knee osteoarthritis (KOA) is a common orthopaedic disease that is the leading cause of disability in the elderly, and can lead to pain, loss of function, and reduced quality of life (QoL) (Felson 2006; Hunter, Schofield and Callander 2014).

Ageing is one of the most considered risk factors for the development of OA, given the physiological decline of joints, especially the knee, hip, and hand. People over 60 years old may develop symptomatic OA. Between 60 and 70 years old, radiographic investigation shows KOA, and over 80 years old the risk of radiographic evidence in the knee increases (Abramoff and Caldera 2020; Jamtvedt et al. 2008; Lespasio et al. 2017; Loeser 2011; Pai et al. 1997).

Specific jobs have a negative effect on the development of OA (Coggon et al. 2000; Cooper et al. 1994; Felson et al. 1991; Jensen et al. 2000). Even some competitive sports can wear down the knee joint in both athletes and younger individuals because repeated traumas, impacts, and excessive loads can damage the articular cartilage (Abramoff and Caldera 2020; Allen et al. 2010; Jamtvedt et al. 2008; Kujala et al. 1995).

Localised cartilage loss can increase focal stress in the joint, which leads to an additional loss of the cartilage itself. If the area of articular cartilage deterioration is very large, the joint will tilt, causing joint malalignment. Malalignment is a major risk factor for joint deterioration because it increases the focal load, causing further damage to the joint that can lead to joint collapse (Felson 2006).

Radiological investigation represents the gold standard for the classification and diagnosis of OA (Abramoff and Caldera 2020; Lespasio et al. 2017). It is commonly represented by a narrowed joint space with osteophyte formation (Abramoff and Caldera 2020; Felson 2006; Lespasio et al. 2017). The most common scale for KOA classification is the Kellgren-Lawrence (KL) system, which evaluates osteophyte formation, articular cartilage narrowing associated with subchondral bone sclerosis, and altered shape of bone ends from grade 0 to grade 4 (Abramoff and Caldera 2020; Kellgren and Lawrence 1957; Lespasio et al. 2017; Zhai et al. 2006).

KL classification:

- Grade 0: no narrowing;
- Grade 1: doubtful articular space constriction, osteophytic lipping is possible;
- Grade 2: permanent osteophytes, potential constriction of the joint space;
- Grade 3: mild osteophytes, definite constriction of the joint space, and potential end-bone deformation;
- Grade 4: severe osteophytes, severe constriction of the joint space, severe sclerosis, and definite deformation of the bone (Abramoff and Caldera 2020; Kellgren and Lawrence 1957; Kohn, Sassoon and Fernando 2016)

The adoption of the KL classification in clinical and research settings is essential to standardise the assessment of OA. However, the integration of this scale with the study of physical activity (PA) in the management of OA has not yet been systematically observed.

The research hypothesis of this study suggests that tailored PA protocols may yield superior outcomes in the treatment of KOA when aligned with the severity levels indicated by the KL classification. The goal is to investigate whether specific exercise regimens can be optimised to address the varying stages of knee OA, potentially leading to improved management of this condition. Further, as the KOA diagnosis is often associated with the use of the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaires, it is beneficial to include in the research hypothesis the classification of PA also based on those tools.

This research aims to determine how PA programs can be effectively classified and customised to align with the stages of knee OA according to the KL classification. This research aims to fill the gap in understanding the relationship between the type and intensity of PA and the stages of OA as defined by the KL classification.

2 | Materials and Methods

2.1 | Search Strategy

This systematic review' protocol was registered in the International Prospective Register of Systematic Review (PROSPERO) with the registration number CRD42024550463. A systematic review of the literature was conducted on DATA, PubMed, Web of Science, and Scopus. The articles discussing the KOA and PA were selected according to the following string: ("Knee Osteoarthritis" OR "Knee arthritis" OR "knee OA") AND ("Articular Cartilage" OR fibrocartilage OR gristle) AND (exercise OR "physical activity" OR fitness OR movement OR sport). Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were used (Page et al. 2021). The criteria of the PICO tool have been fulfilled:

- Population: adults with diagnosis of knee osteoarthritis;
- Intervention: physical activity administration;
- Comparison: healthy control group;
- Outcome: the effect of the physical activity on the knee cartilage health.

2.2 | Eligibility Criteria

The articles were deposited in EndNote 20 (EndNote 20 desktop version, Clarivate, Philadelphia, PA), and duplicate papers were automatically removed. Two independent researchers conducted the screening procedure and analysis separately. Disagreements throughout the selection procedure were settled by a senior investigator. Articles were initially screened by title and abstract, and only those that reported the use of the KL classification for KOA diagnosis and assessed PA outcomes on KOA were selected for further review. Only English written, and peer-reviewed original articles that adopted correlation, randomised, and nonrandomised controlled methods such as quasi-randomised, case-control, and comparative studies were included. Other study designs were excluded. Finally, the full text of the chosen papers was evaluated. Papers that did not consider the KL classification or evaluated PA outcomes were excluded.

2.3 | Data Collection

To gather meaningful information, the full text of each of the screened articles was reviewed. Relevant information taken from the chosen studies is as follows: years, author, KL scale, intervention, age, gender, sample analysed, exercise group, non-exercise group, control group, intervention period, frequency, outcome, and results. The results were disserted discursively in the discussion.

2.4 | Risk of Bias Assessment

The risk of bias in the included studies was assessed using the Newcastle—Ottawa Scale (NOS). This scale rates studies in three categories: selection (up to four points), comparability (up to two points), and outcome (up to three points). The score can range from 0 to 9. A high score indicates better methodological quality of the study (Lo, Mertz and Loeb 2014; Stang 2010). In the comparability section for answer (a) the number of subjects within the groups divided according to the KL scale was selected as an important factor, while for answer (b) the number of subjects within the groups divided by age and sex was selected as an important factor. In the outcome section, for question number 2, an appropriate follow-up time of 4 months was selected for all studies. Instead for question number 3, a score was assigned if there was a drop out less than or equal to 10% at follow-up (Table 1).

3 | Results

3.1 | Study Identification

Using this string, from the search conducted on the database, a total of 2136 studies were found. After removing articles published before January 1, 2013 (n = 572), 1564 articles were screened. A total of 1542 were excluded based on title and abstract. Therefore, 22 full-text articles were examined. After reading full-text articles and eliminating duplicates, a total of 9 studies were included in this systematic review. Figure 1 shows the PRISMA flow chart.

3.2 | Participants

Of nine articles included in this systematic review, a total of 745 participants with KOA were engaged, of which 433 in the exercise group (EG), 264 in the control group (CG), and 48 in NON-exercise training were involved. The sample size of the groups varied between a minimum of 37 (Durmus et al. 2013) and a maximum of 200 subjects (Kangeswari, Murali, and Arulappan 2021) (Table 2).

3.3 | Kellgren-Lawrence Scale

Not all of the single studies were able to classify, in the recruited subjects, the five degrees of severity of the scale. Only one article reported the grade 0 stipulated by the KL scale (Koli et al. 2015), just two articles did not report the grade 1 (Küçük et al. 2018; Roy et al. 2015), all articles reported the grade 2 of KOA through the KL scale, a total of four studies reported the grade 3 (Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Küçük et al. 2018; Roy et al. 2015), and no one of the articles reported the grade 4.

Three articles reported the degree of KOA based on KL classification but did not specify the distribution of severity within groups in the recruited sample (Apparao et al. 2017; Kangeswari, Murali, and Arulappan 2021; Roy et al. 2015) (Table 3).

3.4 | Gender Distribution

Of the 9 articles reviewed, six recruited only women (Durmus et al. 2013; Koli et al. 2015; Küçük et al. 2018; Multanen et al. 2017; Munukka et al. 2016; Waller et al. 2017), while two studies did not report the gender distribution within the groups examined (Apparao et al. 2017; Roy et al. 2015). Only one study reported the percentage of women within the CG and EG groups (Kangeswari, Murali, and Arulappan 2021) (Table 2).

3.5 | Physical Activity Performed

Regarding PA, the included articles comprise various types of exercise protocols. Due to this heterogeneity, a direct comparison of the respective results was not possible. However, as a general grouping of PA, three studies administered resistance training (Munukka et al. 2016; Roy et al. 2015; Waller et al. 2017), two performed aquatic resistance training (Munukka et al. 2016; Waller et al. 2017), and one studied the effects of agility training and dynamic resistance training (Roy et al. 2015). Three studies administered isometric exercise protocols (Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Küçük et al. 2018), in particular one of these, along with isometric training, also performed isokinetic and aerobic exercise programs (Küçük et al. 2018), another one performed a protocol study both with isometric and isotonic exercise (Durmus et al. 2013), and one study performed isometric exercise protocol without any other training programme comparison (Kangeswari, Murali, and Arulappan 2021). One study evaluated the efficacy of stabilisation exercises compared with

TABLE 1 | Risk of bias assessment by the Newcastle—Ottawa Scale (NOS).

Articles	Selection				Comparability		Outcome			
					Comparability of cohort					
	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at the start of the study	Main factor	Additional factor	Assessment of outcomes	Sufficient follow-up time	Adequacy of follow-up	Total 9/9
Waller et al. (2017)	*	*	*	0	*	*	*	*	*	8/9
Munukka et al. (2016)	*	*	*	0	*	*	*	*	*	8/9
Apparao et al. (2017)	*	*	*	0	*	*	*	0	*	7/9
Küçük et al. (2018)	*	*	*	0	*	*	*	0	*	7/9
Kangeswari, Murali and Arulappan (2021)	*	*	*	0	0	0	0	0	*	4/9
Koli et al. (2015)	*	*	*	0	*	*	*	*	*	8/9
Multanen et al. (2017)	*	*	*	0	*	*	*	*	*	8/9
Roy et al. (2015)	*	*	*	0	0	0	0	0	*	4/9
Durmus et al. (2013)	*	*	*	0	*	*	0	0	*	6/9

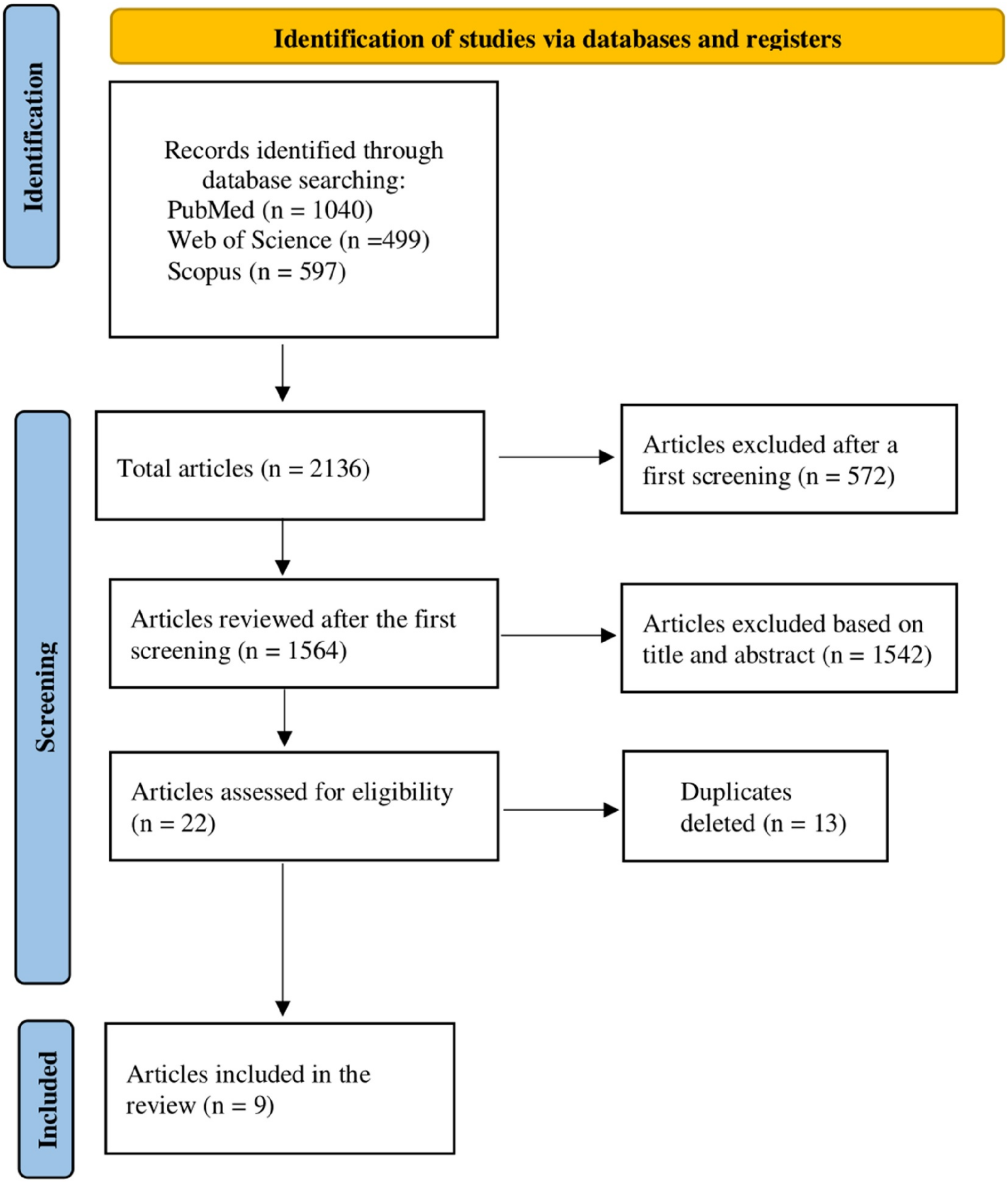

FIGURE 1 | PRISMA flow chart of total records identified through database searching.

conventional physiotherapy (Apparao et al. 2017). We included the study by Apparao et al. in the systematic review because, although they mention conventional physiotherapy, the exercises performed consist of hamstring and quadriceps stretching and strength exercises that can be part of PA protocols (Apparao et al. 2017). Three articles administered aerobic exercise training (Koli et al. 2015; Küçük et al. 2018; Multanen et al. 2017) (Table 3).

3.6 | Duration and Frequency

The duration of PA varies from a minimum of 3 weeks (Roy et al. 2015) to a maximum of 12 months (Koli et al. 2015; Multanen et al. 2017). The frequency of training ranged from a minimum of three times per week in eight studies (Apparao et al. 2017; Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Koli et al. 2015; Multanen et al. 2017; Munukka et al. 2016; Roy et al. 2015; Waller et al. 2017), only one study performed the PA for a maximum of five times per week (Küçük et al. 2018). Seven studies reported the total duration of a single training session (duration of training session in minutes, how many days per week, and total duration of the training protocol in weeks) (Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Koli et al. 2015; Multanen et al. 2017; Munukka et al. 2016; Roy et al. 2015; Waller et al. 2017) (Table 3).

3.7 | Measurement and Outcome Variables

Different measurements were used to evaluate pain, QoL, joint function, and functional performance such as Time-Up and GO (TUG) (Roy et al. 2015), Lower Extremity Function Scale

TABLE 2 | List of studies included in this Systematic Review.

Years	Authors	Study design	Age	Gender	Sample analysed	Exercise group	NON exercise group	Control group	Outcome	Results
2017	Waller et al. (2017)	Randomised controlled trial	60–68 years old	Women only	84	/ 42 /	/	42	DXA body composition, UKK 2 km walking test (walking speed), LTPA, KOOS	Research has shown that the high-resistance training programme reduces fat mass and improves walking speed in women with mild KOA.
2016	Munukka et al. (2016)	Randomised controlled trial	60–68 years old	Women only	84	/ 42 /	/	42	LTPA, transverse relaxation time (T2), dGEMRIC, UKK 2 km walking test, dynamometer chair, KOOS	Results have shown a slight significant change in the biochemical composition of medial posterior femoral cartilage. Furthermore, aquatic resistance training was well tolerated with a low risk of injury and significant improvement in cardiorespiratory capacity, but without significant effects on muscle strength and self-reported symptoms.
2017	Apparao et al. (2017)	Randomised controlled trial	35–65 years old	Not specified	93	/ 45 /	48	/	VAS, ELISA test, KOOS	The study showed significant differences in all KOOS subcomponents in both groups but with no significant differences in pain sub-score and no effect on serum COMP values. In addition, stabilisation exercises were found to be effective in improving knee function.
2018	Küçük et al. (2018)	Comparative study	45–65 years old	Women only	45	15 15 15	/	/	VAS, WOMAC, isokinetic dynamometer, MRI, Lequesne index	The research has shown that isokinetic, aerobic, and isometric training protocols improved all

(Continues)

TABLE 2 | (Continued)

Years	Authors	Study design	Age	Gender	Sample analysed	Exercise group	NON exercise group	Control group	Outcome	Results
										pain outcomes assessed by VAS, WOMAC, and Lequesne index, with no superiority of one type of protocol over another. Peak torque in knee extension was greater in the isokinetic group, while the improvements in peak torque in knee flexion were significant only in the isokinetic group. Only in the isometric group were improvements in patellar cartilage volumes noted.
2021	Kangeswari, Murali, and Arulappan (2021)	Quasi-experimental research design	45–65 years old	Men and women	200	/ 100 /	/	100	WOMAC	The study showed that there were significant reductions in pain and stiffness, and improvements in physical function.
2015	Koli et al. (2015)	Randomised controlled trial	50–65 years old	Women only	76	/ 36 /	/	40	Transverse relaxation time (T2), dynamometer chair, Nottingham power rig, 2-km walk test, KOOS	This study has shown that high and intensive exercises provide proper stimulation and beneficial effects on improving patellar cartilage quality and overall health/physical function in people with mild KOA. Furthermore, the exercise protocol is well tolerated and reduces risk factors for falls.

(Continues)

TABLE 2 | (Continued)

Years	Authors	Study design	Age	Gender	Sample analysed	Exercise group	NON exercise group	Control group	Outcome	Results
2017	Multanen et al. (2017)	Randomised controlled trial	50–65 years old	Women only	76	/ 36 /	/	40	DXA, transverse relaxation time (T2), dGEMRIC, RAND-36, WOMAC	Results have shown that high-impact exercise can positively change femoral neck strength. Progressive high-impact training was shown to be safe for cartilage health. High-impact exercise can be viable in reducing physical performance-related risk factors. No intergroup differences were observed in knee pain, stiffness, and physical function.
2015	Roy et al. (2015)	Comparative study	40–55 years old	Not specified	50	25 / 25	/	/	TUG, LEFS	This study has shown improvements in knee function after intervention protocols. Furthermore, it was observed that the effectiveness of agility and perturbation training is higher than that of dynamic resistance training.
2013	Durmus et al. (2013)	Randomised controlled trial	ExG = 56.94 ± 5.95/ GlucoG = 57.75 ± 6.46	Women only	37	19 / 18	/	/	WOMAC, 6MWT, hand-held dynamometer, enzyme immunoassay kit	In this study improvements in some of the WOMAC sub-scale (pain and physical function), muscle strength and walking distance, and a decrease in leptin levels were found, but with no significant differences between the two groups.

Abbreviations: 6MWT, Six Minute Walking Test; dGEMRIC, delayed gadolinium-enhanced magnetic resonance imaging of cartilage; DXA, dual-energy X-ray absorptiometry; KOOS, Knee Injury and Osteoarthritis Outcome Scores; LEFS, Lower Extremity Function Scale; LTPA, leisure time physical activity; MRI, Magnetic Resonance Imaging; RAND-36, RAND 36-Item Health Survey 1.0 questionnaire; TUG, Timed Up and GO; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 3 | Division of studies by degree of Kellgren & Lawrence severity, type of physical activity performed, intervention period, and frequency.

Years	Authors	Kellgren & Lawrence scale	Physical activity performed	Intervention period	Frequency
2017	Waller et al. (2017)	Grade 1–2	High intensity aquatic resistance training	16 weeks	1 h, 3 times a week
2016	Munukka et al. (2016)	Grade 1–2	Aquatic resistance training	16 weeks	1 h, 3 times a week
2017	Apparao et al. (2017)	Grade 1–2	Conventional physiotherapy and stabilisation exercises	8 weeks	3 times a week
2018	Küçük et al. (2018)	Grade 2–3	Isokinetic, isometric and aerobic training	4 weeks	5 days a week
2021	Kangeswari, Murali, and Arulappan (2021)	Grade 1–2–3	Isometric training	12 weeks	20 min counselling session and isometric exercises daily one-to-one basis for 40 min on six consecutive days; plus 3 times a day exercise at home
2015	Koli et al. (2015)	Grade 0–1–2	Aerobic/step aerobic jumping training	12 months	55 min, 3 times a week
2017	Multanen et al. (2017)	Grade 1–2	High-impact aerobic and step aerobic training	12 months	55 min, 3 times a week
2015	Roy et al. (2015)	Grade 2–3	Agility training and dynamic resistance training	3 weeks	45 min, 3 times a week
2013	Durmus et al. (2013)	Grade 1–2–3	Isometric and isotonic exercise	12 weeks	50 min, 3 times a week

(LEFS) (Roy et al. 2015), Knee Injury and Osteoarthritis Outcome Score (KOOS) (Apparao et al. 2017; Koli et al. 2015; Munukka et al. 2016; Waller et al. 2017), Visual Analogue Scale (VAS) (Apparao et al. 2017; Küçük et al. 2018), Western Ontario and McMaster Universities Arthritis Index (WOMAC) (Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Küçük et al. 2018; Multanen et al. 2017), Lequense Index (Küçük et al. 2018), Rand 36-Item Healthy Survey 1.0 questionnaire (RAND-36) (Multanen et al. 2017), Hand-held dynamometer (Durmus et al. 2013), Enzyme immunoassay kit to measure the leptin level (Durmus et al. 2013), Isokinetic dynamometer (Küçük et al. 2018), Dynamometer chair (Koli et al. 2015; Munukka et al. 2016), Nottingham power rig (Koli et al. 2015), 2-km walk test (Koli et al. 2015), UKK 2 km walking test (Munukka et al. 2016; Waller et al. 2017), 6 Minute Walk Test (6MWT) (Durmus et al. 2013), Leisure time physical activity (LTPA) (Munukka et al. 2016; Waller et al. 2017), Transverse relaxation time (T2) (Koli et al. 2015; Multanen et al. 2017; Munukka et al. 2016), delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) (Multanen et al. 2017; Munukka et al. 2016), Dual-energy X-ray absorptiometry (DXA) scanning (Multanen et al. 2017; Waller et al. 2017), ELISA test to measure serum Cartilage Oligomeric Matrix Protein (serum COMP) (Apparao et al. 2017) and Magnetic resonance imaging (MRI) (Küçük et al. 2018) (Table 2).

4 | Discussion

KOA is a chronic condition impacting the QoL of millions worldwide. The progressive nature of KOA, along with pain, functional limitations, and reduced overall well-being, highlights the need for specific interventions. PA plays a crucial role in the management of KOA, potentially reducing pain, improving function, and enhancing the QoL. This study investigated the potential benefits of classifying and tailoring PA programs based on KOA severity identified by the KL scale. The results of the comprised articles point out the valuable effects of PA to manage the KOA based on the KL scale, reporting positive outcomes for pain and QoL. These outcomes have been measured through KOOS, WOMAC, VAS, and the Lequesne Index (Apparao et al. 2017; Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Koli et al. 2015; Küçük et al. 2018; Munukka et al. 2016; Waller et al. 2017). However, rating scales such as KOOS, WOMAC, and VAS, while valuable, rely on self-reporting. This can introduce potential biases based on the perception of the individual or the desire to minimise or exaggerate symptoms. For instance, Stratford, Kennedy and Clarke (2018) observed that the WOMAC physical function part could provide biases for the assessment of motor functions. As for WOMAC, Roos et al. (1998) found some limitations also for KOOS, such as patients' self-reported outcomes, reliability, validity, and user-friendliness. In particular, subjects may not be as sensitive to variability in pain, joint function, and QoL (Roos et al. 1998). Similar limitations have the VAS scale; Hawker et al. (2011) consider that one of the main limitations may be people's poor subjective assessment; moreover, everyone may assess pain differently, and especially elderly people may have difficulty in completing VAS pain due to possible cognitive impairment or motor problems.

The positive effect of PA on joint cartilage quality in KOA is essential for managing both physiological and psychological aspects of the condition (Petrigna et al. 2022; Trovato et al. 2023). Different studies have found improvements in the knee cartilage volume in those who performed PA. Specifically, aerobic and isometric exercises are the most studied PA programs, suggesting that isometric-type training gives better results at the level of patellar cartilage (Koli et al. 2015; Küçük et al. 2018; Multanen et al. 2017).

Aerobic, isometric, and resistance training represent the major types of exercises used in the reviewed studies for managing KOA since they showed excellent results on pain, QoL, and knee function outcomes (Durmus et al. 2013; Kangeswari, Murali, and Arulappan 2021; Koli et al. 2015; Küçük et al. 2018; Multanen et al. 2017; Munukka et al. 2016; Roy et al. 2015; Waller et al. 2017).

In particular, high-intensity aquatic resistance training offers important results for managing KOA due to its ability to improve fitness while also reducing body mass, a significant risk factor for KOA development (Munukka et al. 2016; Waller et al. 2017). Waller et al. (2017) and Munukka et al. (2016) studied the effects of aquatic resistance exercise; in particular, in the study by Waller et al. (2017), no differences were found between the EG and the CG in any domain of KOOS and, at 12-month follow-up, the improvements found after 4 months of aquatic resistance training, in the EG, regarding fat mass and body weight were lost. Otherwise, walking speed, at 12-month follow-up, remained better in the EG than in the CG (Munukka et al. 2016; Waller et al. 2017). Munukka et al. (2016), instead, showed that the values of T2 and dGEMRIC index changed at the end of the 4-month intervention. A significant decrease in T2 and dGEMRIC index was found in the training group compared with the CG in the full-thickness posterior region of interest (ROI) of the medial femoral cartilage. In addition, significant decreases were found in the training group compared with the CG only in the deep posterior ROI and not in the superficial ROI of the medial femoral cartilage for both T2 and dGEMRIC indexes. Peak cardiorespiratory fitness (VO2) increased in the training group compared with the CG group, while no differences were found between the groups in knee extension or flexion muscle strength and, like Waller et al. (2017), no differences were found between the groups in any of the KOOS domains. Waller et al. (2017) and Munukka et al. (2016) showed that aquatic resistance training can reduce the fat mass and the body weight of the subjects, which is one of the factors influencing the progression of knee osteoarthritis, and also improve the outcomes measured through the walking speed, furthermore, the results of the improvement in walking speed found by Waller et al. (2017) can be matched with the feedback from the study by Munukka et al. (2016), as this study showed that aquatic resistance training improved the cardiorespiratory function of subjects with KOA, underlining that subjects with this chronic problem well tolerated this type of training.

Continuing with the reviewed studies Koli et al. (2015) and Multanen et al. (2017) focused their research on the effects of aerobic training. As in the study of Munukka et al. (2016), Koli et al. (2015) also found changes in T2 at the end of the 12-month intervention. The exercise intervention had an average effect on the T2 values of the total patellar cartilage, the lateral deep zone and the lateral superficial zone, showing an improvement in cartilage quality. In the total deep zone and total lateral segment, the effect of the intervention training was medium. In the medial deep zone, exercise had a small but significant effect. In addition, Koli et al. (2015) found improvements in isometric extension strength and maximal aerobic capacity in the EG. Multanen et al. (2017) in their study, showed that total physical activity load (DISTotal) was significantly higher in the EG than in the CG group, highlighting that the exercise programme showed a difference between the two groups. And that, after 12 months, regarding the relationship between cartilage and bone, an association was found between the change in T2 value (cartilage) in the medial femoral condyle and the change in dGEMRIC index (cartilage) in the lateral femoral condyle and Z (bone), showing that Z increased with decreasing relaxation time in T2 and increasing dGEMRIC index values. Koli et al. (2015) and Multanen et al. (2017) demonstrated that in addition to being well tolerated, aerobic training provides both stimulation and favourable effects on patellar cartilage by not damaging it, improves the overall health status of individuals with KOA, and can be a valid training to reduce risk factors related to physical performance.

Regarding isometric training, Küçük et al. (2018), Kangeswari, Murali, and Arulappan (2021), and Durmus et al. (2013) studied its benefits. Of the previous three studies, Küçük et al. (2018) studied three different protocols of interventions (isokinetic, isometric, and aerobic) and observed significant improvements in pain scores during daily activities after the interventions in all groups, although the difference did not reach significance. In all groups, peak torque values of knee flexion and extension were measured at angular velocities of 60° and 180°/s of the right knee (Küçük et al. 2018). In all three groups, the peak torque values of knee extension at 60° and 180°/s improved significantly after 4 weeks of training. In the isokinetic group, the peak torque values of 60° knee flexion and 180°/s angular velocity improved significantly, whereas no significant changes were found in the aerobic group and the isometric group (Küçük et al. 2018). In addition, the improvements in flexion peak torque and extension peak torque at 60°/s angular velocity and 180°/s angular velocity were not significantly different between the groups (Küçük et al. 2018). Also, the hamstring/quadriceps ratio remained almost unchanged in the isokinetic group and decreased in the aerobic and isometric groups. No significant changes in femoral cartilage volume were observed in any of the groups after the respective interventions. Meanwhile, concerning patellar cartilage volume, there were statistically significant changes in the isometric group, while in the isokinetic and aerobic groups, the changes were not significant (Küçük et al. 2018). Meanwhile, Durmus et al. (2013), in their study, researched the effects of the PA protocol performed through isometric training and isotonic training with glucosamine supplementation, comparing a group that performed only the isometric and the isotonic training and a group that performed isometric and isotonic training with glucosamine supplementation. Durmus et al. (2013) found improvement in both groups in some of the WOMAC sub-scales (pain and physical function), quadriceps muscle strength, walking distance, and a decrease in leptin levels. Also, Kangeswari, Murali, and Arulappan (2021), who performed only an isometric training protocol, at the end of it, found pain reduction, and improvements in stiffness and physical function in the EG, and at the same, they also found a reduction of pain and improvements in stiffness and physical dysfunction in the CG, but these differences were not statistically significant, as in the EG. In particular, the results showed that after the intervention, the difference in the level of pain in the exercise and CG was significant in 30, 60, and 90-day post-tests (Kangeswari, Murali, and Arulappan 2021). Specifically, the differences between groups on pain, stiffness, and physical dysfunction of subjects with KOA were statistically significantly high at 60 and 90 days after intervention (Kangeswari, Murali, and Arulappan 2021). Furthermore, Kangeswari, Murali, and Arulappan (2021) showed that the reduction of pain level score was higher in the experimental group compared with the CG.

Therefore, based on the findings of this systematic review, resistance, aerobic, and isometric training should be considered as primary exercise recommendations for individuals with KOA.

Additionally, stabilisation exercises, agility training, and dynamic resistance training demonstrated positive outcomes and can be valuable components of comprehensive exercise programs (Apparao et al. 2017; Roy et al. 2015).

Roy et al. (2015) demonstrated how even agility and dynamic resistance training can improve knee function after 21 days of training at a frequency of 3 days per week and 45 min of exercise. They showed that the LEFS outcomes test increased in both the agility training group and the dynamic resistance training group by comparing the same test from day 0 to day 21, and the same thing can be said for the TUG test, in both training groups there was a decrease in outcome parameters (Roy et al. 2015). Apparao et al. (2017) showed that all KOOS score subcomponents and within-group changes in serum COMP values from baseline to post-test in both the control and experimental groups were statistically significant. There was a significant difference in all KOOS score subcomponents between the groups, but no significant difference was found in the KOOS pain subcomponent. In addition, there was no significant difference between the groups in the mean VAS scores at baseline and post-test, but within-group changes in the VAS measure from baseline to post-test in both the control and experimental groups were significant (Apparao et al. 2017). This indicated that both stabilisation exercise training and conventional physiotherapy can provide excellent results in the management of subjects with KOA. In particular, stabilisation exercise training was found to have more effect in terms of joint function when compared with conventional physiotherapy intervention (Apparao et al. 2017).

There are many studies in the scientific literature that validate the beneficial effects of PA on individuals with KOA, going on to improve the QoL, reducing pain and improving joint function and performance of the subjects; in this regard, reference can be made to the studies by Vincent et al. (2019) and Vincent and Vincent (2020) that employed the sit-to-stand, stair climb, 6-min walking test, knee flexion, and knee extension tests to evaluate the outcomes of their intervention. The authors administered concentric and eccentric resistance training, finding an increase in leg muscle strength and improvement in sit-to-stand and stair climb functional tests. Their findings suggest that improving knee flexion strength can significantly reduce pain as reported by subjects through the WOMAC (Vincent et al. 2019; Vincent and Vincent 2020). Therefore, it can be underlined that Vincent et al. (Vincent et al. 2019; Vincent and Vincent 2020) in their studies found that both types of resistance training reduced the pain caused by KOA, that concentric resistance training significantly reduced the severity of pain compared to eccentric resistance training, and also both types of resistance training significantly increased leg strength. Finally, it cannot be evinced from the studies which of the two types of training is better than the other, so the choice and use of either resistance programme may be determined by preference, objectives and equipment availability (Vincent et al. 2019; Vincent and Vincent 2020).

A great heterogeneity was found in the articles reviewed in this systematic review regarding the results and the choice of the best type of PA according to the severity of the knee osteoarthritis, but the consistent use of the KL classification in all articles, although different types of PA are present, allowed us to achieve the goal of this systematic review by classifying specific PA protocols based on the KL scale (Table 4).

TABLE 4 | The table shows the different types of physical activity performed according to the degree of severity of knee osteoarthritis assessed using the KL scale.

Grade	Aerobic training	Isometric training	Isokinetic training	Resistance training	Agility training	Stabilisation exercise	NON exercise training
0	X	—	—	—	—	—	—
1	X	X	—	X	—	X	X
2	X	X	X	X	X	X	X
3	—	X	X	X	X	—	—
4	—	—	—	—	—	—	—

5 | Conclusion

Physical exercise programs seem to be both safe and beneficial for people with KOA. Therefore, there is consistent proof of the effects of physical exercise on decreasing pain, strength, knee function, and QoL. Regarding the other variables studied, additional studies are needed to confirm the positive effect of exercise on its improvement. Although aerobic, resistance and isometric training were the most performed among the studies reviewed, according to our systematic review, to achieve optimal benefits, physical activities, whether they are resistance, aerobic, isokinetic, isometric, stabilisation, or agility programs, should be performed for a minimum of 3 to a maximum of 5 sessions per week with a duration of 1 h. Exercise programs can play an important role in the rehabilitation of patients with KOA and in managing the progress of chronic disease. Finally, at an early stage, in order to understand the degree and severity of KOA, it is recommended to perform an X-ray of the joint district based on the KL scale before starting the rehabilitation and reeducational programme, so as to better manage the chronic issue. Next, according to what has been researched in the literature, operators are recommended to assess the subject's health status and QoL through questionnaires, such as the WOMAC, KOOS or RAND-36, through pain rating scales, such as the VAS, through functional performance assessment tests, such as the 6MWT, the TUG, the 2 km walk test and through the use of isokinetic dynamometers for the assessment of muscle strength. Finally, during the rehabilitation and functional reeducation process, it is also recommended to conduct joint assessments through MRI.

Author Contributions

Alberto Canzone: conceptualization, data curation, formal analysis, writing—original draft, writing—review and editing. **Federico Roggio**: conceptualization, data curation, formal analysis, writing—original draft. **Antonino Patti**: supervision, visualization, methodology, writing—review and editing. **Valerio Giustino**: supervision, methodology, writing—review and editing. **Carmen Mannucci**: conceptualization, writing—original draft, visualization, writing—review and editing. **Debora Di Mauro**: visualization, methodology, writing—review and editing. **Giuseppe Musumeci**: Funding acquisition, visualization, supervision, methodology. **Antonino Bianco**: funding acquisition, supervision, methodology. **Fabio Trimarchi**: project administration, funding acquisition, visualization.

Acknowledgements

'The work was carried out as part of the PRIN 2022 project entitled "Predictive model of osteoarthritis through the use of inertial knee brace and thermography applied to movement analysis. Get back to move!" announcement D.D. n. 104 del 2 febbraio 2022 financed by the European Union – NextGenerationEU - The Italian Ministry of University and Research (MUR)'.

Open access publishing facilitated by Universita degli Studi di Palermo, as part of the Wiley - CRUI-CARE agreement.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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