

Concentric or eccentric physical activity for patients with symptomatic osteoarthritis of the knee: a randomized prospective study

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Abstract

Background: Knee osteoarthritis-related pain limits physical function and leads to functional disability. Physical activity is one of the central recommendations for the management of knee osteoarthritis. Although concentric muscle activities are often preferred to eccentric ones, the corresponding rationale remains controversial.

Objective: To explore the effect of a 6-week exercise program on function, pain, and performance in patients with symptomatic knee osteoarthritis.

Methods: Patients with symptomatic knee osteoarthritis were included in the prospective EX-ART project (Walking performance in osteoARThritic subjects: effect of an ECCentric muscle strengthening program) and randomized in a 6-week rehabilitation program including either eccentric or concentric activities. Metrics of interest chosen as end points measured before and after the rehabilitation were WOMAC score, pain, and muscular performance (quadriceps power P_{MAX} and contraction strength M_{MAX}). MRI was also used to assess muscle volume and fat infiltration changes.

Results: 30 patients were included in each group; mean age was 74 (± 7.6); 69% were women. At week 6, both groups showed a significant improvement in the WOMAC without difference between the two groups ($p=0.7$). No difference between the two groups was identified for the pain reduction ($p=0.7$). A significant improvement in the change in P_{MAX} and M_{MAX} at high velocity ($p=0.001$ and $p=0.002$) was observed in the eccentric group only. A vastus medialis hypertrophy was quantified in the eccentric group only ($p=0.002$), whereas fat infiltration in the quadriceps muscles was unchanged.

Conclusion: Physical activity, whether eccentric or concentric, has a benefit on function and pain in patients with symptomatic knee osteoarthritis. A few differences have been identified between the two types of rehabilitation. More particularly, a gain in muscle performance and vastus medialis volume was found with eccentric rehabilitation only.

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Keywords: concentric, eccentric, knee, osteoarthritis, quadriceps, rehabilitation

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Introduction

Knee osteoarthritis causes pain and limits physical function leading to functional disability.^{1,2} Recent advances in the knowledge of the pathophysiology of osteoarthritis have shown that it involves the entire joint including the crosstalk

between cartilage, synovial tissue, and periarticular muscles. Osteoarthritis is influenced by modifiable lifestyle factors (overweight, physical activity, etc.) or nonmodifiable factors (age, sex, genetic background, etc.).³ Loss of muscle mass and muscle strength is independently associated

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with knee osteoarthritis symptoms.⁴ Weakness of the thigh extensors is associated with a higher risk of developing symptomatic knee osteoarthritis.^{5,6} Studies have also demonstrated that patients with knee osteoarthritis have greater fat infiltration and quadriceps weakness, and that a reduction in vastus medialis (VM) fat infiltration is associated with a decrease in annual loss of medial tibiofemoral and patellofemoral cartilage.^{7,8} A wide range of rehabilitation programs have been proposed.^{9,10} A literature review covering 54 studies confirmed a marked effect of rehabilitation on pain at least equivalent to that of nonsteroidal anti-inflammatory drugs (NSAIDs) and a lesser effect on function.^{10–12} These improvements can last for more than 6 months postintervention.¹⁰ As a consequence, current international guidelines place physical activity at the center of knee osteoarthritis management, and particularly muscle strengthening against resistance.¹³ Concentric muscle strengthening is often preferred, and yet eccentric contractions play an important role in controlling knee flexion and knee stability, and develop a high level of strength at low energy cost.^{14,15} In the past decade, greater interest has been shown for including eccentric contractions in the muscle strengthening program, although recent studies have not shown a superiority of one or the other of these techniques.¹⁶ For some authors, comparable gains in terms of function, muscle mass and pain relief can be obtained from the two types of exercises; while for others, exercises focusing on eccentric contractions present a greater benefit in terms of function and muscle strength gain.^{17–20} The choice of physical activity to manage symptomatic knee osteoarthritis therefore remains controversial.

The objective of our study is to compare the effects after a 6-week rehabilitation program based on concentric muscle strengthening with those of a 6-week program based on eccentric muscle strengthening in patients with symptomatic knee osteoarthritis.

Materials and methods

Study design and patients

This study is a post hoc analysis of an original study called EXART, which was a prospective single-center randomized study aimed at comparing the effect on fatigue of 6 weeks of concentric *versus* eccentric physical activity in subjects with

symptomatic tibiofemoral knee osteoarthritis. Participants were recruited consecutively starting on September 25, 2017, from among the patients scheduled for appointments within the rheumatology department of the Nice University Hospital Center. The study only included patients aged 40 to 85 years who were ambulatory and suffered from symptomatic knee osteoarthritis meeting ACR (American College of Rheumatology) criteria with a Kellgren–Lawrence (KL) radiological grade of 2 or 3.^{21,22} Patients with a KL radiological grade of 1 were excluded as were patients in severe stages with a radiological grade of 4. The study did not include patients with isolated symptomatic patellofemoral osteoarthritis and patients with MRI contraindications or co-morbidities, particularly cardiovascular ones, which prohibit specific physical activities. Symptomatic osteoarthritis at the radiological grade of 4 according to KL or a knee prosthesis on the contralateral knee was also a reason for exclusion. Inclusion was determined during the first appointment at the center. Patients were randomized regarding the concentric or eccentric activity. Randomization was performed centrally by the delegation of clinical research and innovation of the Nice University Hospital, using the RedCap integrated randomization module. The randomization lists were created using the nQuery Advisor v7.0 software. Randomization was balanced one-to-one between groups, without stratification on gender. All patients underwent two sessions per week of supervised rehabilitation over a period of 6 weeks. After this period, they were assessed once again by the same person who conducted the baseline at inclusion (C.R.). This assessment was carried out blind from the data collected during the rehabilitation sessions. A muscle MRI was performed at inclusion and at 6 weeks on a subgroup of patients.

Collection of data

All participants had a clinical examination during the baseline appointment and data were collected regarding their age, sex, weight, height, BMI, analgesics prescribed, medical and surgical history, and pain intensity on the standard numerical rating scale (NRS). Patients filled out a WOMAC questionnaire (Western Ontario and McMaster Universities Osteoarthritis Index) and completed a 6-min walk test (6WT). A subset of patients was given a muscle MRI of the thigh. These data were also collected after 6 weeks. An NRS pain rating was collected in addi-

tion at each interim appointment at the rehabilitation center.

Groups of exercises. After randomization (1:1), subjects were assigned to either a group assigned concentric quadriceps exercises or a group given eccentric contraction exercises. An experienced engineer specialized in designing physical activities supervised the exercise protocols for two 1-h sessions per week. The protocols followed the recommendations of the American College of Sports Medicine (ACSM) for aerobic, flexibility, balance, and muscle strengthening exercises.²³ The sessions were therefore similar for the two groups except for the muscle strengthening exercises (concentric *versus* eccentric). Both groups used resistance bands and weights to increase muscle strain. The maximum level of pain tolerated during exercising was ≤ 5 on the numerical rating scale. The exercises were adjusted if pain increased.

Protocol for measuring performance data. After installing participants in optimum conditions on the isokinetic ergometer, all participants completed a 10-min warm-up exercise on a cycle ergometer at a power of 50 W and 50 to 60 rotations per minute to become familiar with the isokinetic extension of the lower limbs. The subjects then performed three maximum contractions at six preset velocities (180, 150, 120, 90, 60, and 30°/s). Only the best of the three trials was retained for statistical analyses. Participants were verbally encouraged during each trial. Subjects were allowed a 4-minute rest period between each test to avoid a phenomenon of fatigue.

The maximum torque (maximum force) was identified as the highest value achieved during the movement at each constant velocity. Instantaneous maximum power is the product of torque (force) times velocity. The linear moment–velocity relationship was obtained from the maximum torque value obtained at each imposed velocity. The power (P)–velocity (V) relationship was described using a second-order polynomial relationship of the type: $P = a \cdot V^2 + b \cdot V + c$, where a , b , and c are coefficients of the polynomial regression. From this equation, the maximum power (P_{MAX}), and the corresponding optimum velocity (V_{OPT})

were determined such that: $V_{OPT} = -\frac{b}{2a}$ and $P_{MAX} = -\frac{b^2}{4a} + c$. The theoretical maximum

moment (M_{MAX}) and the theoretical maximum velocity (V_{MAX}) were obtained by extrapolating the linear relationship when this relationship reached, respectively, the x-axis for $M=0$ and the y-axis for $V=0$. All of these relationships and parameters were processed by creating a MATLAB script (R2008b, The MathWorks, Natick, MA, USA).

MRI

For financial reasons, only 40 patients (20 in each group) were able to have MRI follow-up. They were selected in consecutive order of appearance. The muscle MRI was performed using an Optima MR450w GEM 1.5 T scanner. T1-weighted images (T1 W) in the axial plane (35–50 slices depending on the patient's size) were recorded with the following parameters: 400 mm field of view, 160×320 acquisition matrix, 4-mm section thickness, 2-mm intersection gap. The TR-TE (ms) values were 578-11, the tilt angle was 90°, and the refocusing flip angle was 120°. The total acquisition time was 2.21 min. Image uniformity correction was used to reduce signal inhomogeneities caused by the receiving coils.

Image processing. A four-step processing pipeline was used:²⁴

Step 1: Each image was first corrected for any remaining inhomogeneity.

Step 2: Regions of interest (masks) on each image were carefully outlined manually by the same observer (M.C.T.) using FSLview. We were careful not to select areas of the subcutaneous fat compartment (Figure 1).

Step 3: Pixel intensity distribution (histograms) in each region of interest was normalized with a linear interpolation using the bone marrow intensity in the lumen of the femur as a 100% reference.

Step 4: The mean pixel intensity (MPI) value in each region of interest was quantified. This value is proportional to the fat infiltration.

Assessment criteria

The primary criteria in our study were the WOMAC questionnaire, which is specifically designed to measure functional disability due to osteoarthritis.²⁵ The questionnaire comprises 24 items divided into three categories: pain (five questions, 20 points), stiffness (two questions,

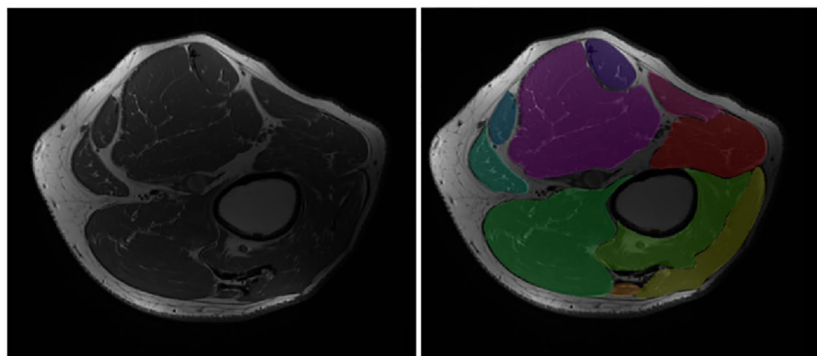


Figure 1. MRI image processing. Step 2, masks were created for each image using FSLview to outline each muscle head of the thigh. The bone, vasculo-nervous, and subcutaneous adipose compartment were excluded.

8 points) and physical function (17 questions, 68 points). The value assigned to each question varies from 0 to 4: *null* = 0; *minimal* = 1; *moderate* = 2; *severe* = 3; *extreme* = 4. The maximum score for the Likert-type variant of the questionnaire is 96 points (worst function, stiffness, and severe pain). A low score indicates a better articulation condition or a better result.

Secondary assessment criteria included pain, assessed on a standard Numerical Rating Scale (NRS, 0 = no pain, 10 = extreme pain), and walking distance covered, assessed by the 6-minute walk test (6WT) which counts the number of round trips completed between two cones spaced 30 m apart on a flat surface over 6 min.^{26,27} The total distance walked was recorded using OptoGait. Muscle performance of the quadriceps was also measured by calculating the theoretical maximum moment (M_{MAX}) and maximum power (P_{MAX}) using an isokinetic ergometer.

The MRI before and after the intervention measured the fat infiltration rate (given by the MPI value expressed in arbitrary units) and the volume (in cm^3) of the vastus lateralis (VL) and vastus medialis (VM).

Statistical analysis

Results are presented as mean values with standard deviations. According to the data distribution, groups were compared using either Student's *t*-test or Mann-Whitney *U* tests. For each group, the intervention effect was analyzed using paired tests. All the analyses were conducted using R Studio and a *p*-value lower than 0.05 was considered as significant.

Results

Patient characteristics

The flowchart presented in Figure 2 shows that out of 80 patients screened, 60 were included in the study and randomized into two groups. After 6 weeks, a total of 25 in the concentric group and 28 patients in the eccentric group completed the assessment. The mean age of the patients was 72 years (± 6.8 years) in the concentric group, and 74.5 years (± 8.3 years) in the eccentric group. The mean BMI was 26.9 (± 4.7) and 27.5 (± 4.1) kg/m^2 , respectively, for both groups. 84% of patients were women in the concentric group and 57% in the eccentric group ($p = 0.03$). Patient characteristics are presented in Table 1. Regarding patients with inflammatory rheumatism, only patients with prolonged clinical remission (> 1 year) were eligible. The groups were comparable, apart from the higher proportion of women in the concentric group.

Effect of 6 weeks of supervised training

We did not observe any difference between the two groups in the improvement of the WOMAC total score ($p = 0.7$) or of the score in any of its three categories after 6 weeks (Table 2). However, we observed a significant improvement in the WOMAC total score in each group ($p < 0.0001$ for each) and in the WOMAC function score of the concentric group only ($p = 0.008$) (Table 2).

There was no difference in the change in pain intensity between the two groups after 6 weeks of training ($p = 0.7$). However, both groups showed a significant reduction in pain of -2.3 ± 2.3 points on average in the concentric group ($p < 0.001$) and

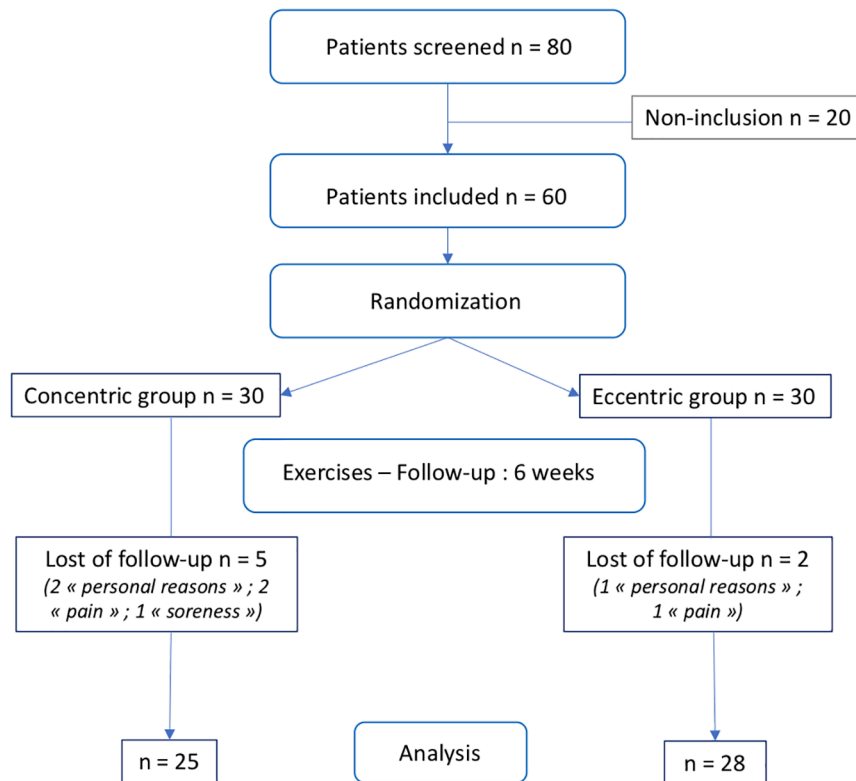


Figure 2. Flowchart summarizing study design.

of -2.3 ± 2 points on average in the eccentric group ($p < 0.0001$). There was no difference in the 6WT between the two groups after 6 weeks of training ($p = 0.37$), but a significant improvement was noted in the distance covered by members of the concentric group ($+32 \pm 61$ m) on average ($p = 0.02$).

An improvement in performance was observed in the group that performed eccentric exercises (Table 2 and Figure 3). This included a significant improvement in power (Watts) in the eccentric group that was not replicated in the concentric group [eccentric: 179 ± 62.3 final – 158.3 ± 59 baseline ($p = 0.001$); concentric: 164.9 ± 56 final – 160.2 ± 69 baseline ($p = 0.52$), with a trend toward significance for the difference between the two groups ($p = 0.09$]. We also found a significant improvement in strength at fast velocities (maximum moment, 150 and 180°/s) in the eccentric group only (eccentric 150°/s: 66.7 ± 24.1 final – 58.4 ± 25 baseline ($p = 0.002$); concentric 150°/s: 57.7 ± 19 final – 55.8 ± 22.4 baseline ($p = 0.27$)], with a significant result for the difference between the two groups ($p = 0.037$). There was no difference in

the M_{MAX} between the two groups after 6 weeks of training ($p = 0.4$).

MRI assessment

A total of 20 patients per group underwent an MRI of the thigh before and after training. The MRI scans of 10 patients in the concentric group and 13 patients in the eccentric group have been discarded due to movement artifacts in the corresponding MR images. MRI scans could be analyzed for a total of 10 patients in the concentric group, and 7 in the eccentric group. The characteristics of these patients are not presented (Supplementary Data).

We observed a significant increase in the volume of the VM in cm^3 in the eccentric group (VM 15.9 ± 5.8 initial, 16.7 ± 5.8 final, $p = 0.002$) that was absent in the concentric group (12.5 ± 5.8 initial, 12.7 ± 5.2 final, $p = 0.64$) (Figure 4(a)). The volume of the vastus lateralis did not change in both groups (concentric: 9.8 ± 2.5 initial, 9.3 ± 2.5 final, $p = 0.46$; and eccentric 10.4 ± 3 initial, 10.2 ± 2.6 final,

Table 1. Patient characteristics at inclusion in the cohort and in each group.

	Total, <i>n</i> = 53	Concentric group, <i>n</i> = 25	Eccentric group, <i>n</i> = 28
Gender, women, <i>n</i> (%)	37 (69)	21 (84)	16 (57)
Age, years, mean ± SD	74.3 ± 7.6	72 ± 6.8	74.5 ± 8.3
BMI, kg/cm ² , mean ± SD	27.2 ± 4.4	26.9 ± 4.7	27.5 ± 4.1
Duration of condition, years, mean ± SD	10 ± 6.9	10 ± 7.7	8.5 ± 6
Hip osteoarthritis, <i>n</i> (%)	6 (11.3)	2 (8)	4 (14.2)
Hand osteoarthritis, <i>n</i> (%)	21 (39)	11 (44)	10 (35.7)
Menisectomy, <i>n</i> (%)	8 (15)	4 (16)	4 (14.2)
Radiological chondrocalcinosis, <i>n</i> (%)	8 (15)	4 (16)	4 (14.2)
Inflammatory rheumatism, ^a <i>n</i> (%)	7 (13)	3 (12)	4 (14.2)
Daily intake of paracetamol, <i>n</i> (%)	18 (33.9)	7 (28)	11 (39.2)
Daily intake of tramadol, <i>n</i> (%)	6 (11.3)	3 (12)	3 (10.7)
Charlson Score, med (min–max)	3 (1–7)	3(2–5)	3 (1–7)
10-year survival rate (%)	77	77	77
WOMAC total, mean ± SD	49.2 ± 19	49.7 ± 17.4	48.8 ± 20
WOMAC function, mean ± SD	34.4 ± 15	34.8 ± 12.3	34 ± 17
WOMAC stiffness, mean ± SD	4.5 ± 1.8	4.7 ± 1.7	4.4 ± 1.9
WOMAC pain, mean ± SD	10.3 ± 4	10.2 ± 3.2	10.3 ± 4
NRS, mean ± SD	5.3 ± 1.8	5.3 ± 2	5.2 ± 1.7
6WT, meters, mean ± SD	424 ± 80	417 ± 80	430 ± 82.3
M _{MAX} , Nm, mean ± SD	104.9 ± 42	95.7 ± 32	117.4 ± 48.4
Max power, W, mean ± SD	159.2 ± 63.5	160.2 ± 69	158.3 ± 59
Theoretical max velocity, °/s, mean ± SD	334.9 ± 85.1	370.9 ± 96.8	301.7 ± 56.3
Optimum velocity, °/s, mean ± SD	179.6 ± 52.3	198.1 ± 59.8	162.7 ± 38
Max moment 150°/s, Nm, mean ± SD	57.2 ± 23.6	55.8 ± 22.4	58.4 ± 25
Max moment 180°/s, Nm, mean ± SD	47.1 ± 18.6	48.1 ± 20.2	42.3 ± 17.3

Values are means with standard deviation (SD) or percentage of the group.
 BMI, body mass index; med, median; M_{MAX}, theoretical maximum moment; NRS, numerical rating scale; WOMAC, West Ontario and McMaster Universities Osteoarthritis Index; 6WT, 6-min walk test.
^aLong-term clinical remission.

p = 0.55) (Figure 4(a)). The rate of fat infiltration in the vastus did not change within each group (concentric group: 34.1 ± 1.6 initial VM, 33.6 ± 1.7 final VM, *p* = 0.59 – 32.9 ± 5 initial

VL, 34.1 ± 4.3 final VL, *p* = 0.38; eccentric group: 34.1 ± 1.64 initial VM, 34.7 ± 2.5 final VM, *p* = 0.871 – 32.9 ± 5 initial VL, 35.4 ± 4.3 final VL, *p* = 0.09) (Figure 4(b)).

Table 2. Comparison of the changes in the parameters studied in each group and between groups.

	Concentric group <i>n</i> = 25			Eccentric group <i>n</i> = 28			Change Mean of changes		
	Inclusion	After 6 weeks	<i>p</i> *	Inclusion	After 6 weeks	<i>p</i> **	Concentric	Eccentric	<i>p</i> ***
WOMAC total, mean ± SD	49.2 ± 19	43 ± 18.7	<0.0001	49.7 ± 17	45 ± 19.7	<0.0001	7.5 ± 12	4.5 ± 12	0.701
WOMAC function, mean ± SD	34.4 ± 15	29.6 ± 12	0.008	34.8 ± 12	31 ± 14.5	0.052	5.8 ± 9	3.9 ± 9.9	0.912
WOMAC stiffness, mean ± SD	4.5 ± 1.8	4.3 ± 2.2	0.077	4.7 ± 1.7	4.7 ± 2.4	0.377	0.5 ± 1.3	-0.4 ± 2.3	0.213
WOMAC pain, mean ± SD	10.3 ± 4	9 ± 3.8	0.093	10.2 ± 3	9.3 ± 4.6	0.154	1.2 ± 3.1	0.9 ± 3.1	0.661
NRS, mean ± SD	5.3 ± 1.8	3 ± 2.4	0.001	5.3 ± 2	2.7 ± 2.4	< 0.0001	2.3 ± 2.3	2.3 ± 2	0.687
6WT, meters, mean ± SD	424 ± 80	448 ± 91	0.022	417 ± 80	437 ± 73	0.425	32 ± 61	10 ± 63	0.37
<i>M</i> _{MAX} , N m, mean ± SD	105 ± 42	99 ± 32	0.33	95.7 ± 32	116 ± 43.5	0.783	3.2 ± 16	-0.9 ± 16	0.415
<i>P</i> _{MAX} , W, mean ± SD	160 ± 69	165 ± 56	0.52	158 ± 59	179 ± 62	0.001	4.8 ± 36	21 ± 29	0.09
<i>V</i> _{MAX} , °/s, mean ± SD	371 ± 97	394 ± 141	0.27	302 ± 56	377 ± 125	0.006	23 ± 102	75 ± 128	0.1
<i>V</i> _{OPT} , °/s, mean ± SD	198 ± 59	203 ± 57	0.7	163 ± 38	184 ± 40.7	0.006	4.9 ± 63.5	21 ± 36	0.3
MM 150°/s, N m, mean ± SD	56 ± 22.4	57.7 ± 19	0.27	58.4 ± 25	66.7 ± 24	0.002	1.9 ± 8.2	8.3 ± 13	0.037
MM 180°/s, N m, mean ± SD	48 ± 20.2	50 ± 16.6	0.36	2.3 ± 17	54 ± 20.4	0.006	1.8 ± 9.3	7.7 ± 13.1	0.07

Values are means with standard deviation (SD).
MM, maximum moment; *M*_{MAX}, theoretical maximum moment; NRS, numerical rating scale; *P*_{MAX}, maximum power; *V*_{MAX}, theoretical max velocity; *V*_{OPT}, optimum velocity; 6WT, 6-min walk test.
**p*: change in the parameters studied in the concentric group between inclusion and 6 weeks.
***p*: change in the parameters studied in the eccentric group between inclusion and 6 weeks.
****p*: difference in the change in the parameters studied (relative, normalized compared with the baseline score) between the concentric and eccentric group.

We did not find any correlation between VM muscle volume gain and clinical data (respectively $r^2 = 0.008$, $p=0.7$ for the WOMAC score; $r^2 = 0.003$, $p=0.8$, for pain) (results not shown).

Discussion

We studied the effectiveness of a 6-week program of supervised physical activity that allowed us to compare the effect of eccentric and concentric training methods on the WOMAC score, on pain, and on muscle performance.

We were unable to show superiority of one type of physical activity over the other as regards the total

WOMAC score. However, each of the two types of rehabilitation exercises (eccentric and concentric) contributed to a significant improvement in the total WOMAC score. Similarly, pain assessed by the NRS was reduced in both groups, but no type of exercise showed an advantage over the other. Only the eccentric exercises contributed to a gain in vastus medialis muscle volume and an improvement in muscle strength.

The functional results corroborate data in the recent literature that do not show superiority of one type of resistance exercise over the other, and confirm earlier data that demonstrate the benefit of any type or duration of physical activity in

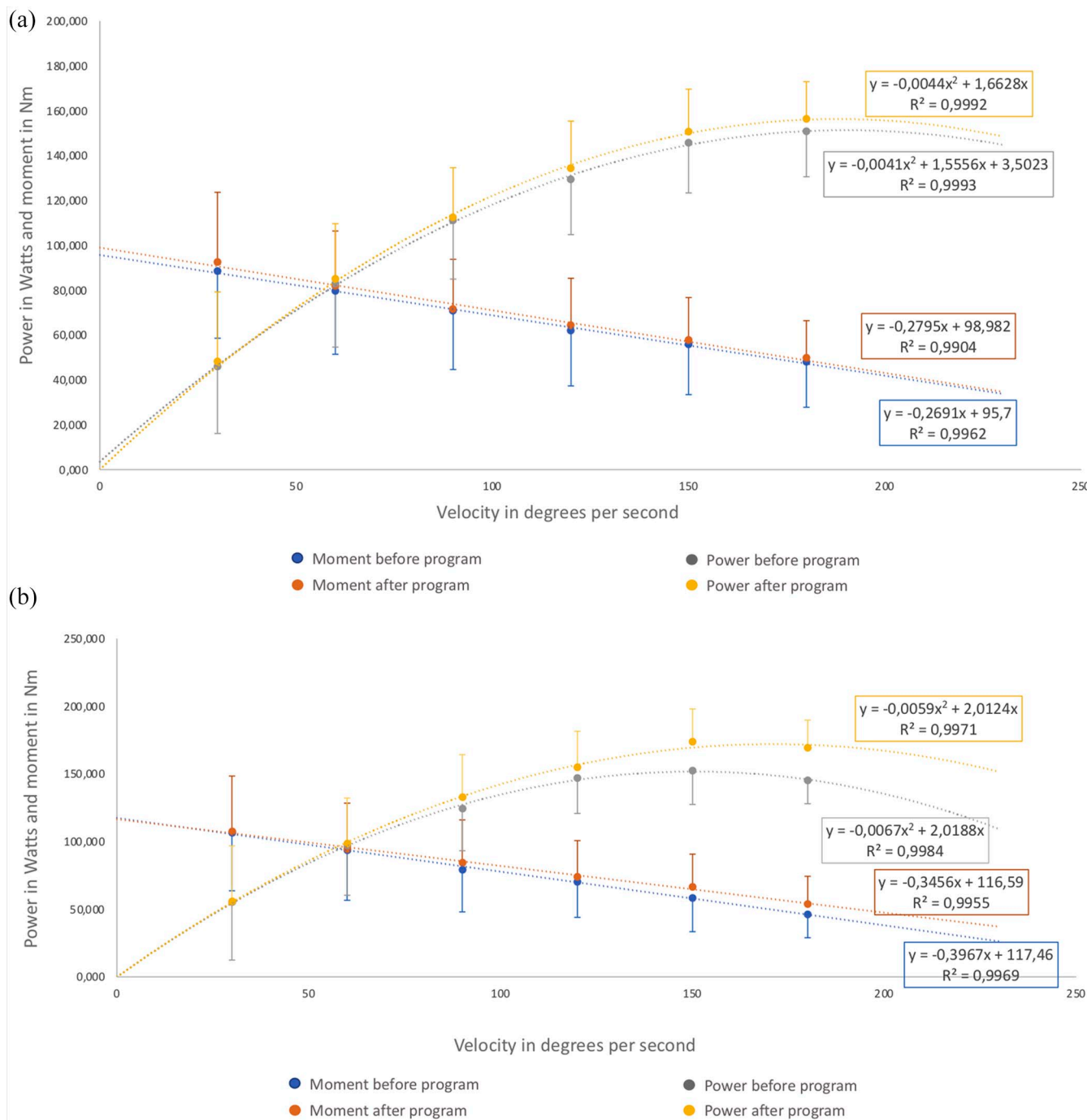


Figure 3. Moment–velocity and power–velocity relationship in each group: (a) concentric group and (b) eccentric group.

treating symptomatic knee osteoarthritis.^{10,18} Furthermore, results showed that physical function measured by the 6-minute walk test and the WOMAC score for function only significantly improved in the concentric group. This is consistent with the results presented by Vincent and Vincent¹⁹ in their 2020 study opposing eccentric to concentric rehabilitation, in which a benefit in reducing walking pain or ‘ambulatory pain’, as

assessed by a 6-minute walk test, was only observed in the concentric group.

Our results showed an improvement in muscle performance, including an improvement in P_{MAX} in the eccentric group only. Muscle strength and contraction velocity are essential in assessing a subject’s muscle performance. Several studies have demonstrated the benefit of eccentric

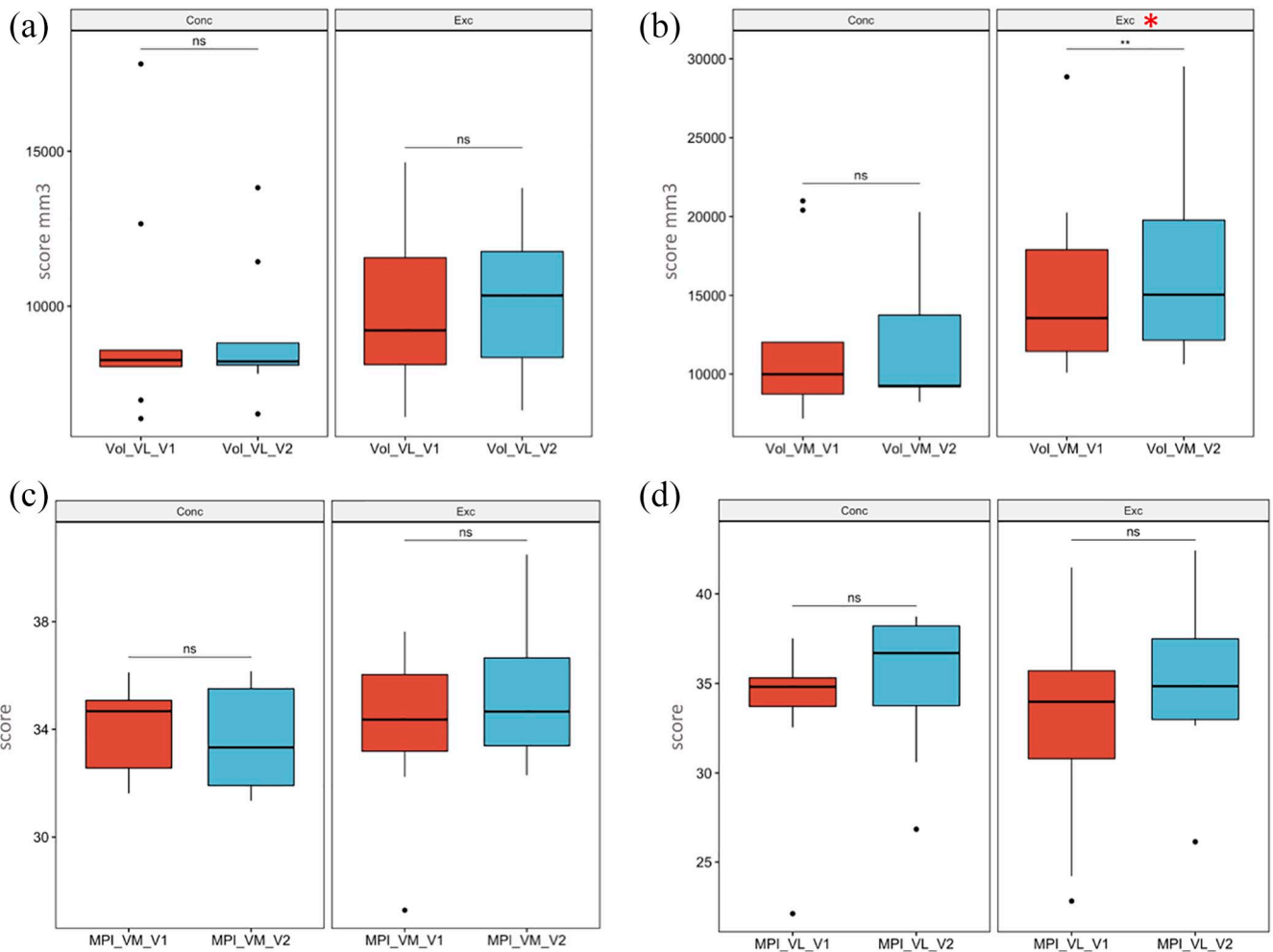


Figure 4. Change in the muscle parameters assessed by MRI between inclusion and after 6 weeks in each group: (a) Comparison of VM and VL muscle volume (cm^3) between the concentric group and the eccentric group at inclusion and after 6 weeks of training (*) significant result, $p < 0.05$. (b) Comparison of VM and VL fat infiltration between the concentric group and the eccentric group at inclusion and after 6 weeks of training.

rehabilitation in terms of muscle strength gain compared with concentric reinforcement, while other authors found no difference between the two types of exercises.^{20,28–30} In our study, although we did not find any improvement in M_{MAX} , we identified an increase in muscle contraction at rapid velocity (M_{MAX} 150°/s) in the eccentric group and an increase in P_{MAX} muscle power. This can be explained by the fact that power is equal to the product of force and velocity. It is interesting to note that another parameter, optimum velocity (V_{OPT}), can be used to assess muscle performance. It corresponds to the orthogonal projection of the maximum power (P_{MAX}) on the velocity axis. The V_{OPT} also increased in our eccentric group, but did not change in the concentric group. In the literature, maximum power and optimum velocity have been shown to be important determinants of

physical performance and mobility in the elderly.³¹ Also, the higher the V_{OPT} , the greater the proportion of fast-twitch muscle fibers (type II) compared with slow-twitch fibers (type I), the V_{OPT} is therefore considered a direct indicator of the proportion of fast-twitch fibers.³² In addition, we were able to observe an increase in VM muscle volume measured by MRI in the eccentric group, clearly greater than that obtained in the concentric group. We suggest that this volume gain corresponds to the formation of type II fibers, consistent with improved performance, such as P_{MAX} and V_{OPT} increases, in the eccentric group. This result corroborates literature data suggesting that exercises focusing on eccentric muscle strengthening contribute to a greater muscular hypertrophy due in particular to the generation of a greater force, or in our case greater muscle power, neuromuscular

adaptation, IGF-1 mRNA expression, satellite cell activation and proliferation, and a more rapid increase in protein synthesis.^{17,28,29,33} A 2017 review sought to demonstrate that eccentric strength training was more effective in terms of volume gain, but did not achieve a statistically significant result ($p=0.076$).³⁴ Note that these data remain controversial and that other authors suggest that the two types of resistance training achieve a similar muscle volume gain.^{17,35}

Some authors have demonstrated a correlation between the improvement in muscle parameters (muscle strength) and the improvement in clinical parameters (pain, function).³⁶ This was not the case in our study, where improvement in VM volume in the eccentric group did not correlate with improvement in function and pain, and where, despite improvement in muscle performance in the eccentric group, no superiority could be found over the concentric group. This clearly shows the complexity of factoring in muscle parameters and the need to find a consensus on how to use them in clinical practice.

Our training protocol did not identify any change in the rate of fat infiltration of the quadriceps, and in particular of the VL and VM, including in the eccentric group despite the VM volume gain. Few studies have been conducted to examine the relationship between physical activity and quadriceps fat infiltration. A study in 2015 demonstrated the reversible nature of the VM fat infiltration determined by MRI and its connection with physical exercise.⁸ The decrease in VM fat infiltration was also linked to reduced cartilage loss.⁸ The advantage of the 2015 longitudinal study was a longer prospective follow-up, but the physical activity was not supervised and was assessed by a questionnaire. In addition, the method for assessing VM fat infiltration relied on a manual count of the number of T1-hypointense lesions on five consecutive slices, whereas our assessment was automated and validated in a previous study.^{8,24} In this context, it is difficult to compare our results with the results of the literature. However, the absence of change in the VM fat fraction in our study despite its increase in volume allows us to suggest that a longer intervention would be required to observe a significant change in this parameter.

Our study has several limitations. First, it was carried out on a relatively small number of patients, even if the number remains higher or comparable

with recent randomized protocols dealing with the same subject.^{18,20} Our study was conducted voluntarily over a shorter period of time than the other current randomized prospective protocols (ranging from 8 weeks to 4 months) to correspond to treatment durations usually prescribed: 12 to 15 physiotherapy sessions, that is, two sessions per week for 6 weeks.^{18–20,37} Thus, we know that after 6 weeks of well-conducted physical exercise, its marked benefits can be observed on the symptoms of knee osteoarthritis in a selected population. The absence of a control group without a rehabilitation protocol could also be considered a limitation. However, it has been established that physical activity is effective and is recommended by various learned societies for treating knee osteoarthritis.^{13,38,39} If patients had not been offered physical activity, it would have been a lost opportunity for them. It might also have been interesting to carry out a long-term follow-up to evaluate the persistence of the benefits obtained. Finally, the number of subjects in the MRI subgroup is a limitation, but given financial constraints, we were unable to perform more MRI scans.

In conclusion, this study demonstrated that physical activity, whether eccentric or concentric, significantly improves the WOMAC score and reduces pain assessed on a standard numerical rating scale in patients with symptomatic tibiofemoral osteoarthritis. Concentric exercises were the only type of training that significantly improved the WOMAC score for physical function, without demonstrating a significant difference between the groups. Eccentric physical exercises allowed patients to obtain greater gains in performance and in muscle volume, in particular of the vastus medialis, compared with concentric exercises. Further studies are needed to confirm that eccentric exercises increase quadriceps muscle volume and power in patients with knee osteoarthritis and to prove the clinical impact of these parameters on function and pain.

Declarations

Ethics approval and consent to participate

The study was conducted in compliance with the recommendations of the Declaration of Helsinki and was approved by the *Committee for the protection of persons (Sud Est II)* as suitable for local clinical research (ID-RCB: 2017-A00164-49). All subjects signed a consent form. The study was registered on the website www.ClinicalTrials.gov (registration number: NCT03167502).

Consent for publication

Not applicable.

Author contribution(s)

Marie-Charlotte Trojani: Data curation; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Frédéric Chorin: Data curation; Formal analysis; Funding acquisition; Writing – original draft.

Pauline Gerus: Formal analysis; Writing – review & editing.

Véronique Breuil: Supervision; Validation; Writing – review & editing.

Constance Michel: Data curation; Funding acquisition; Software; Writing – original draft.

Sandrine Guis: Methodology; Supervision; Writing – review & editing.

David Bendahan: Conceptualization; Formal analysis; Resources; Software; Writing – review & editing.

Christian Roux: Conceptualization; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing – original draft; Writing – review & editing.

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Availability of data and materials

Not applicable.

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