

# Rate of Force Development in the Quadriceps of Individuals With Severe Knee Osteoarthritis: A Cross-Sectional Study

Yusuke Suzuki (✉ [yusuke-suzuki@nuhw.ac.jp](mailto:yusuke-suzuki@nuhw.ac.jp))

Department of Physical Therapy, Faculty of Rehabilitation, Niigata University of Health and Welfare, Niigata

Hiroataka Iijima

Department of System Design Engineering, Faculty of Science and Technology, Keio University, Yokohama

Masatoshi Nakamura

Department of Physical Therapy, Faculty of Rehabilitation, Niigata University of Health and Welfare, Niigata

Tomoki Aoyama

Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto

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## Research Article

**Keywords:** KOA, RFD, isometric

**Posted Date:** January 29th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-152970/v1>

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**Version of Record:** A version of this preprint was published at PLOS ONE on January 11th, 2022. See the published version at <https://doi.org/10.1371/journal.pone.0262508>.

# Abstract

We tested the following hypotheses: individuals with severe knee osteoarthritis (KOA) would display a significantly decreased quadriceps rate of force development (RFD); and this decrease would be greater than the decrease in maximum quadriceps strength. Maximum isometric strength of the quadriceps was assessed in individuals with mild (Kellgren and Lawrence [K&L] grade 1–2) and severe KOA (K&L grade 3–4). RFD was analyzed at 200 ms from torque onset and normalized to body mass and maximum voluntary isometric contraction torque. The decrease in quadriceps RFD and the difference between this and the decrease in maximum quadriceps strength was tested with logistic regression analysis with a propensity-score-adjusted model and analysis of covariance, respectively. Effect size by Hedges' *g* with a 95% confidence interval (CI) was calculated for the quadriceps RFD and maximum quadriceps strength. Sixty-six participants were analyzed. Individuals with severe KOA displayed significantly decreased quadriceps RFD (odds ratio: 0.50; 95% CI: 0.26-0.82), the decrease being greater than that in maximum quadriceps strength (between-group difference, ES: 0.88, -1.07 vs. 0.06, -0.22). The results suggest that a decreased quadriceps RFD is a modifiable risk factor for progressive KOA. This could lead to the early detection and prevention of severe KOA.

## Introduction

Knee osteoarthritis (KOA) is a common form of arthritis and a leading cause of knee pain and disability through irreversible cartilage degeneration<sup>1</sup>. Deterioration of physical function is common among individuals with KOA<sup>2</sup>. However, there is currently no available radical treatment for KOA, and no treatment approaches for controlling KOA progression have been reported. The risk factors of KOA were detected in a previous review<sup>3</sup>; however, the prognostic factors identified in this review (having KOA and a high serum level of hyaluronic acid) are not modifiable and can only be used to identify patients at high risk for high rates of disease progression. Identifying and updating modifiable risk factors is, therefore, a critical unmet need.

Skeletal muscles provide shock absorption and distribute the load across the joint<sup>4</sup>. Failure of the protective mechanisms from weakened quadriceps muscle strength can lead to harmful load distribution in the knee joint<sup>5</sup>. Therefore, the quadriceps muscle functions as a general shock absorber to protect articular knee joint surfaces during loading. However, reports on the relationship between maximum quadriceps strength and radiographic severity, which reflects reduced cartilage thickness of the knee joint in patients with KOA, have been equivocal. A systematic review and meta-analysis showed the quadriceps muscle weakness at baseline to be a risk factor for later radiographic KOA<sup>6</sup>. On the other hand, previous meta-analyses have reported that knee extension strength is not associated with the radiographic severity of KOA<sup>7</sup>. Indeed, a prospective cohort study reported that greater quadriceps strength did not influence cartilage loss at the tibiofemoral joint in KOA<sup>8</sup>. Therefore, it may be insufficient to focus solely on maximum quadriceps strength to prevent the progression of KOA.

The rate of force development (RFD) is an index reflecting explosive muscle strength. The RFD has recently received focus as a measure of muscle strength, distinct from maximum strength. In terms of muscle contraction time, maximum strength requires more than 300 ms for exertion, whereas the RFD is exerted in 50–200 ms<sup>9</sup>. Muscle activity in daily life is performed over a muscle contraction time of 50–200 ms<sup>10, 11</sup>. Therefore, with regard to muscle contraction time, the RFD may be more closely related to daily activities than maximum strength. In fact, it has been reported that RFD in KOA patients was significantly associated with activities of daily living score<sup>12</sup> and biomechanical gait variables<sup>13</sup>. These findings collectively suggest that the RFD is more closely associated with daily activities than maximal strength. Besides, radiographic severe KOA (Kellgren and Lawrence [K&L] grade > 2) patients have significantly more impairments of daily activities than mild KOA patients (K&L grade 1–2)<sup>14</sup>. For these reasons, individuals with radiographic severe KOA may have a more significantly decreased quadriceps RFD than maximum quadriceps strength. However, the relationship between RFD and radiographic KOA severity has not been investigated to date.

We therefore tested hypotheses that (1) individuals with severe KOA would display a significantly decreased quadriceps RFD and (2) the decrease in the quadriceps RFD would be greater than the decrease in maximum quadriceps strength in individuals with severe KOA.

## Results

In total, 150 participants were recruited. Of these, 69 (46.0%) were excluded due to the absence of pain in the knee; four (2.6%) due to pre-radiographic KOA; and 11 (7.3%) due to missing data. A total of 66 participants were included in the final analysis (Fig. 1). Table 1 shows the group differences between participants with mild and severe KOA. Figure 2 shows the isometric force-time curve indicating the maximum strength and RFD in mild and severe KOA.

Table 1  
 Characteristics of participants with mild and severe KOA.

	Mild KOA* (n = 58)	Severe KOA* (n = 8)	p-value <sup>†</sup>
Age (years)	74.05 ± 5.09	75.87 ± 4.45	0.23
Women (%)	50 (86.2)	6 (75.0)	0.59
Height (cm)	154.41 ± 8.73	157.75 ± 10.84	0.23
Weight (kg)	53.43 ± 9.08	56.37 ± 7.02	0.24
BMI (kg/m <sup>2</sup> )	22.35 ± 2.91	22.75 ± 2.72	0.62
K&L grade			
Grade 1	17 (29.3)	-	
Grade 2	41 (70.7)	-	
Grade 3	-	6 (75.0)	
Grade 4	-	2 (25.0)	
Knee pain VAS (mm)	25.06 ± 22.05	29.0 ± 23.13	0.56
BMI: Body Mass Index; K&L grade: Kellgren and Lawrence grade; VAS: Visual Analogue Scale			
* Values are expressed as mean ± SD or number (percentage)			
† Based on the unadjusted analysis (Wilcoxon signed-rank test) between participants with early and severe KOA			

## Decreased quadriceps RFD in severe KOA

When adjusted for propensity as a function of age, sex, and knee pain visual analog scale (VAS), participants with severe KOA displayed a significantly decreased quadriceps RFD (odds ratio [OR]: 0.50; 95% CI: 0.26–0.82) (Table 2). Conversely, participants with severe KOA did not display significantly decreased maximum quadriceps strength (OR: 0.57; 95% CI: 0.09–2.88) (Table 3).

Table 2  
The association between severe KOA and quadriceps RFD

	Mild KOA*	Severe KOA*	Odds ratio (95% CI)	
			Crude model	Propensity-adjusted model **
Quadriceps RFD (%MVC/s*kg)	6.97 ± 1.72	5.10 ± 1.71	<b>0.52 (0.28– 0.83)‡</b>	<b>0.50 (0.26–0.82)†</b>
RFD: rate of force development; 95% CI: 95% confidence interval				
* Values are expressed as mean ± SD				
** Adjusted for propensity to prescribe as a function of age (years), sex and knee pain VAS (mm)				
† p < 0.05				
‡ p < 0.01				

Table 3  
The association between severe KOA and quadriceps strength

	Mild KOA*	Severe KOA*	Odds ratio (95% CI)	
			Crude model	Propensity-adjusted model **
Maximum quadriceps strength (Nm/kg)	1.49 ± 0.41	1.39 ± 0.69	0.59 (0.10– 3.25)	0.57 (0.09–2.88)
RFD: rate of force development; 95% CI: 95% confidence interval				
* Values are expressed as mean ± SD				
** Adjusted for propensity to prescribe as a function of age (years), sex, and knee pain VAS (mm)				

## Greater decrease in the quadriceps RFD than in maximum quadriceps strength in severe KOA

When adjusted for age, sex, and knee pain VAS, participants with severe KOA exhibited a significantly decreased quadriceps RFD (between-group difference: 0.88; 95% CI: 0.23 to -1.54). The quadriceps RFD exhibited a large effect (ES: -1.07; 95% CI: -1.83 to -0.30) (Table 4). When adjusted for age, sex, and knee pain VAS, participants with severe KOA did not exhibit significantly decreased maximum quadriceps strength (between-group difference: 0.06; 95% CI: -0.09 to 0.21). Maximum quadriceps strength exhibited a small effect (ES: -0.22; 95% CI: -0.96 to 0.52) (Table 5).

Table 4  
Between-group differences and effect size in the quadriceps RFD for mild and severe KOA

	Mild KOA	Severe KOA	Between-group difference	95% CI	Effect size	
	(n = 58)	(n = 8)			Hedges	95% CI
Quadriceps RFD (%MVC/s*kg)	6.97 ± 1.72	5.10 ± 1.71	0.88	0.23–1.54	-1.07	-1.83 to -0.30
RFD: rate of force development; 95% CI: 95% confidence interval						
Adjusted for age (years), sex, and knee pain VAS (mm)						

Table 5  
Between-group differences and effect size in maximum quadriceps strength for mild and severe KOA

	Mild KOA	Severe KOA	Between-group difference	95% CI	Effect size	
	(n = 58)	(n = 8)			Hedges	95% CI
Maximum quadriceps strength (Nm/kg)	1.49 ± 0.41	1.39 ± 0.69	0.06	-0.09 to 0.21	-0.22	-0.96 to 0.52
95% CI: 95% confidence interval						
Adjusted for age (years), sex, and knee pain VAS (mm)						

## Discussion

The study findings supported our hypotheses and demonstrated that individuals with severe KOA displayed a significantly decreased quadriceps RFD. Moreover, the decrease in the quadriceps RFD was greater than that in maximum quadriceps strength in individuals with severe KOA based on a comparison of the ES between the quadriceps RFD and maximum quadriceps strength.

The mechanism of the early (range 0-100 ms) RFD was associated with neural drive, contractile properties, and fiber type composition, and the late (range 0-200 ms) RFD was associated with muscle size, muscle strength, neural drive, and the stiffness of the tendon-aponeurosis complex<sup>15</sup>. For fiber type, skeletal muscle fibers are broadly classified as “slow-twitch” (type I) and “fast-twitch” (type II). The RFD is an index that reflects explosive muscle strength and is thus indicative of type II muscle fibers<sup>16</sup>. Type II muscle fibers are more affected by age-related atrophy than type I muscle fibers<sup>17</sup>. However, it has been reported that atrophy of type II muscle fiber is not observed in patients with severe KOA compared with that in age-matched elderly controls<sup>16</sup>. Moreover, there was no significantly decreased early RFD in severe KOA in this study (data not shown). Therefore, the involvement of fiber type in this study is considered to be small. For neural drive, neural activation and rapid neuromuscular activation of the quadriceps were

impaired in KOA patients<sup>18,19</sup>. Moreover, in this study, RFD was adjusted for peak torque; therefore, the effects of muscle size and muscle strength were considered to have been excluded. For this reason, individuals with severe KOA displayed a significantly decreased quadriceps RFD, and the quadriceps RFD exhibited a large ES due to the effect of neural drive and the stiffness of the tendon-aponeurosis complex.

In this study, participants with severe KOA did not exhibit significantly decreased maximum quadriceps strength. A systematic review reported that decreased maximum quadriceps strength was associated with an increased risk of symptomatic and functional deterioration but not radiographic tibiofemoral joint space narrowing (JSN)<sup>7</sup>. The results of the maximum quadriceps strength in this study support this review. Therefore, in this study, participants with severe KOA did not display decreased maximum quadriceps strength, and maximum quadriceps strength exhibited a small ES.

For these reasons, individuals with severe KOA displayed a significantly decreased quadriceps RFD rather than maximum quadriceps strength, as the ES was larger for the quadriceps RFD than for maximum quadriceps strength.

The clinical implications of our results are described as follows. First, weakness in the quadriceps RFD may be related to the early detection of severe KOA development. Therefore, the development of severe KOA, which can be determined only by radiography or magnetic resonance imaging (MRI), may be easily determined by measuring the quadriceps RFD if causal relationships are identified in future investigations. Second, interventions for RFD of the quadriceps muscle may lead to the prevention of severe KOA. Since the weakened quadriceps muscle strength can lead to a failure of harmful load distribution in the knee joint<sup>4,5</sup>, the quadriceps muscle functions seem to be a general shock absorber during knee joint load. Moreover, excessive mechanical stress on knee cartilage due to muscle weakness has been suggested to contribute to degenerative processes<sup>20</sup>. In the present study, quadriceps RFD was found to be more strongly related to severe KOA than maximal quadriceps strength. Therefore, if a causal relationship between quadriceps RFD and radiographic severity is found, improving the quadriceps RFD may lead to the prevention of severe KOA.

## Study Limitations

This study has several limitations. First, the participants were motivated individuals given that they actively enrolled by responding to e-mails and were recruited via public relations magazine advertisements; thus, there may have been selection bias. Second, since a power calculation was not performed, the relationship between severe KOA and weakness of maximum quadriceps strength cannot be determined. Third, there was a small number of individuals with severe KOA, which may bias the incidence of severe KOA events. Therefore, in the present study, univariate analysis was performed at the same time as multivariate analysis, and the results of the multivariate analysis were confirmed to be unchanged. Moreover, to reduce the number of independent variables and reduce the effect of bias in the

logistic regression analysis, we conducted the logistic regression analyses using a propensity-adjusted model. However, it is necessary to increase the sample size and confirm the results with different analysis methods in the future. Finally, given the cross-sectional nature of this study, causal associations between severe KOA and the quadriceps RFD could not be determined. Further investigations, including prospective studies that clarify causal associations, are required to confirm our results.

## Conclusions

We demonstrated that individuals with severe KOA displayed significantly decreased quadriceps RFD. Moreover, the decrease in the quadriceps RFD was greater than that in maximum quadriceps strength in individuals with severe KOA. These findings indicate that a decreased quadriceps RFD may be a modifiable risk factor for progressive KOA, which should be verified in future longitudinal studies.

## Methods

### Participants

This study employed a cross-sectional design. Elderly participants who reported current knee pain were identified via a mailed survey and were invited to visit a research center in Kyoto in September 2019. This study was conducted in accordance with the Declaration of Helsinki and with the approved by the ethics committee of Kyoto University (approval No. R2151-1). Written informed consent was obtained from all of the participants before their enrolment. All of the recruited participants had a history of pain in one or both knees. The eligibility criteria were (1) age  $\geq$  45 years, (2) knees with early and severe osteoarthritis (OA) (i.e., K&L grade 1–2 and 3–4, respectively, according to the original version; Kellgren et al., 1957) in one or both knees in the medial tibiofemoral compartment as evaluated using weight-bearing anteroposterior radiographs, and (3) ability to walk independently on a flat surface without the use of any ambulatory assistive device. Participants with bilateral KOA were not considered separately from the unilateral cases because it was necessary to increase the sample size. The exclusion criteria were (1) a history of knee surgery, (2) rheumatoid arthritis, (3) periarticular fracture, (4) concurrent neurological problems, or (5) knees with pre-radiographic OA (i.e., K&L grade 0).

### Measurements

For all of the participants, demographic data and knee pain were evaluated as individual characteristics and covariates. Outcome measures were radiographic evaluation and measurement of maximum quadriceps strength and the RFD.

### Demographic data and knee pain

Data on age, sex, and height were self-reported by participants. Weight was measured on a scale, with the participants clothed but barefoot. Body mass index was calculated by dividing weight in kilograms by the square of height in meters. Knee pain over several days prior was evaluated using a VAS.

# Radiographic evaluation

Anteroposterior radiographs of both knees in the fully extended weight-bearing and foot map positions were obtained at enrolment. The radiographic severity of the medial compartment in the tibiofemoral joint was assessed by a trained examiner. The K&L grade was scored as follows: 0, normal; 1, doubtful JSN and possible osteophyte; 2, definite osteophyte and possible JSN; 3, multiple osteophytes, definite JSN, some sclerosis, and possible deformity of bone ends; and 4, large osteophyte, marked JSN, severe sclerosis, and definite deformity of bone ends. The intra- and inter-rater agreements for the K&L grade determination were excellent (intra-rater:  $\kappa = 0.88$ , 95% CI = 0.83–0.92; inter-rater:  $\kappa = 0.84$ , 95% CI = 0.79–0.90)<sup>22</sup>. To permit analysis of the association between outcome measures and radiographic severity, the present sample was dichotomized, as reported previously<sup>23</sup>, into mild KOA (K&L grade 1–2) and severe KOA (K&L grade 3–4).

## Maximum quadriceps strength and RFD

The maximum voluntary isometric contraction (MVC) in both legs was measured using a handheld dynamometer (HHD) (Mobie, Sakai Medical Co., Ltd, Japan; accuracy:  $\pm 2\%$  rated output), in accordance with a previously validated method for community-dwelling elderly patients prone to falling<sup>24,25</sup>. The HHD is a simple tool for objectively quantifying muscle strength and is widely used in clinical practice. Participants were instructed to remain seated in an upright position. The knee was placed at 90° flexion. The HHD was attached 10 cm proximal to the lateral malleolus and held in place with an inelastic strap looped around the therapy bed and fastened. The length of the straps allowed for an isometric contraction to be performed with the knee at 90° flexion during testing. Participants were instructed to extend their leg for 5 seconds as fast and as hard as possible. A few practices were done before the measurement. Strong verbal encouragement was provided to ensure a maximal effort. There were no complaints of knee pain from the subjects during the RFD and maximal muscle strength measurements. MVC was recorded in Newtons (N), and two repetitions were performed for each test. Force measures were acquired and passed through an analog-to-digital converter (Power Lab, AD Instruments, Australia) sampling at 1,000 Hz and plotted using LabChart 8 software (AD Instruments, Australia). The distances from the center of the force pad to the knee were recorded for each participant and used to convert measured forces into joint torques. The torque values were calculated by multiplying the obtained force values by the distances from the center of the force pad to the knee. The average of two repetitions was used for statistical analysis.

MVC in the quadriceps was defined as the maximal torque value obtained from two attempts. We assessed the RFD over the first 200 ms of the maximal isometric contraction, whereby the onset of contraction was deemed as the point at which torque had risen 4 Newton-meter (Nm) above the baseline value<sup>26</sup>. The RFD was analyzed at 200 ms from the onset of torque<sup>9</sup>. The RFD was normalized to body mass and MVC torque to exclude the effects of muscle strength<sup>26,27</sup>.

The intraclass correlation coefficient of measured maximum muscle strength and RFD was 0.974 (95%CI: 0.958–0.985) and 0.873 (95%CI: 0.797–0.922), respectively.

## Statistical analysis

To minimize any bias introduced by similarities between the right and left knees of the same subjects, only one knee per subject (index knee) was analyzed. The index knee was defined as the more painful knee in either the past or present. For subjects who reported equally painful knees, the index knee was selected randomly using a computer-generated permuted block randomization scheme<sup>28</sup>.

The characteristics of participants are presented as mean  $\pm$  standard deviation (SD) for continuous variables and as numbers and percentages for nominal and ordinal variables. Wilcoxon signed-rank test was used to determine group differences between participants with mild and severe KOA as the dependent variable was not normally distributed as determined by the Shapiro-Wilk test.

To test the hypothesis that individuals with severe KOA would display a significantly decreased quadriceps RFD, logistic regression analysis was performed. Logistic regression analyses were performed first with an unadjusted model followed by a propensity-adjusted model. Due to the small sample size, we used propensity score adjustment, including covariates. The presence or absence of severe KOA (0, absence; 1, presence of severe KOA) was included as a dependent variable. Maximum quadriceps strength or the RFD was included as an independent variable. Age (years), sex, and knee pain VAS (mm) were included as covariates. To test the hypothesis that the decrease quadriceps RFD would be greater than the decrease in maximum quadriceps strength in individuals with severe KOA, the following analysis was performed. To compare between-group differences for mild and severe KOA, an independent measures analysis of covariance was performed, with age (years), sex, and knee pain VAS (mm) as covariates. The ES was calculated by Hedges' *g* with 95% CI for the quadriceps RFD and maximum quadriceps strength. Data analyses were performed using JMP Pro 15.0 (SAS Institute, Cary, NC, USA). A *p*-value of  $< 0.05$  was considered statistically significant.

## Declarations

### Data availability

The datasets generated and/or analyzed in the present study are available from the corresponding author on reasonable request.

### Acknowledgments:

The authors thank the students of Human Health Sciences at Kyoto University for their help with data collection. We would like to thank Editage ([www.editage.jp](http://www.editage.jp)) for English language editing.

### Author contributions:

All authors: conceptualization and design of the study. All authors: collection and assembly of data. YS: analysis of data. All authors: interpretation of data. YS: first draft of the manuscript. HI: statistical expertise. MN: collection of data and statistical expertise. TA: obtaining of funding. All authors: critical revision of the manuscript for important intellectual content and approval of the final version.

### Funding:

This work was supported by a Grant-in-Aid for Research B from the Niigata University of Health and Welfare, 2019. This funding source had no involvement in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

**Competing Interests:** none

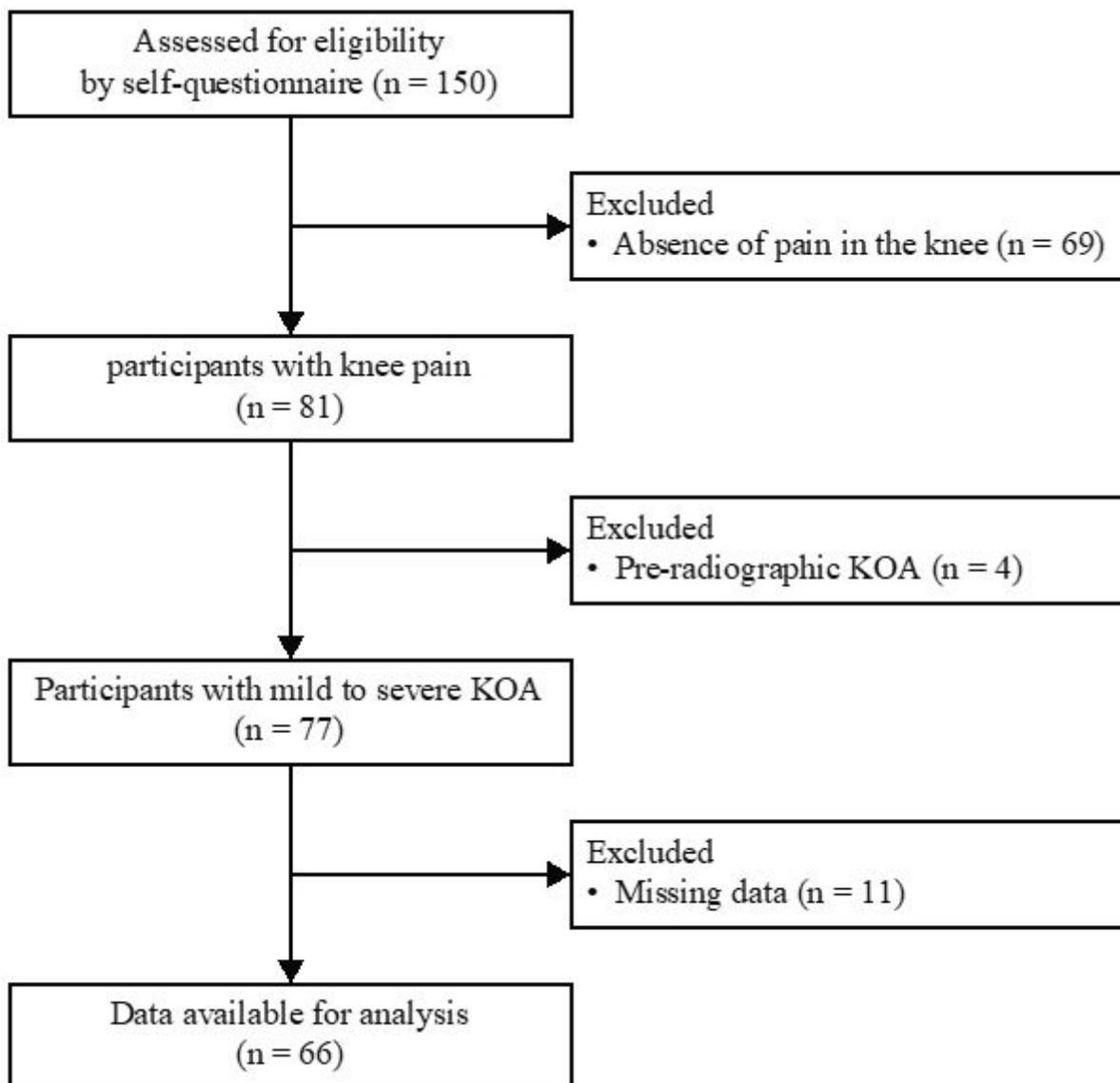
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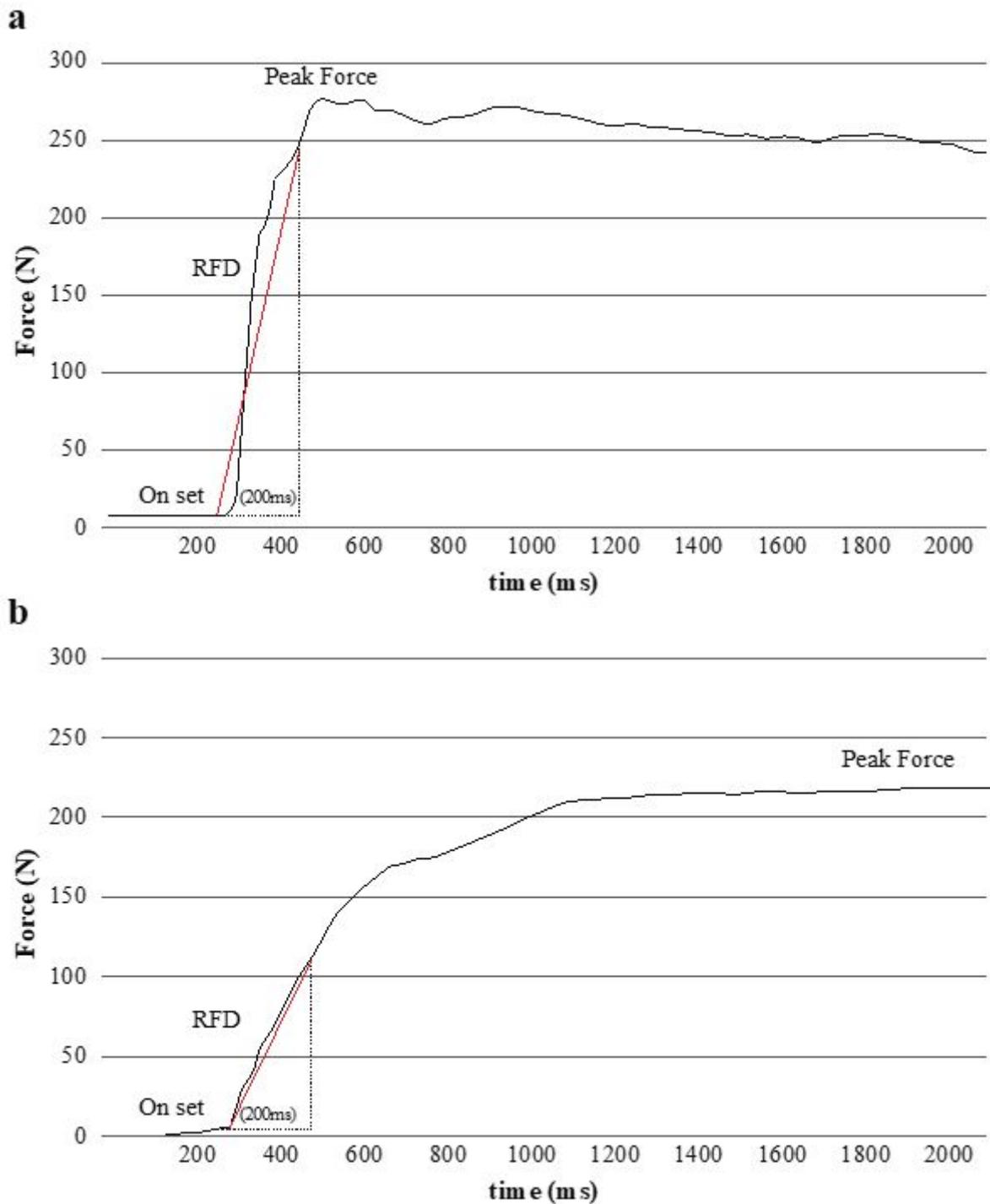
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## Figures



**Figure 1**

Flow diagram of the study protocol.



**Figure 2**

(a) Isometric force-time curve indicating the maximum strength and RFD in individuals with mild KOA. (b) Isometric force-time curve indicating the maximum strength and RFD in individuals with severe KOA.

## Supplementary Files

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