

Influence of Knee Osteoarthritis Severity, Knee Pain, and Depression on Physical Function: A Cross-Sectional Study

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Purpose: Decreased physical function with increasing life expectancy is a public health concern worldwide. Knee osteoarthritis (KOA) is considered one of the primary illnesses causing decreased physical function. Depression affects decreased physical function and is closely related to knee pain in KOA. However, the effect of these interacting factors on physical function is not clear.

Patients and Methods: We conducted a cross-sectional analysis of the baseline data of 1106 subjects of the 2009 Locomotive Syndrome and Health Outcome in Aizu Cohort Study (LOHAS). We determined the association between their Timed Up and Go test (TUG) scores and radiographic KOA, knee pain, and depression in a multivariate analysis.

Results: Severe knee pain was significantly associated with decreased physical function (the odds ratio [OR] was 2.13, 95% confidence interval [CI]: 1.32–4.89), as was depression (OR 2.64, 95% CI 1.61–4.33). Only Kellgren-Lawrence (KL) grade 4 was significantly associated with decreased physical function in the radiographic KOA severity (OR 6.58, 95% CI 1.75–24.68).

Conclusion: Severe knee pain and depression were significantly associated with decreased physical function, but not radiographic KOA severity except for KL grade 4. The limitations of using radiographic KOA severity alone as the indicator of assessment for physical function were suggested. When assessing decreased physical function, the clinical focus tends to be on radiographic KOA severity, but it is important to consider the patient's knee pain and psychological factors.

Keywords: knee osteoarthritis, knee pain, physical function, depression, aging, TUG test

Introduction

Disability is conceptualized by the World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF). A health condition (eg, arthritis) can impair body functions and structures (eg, joints), limit activities (eg, reduced mobility) and restrict participation (eg, reduced social engagement).¹ Disability contributes to increased healthcare costs² and mortality³ and a decline in quality of life (QOL),⁴ especially among the elderly. One of the frequently reported functional limitations among older people is decreased physical function.⁵ Poor physical functioning is associated with total mortality,⁶ increased healthcare costs,⁷ and adverse health outcomes.⁸ Decreased physical function in combination with increasing life expectancy is a worldwide public health problem that needs to be solved.⁹

Knee osteoarthritis (KOA) is a common musculoskeletal disorder in the elderly. It causes significant loss of joint function,¹⁰ with pain, inflammation, and dysfunction due to progressive articular cartilage degeneration¹¹ and synovitis.¹² The global prevalence of KOA is predicted to reach 40% by 2025.¹³ KOA-related functional decline leads to decreased mobility, limited activities of daily living (ADLs),¹⁴ and an increased frequency of limited participation in social and community activities.¹⁵ Difficulties in social participation can lead to social isolation and heightened economic burdens.¹⁶

KOA is often diagnosed basis of subjective symptoms such as pain, stiffness, limited joint range of motion and crepitus, and plain radiographs such as osteophyte formation and narrowing of joint space.¹⁷ Based on the European League Against Rheumatism (EULAR) evidence-based recommendations,¹⁸ the most typical symptom of KOA is pain. In patients with symptomatic KOA, knee symptoms such as knee pain and physical function assessed by TUG score are negatively correlated.¹⁹ However, musculoskeletal pain and depression interact with each other, with knee pain also being closely related to depression.^{20–22} Furthermore, depression itself also reduces physical function in adults,²³ but there are few quantitative evaluation reports.²⁴ As regards imaging findings, the association between radiographic KOA itself and physical function assessed by TUG score has been described in two cross-sectional studies, one of which found that radiographic KOA severity is not associated with physical function²⁵ and the other of which reported a positive correlation.²⁶ Thus, this association remains controversial. However, these studies did not evaluate interacting factors that may affect physical function, such as pain or depression. The purpose of this study was to clarify how knee pain, a common symptom of KOA, radiographic KOA severity, and depression affect decreased physical function.

Material and Methods

Participants

In this study, we analyzed data from the Aizu Cohort Study on Locomotive Syndrome and Health Outcomes (LOHAS). LOHAS is a cohort study to assess the risk of cardiovascular disease, QOL, healthcare costs and mortality attributable to locomotor dysfunction.²⁷ Cohort participants were recruited from residents between 40 and 80 years old who received regular health check-ups conducted by local government each year between 2008 and 2010 in Minami-Aizu Town and Tadami Town in Fukushima Prefecture, Japan. Musculoskeletal examination included physical examination of the cervical spine, lumbar spine, upper and lower limbs and assessment of physical functions such as grip strength, and Timed Up and Go (TUG) test. A self-administered questionnaire survey was also conducted. This cross-sectional analysis used data from the 2009 LOHAS baseline survey, which included 3790 subjects. Previously, we have reported using the same database.²⁸ The 1,484 subjects who requested to be examined underwent plane radiography of both knee joints in the standing position and a TUG test. Twenty-six subjects with a history of knee surgery, trauma, rheumatoid arthritis, or joint disease other than KOA were excluded from this study. Another 352 subjects with missing data were also excluded from the study. Ultimately, 1,106 subjects were included in the present analyses (Figure 1).

Ethical Consideration

We complied with the Declaration of Helsinki and provided written informed consent for the use of the collected data to all subjects. The present study was approved by the Research Ethics Committee of Fukushima Medical University (No. 673).

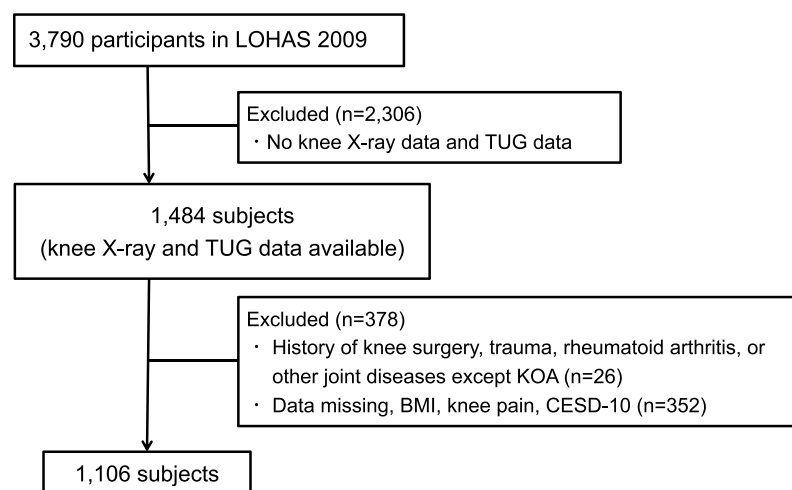


Figure 1 Flowchart for the study. A total of 1,106 subjects were included in the analysis. LOHAS: the Locomotive Syndrome and Health Outcome in Aizu Cohort Study; KOA: knee osteoarthritis; BMI: body mass index; CESD-10: Center of Epidemiologic Studies Depression Scale-10.

Data Collection

Knee Symptoms

Knee pain is based on subjects' self-administered questionnaire reports, the degree of knee pain was described on a six-point Likert scale (0 points: complete absence of pain; 1 point: very slight pain; 2 points: slight pain; 3 points: moderate pain; 4 points: very painful; 5 points: severe pain). For the purposes of the present analyses, knee pain was classified 0 points as no pain, 1 or 2 points as mild pain, 3 points as moderate pain, and 4 or 5 points as severe pain.

Radiological Assessment

As in our previous reports,²⁸ the radiographic KOA severity was assessed by two well-trained knee surgeons with more than 20 years' experience and more than 200 cases per year based on the Kellgren-Lawrence classification (ie KL grade).²⁹ In the present study, the KL grades on the subject's more severe side were used.

Psychological Factors

The CESD-10 score was used as the psychological factors questionnaire in LOHAS. The CESD-10 is a short form of the Center of Epidemiologic Studies Depression Scale³⁰ as a 10-item questionnaire that provides a simple assessment of depression which has been translated and validated into Japanese,³¹ scores of ≥ 10 points indicate the presence of clinical depression.³²

Physical Function

We assessed the subjects' physical function by the TUG test. The TUG score is calculated from the time taken to rise from a chair without armrests, walk 3 meters, return to the chair, and sit down. The TUG test is a performance-based measure recommended by the Osteoarthritis Research Society International (OARSI) to assess physical function in individuals diagnosed with KOA.³³ Although there are various reports on cut-off values for TUG time,^{34–36} we defined normal physical function as < 10 and decreased physical function as ≥ 10 sec, which is considered a general indication of physical function.³⁶

Statistical Analysis

The data from 1,106 subjects with complete data were included in the primary analysis.

Descriptive statistics were calculated for the baseline characteristics of subjects, with continuous data presented as means and standard deviations. Binomial or categorical data were presented as proportions. The χ^2 -test was used to compare categorical variables. Univariate and multivariate logistic analyses were conducted to examine the association between mobility and each factor, with the categorical variable TUG score as the dependent variable. Categorical variables of age, gender, BMI, knee pain, CESD-10 and radiographic KOA severity were included in the analysis as independent variables, regardless of the results of the univariate analysis, as they were considered clinically important. The variance inflation factor (VIF) indicates multicollinearity in multivariate analysis and expresses the correlation between independent variables. VIF ≥ 10 was considered to be multicollinearity.³⁷ The odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from logistic analysis. All tests were two-sided, and probability (p)-values < 0.05 were considered statistically significant. The sample size required for logistic regression analysis is proposed to be $n = 10k/p$ (K: number of terms in the independent variables, p: proportion of the smaller of the two groups of dependent variables).³⁸ The sample size required for this study was $n = 10 * 6 / 0.127 = 472.4$. The data we used in this study of 1106 individuals was sufficient for the required sample size. All statistical analyses were conducted using JMP PRO 16 (SAS, Cary, NC, USA).

Results

The Subjects' Characteristics

We summarized the characteristics of the 1,106 subjects and 352 excluded from the analysis due to missing data in [Table 1](#). The subjects included in present analysis tended to be older and more male compared to the missing data subjects.

Relationship Between Subjects' Depression and Knee Pain

[Table 2](#) shows the present data concerning the relationship between depression and knee pain. Depression was significantly associated with the severity of the subjects' knee pain.

Table 1 Subject Characteristics

(n, [%])	All Subjects (n=3790)	Excluded Subjects (n=2332)	Excluded Subjects : Missing Data (n=352)	Analyzed Subjects (n=1106)	P value (Excluded Subjects: Missing Data and Analyzed Subjects)
Age (mean, [95% CI])	67.5 (58.4–76.5)	67.0 (57.5–76.5)	67.1 (57.7–76.4)	68.7 (60.9–76.5)	<0.0001
Age (years; n, [%])					<0.0001
<65 years	1200 (31.7)	807 (34.6)	128 (36.4)	265 (24.0)	
65–74 years	1640 (43.2)	949 (40.7)	125 (35.5)	566 (51.2)	
≥ 75 years	950 (25.1)	576 (24.7)	99 (28.1)	275 (24.9)	
Gender (n, [%])					<0.0001
Male	1560 (41.2)	1100 (42.9)	102 (29.0)	458 (41.4)	
Female	2230 (58.8)	1332 (57.1)	250 (71.0)	648 (58.6)	
BMI (n, [%])					0.4762
<18.5	98 (3.1)	66 (3.4)	3 (3.6)	29 (2.6)	
18.5–24.9	1981 (63.6)	1245 (64.6)	48 (57.2)	688 (62.2)	
25.0–29.9	921 (29.6)	546 (28.4)	27 (32.1)	348 (31.5)	
≥ 30	116 (3.7)	69 (3.6)	6 (7.1)	41 (3.7)	
Knee pain (n, [%])					0.2446
No pain	1797 (47.4)	1249 (53.6)	119 (33.8)	429 (38.8)	
Mild pain	170 (4.5)	742 (31.8)	156 (44.3)	427 (38.6)	
Moderate pain	196 (5.2)	219 (9.4)	47 (13.4)	159 (14.4)	
Severe pain	47 (1.2)	122 (5.2)	30 (8.5)	91 (8.2)	
Radiographic KOA severity (n, [%])					0.2288
KL grade 0	–	–	35 (9.9)	83 (7.5)	
KL grade 1	–	–	110 (31.3)	330 (29.9)	
KL grade 2	–	–	77 (21.9)	304 (27.5)	
KL grade 3	–	–	101 (28.7)	298 (26.9)	
KL grade 4	–	–	29 (8.2)	91 (8.2)	
CESD-10 (n, [%])					0.1129
No depression	3139 (87.3)	1930 (87.7)	257 (90.0)	952 (86.1)	
Depression	455 (12.7)	271 (12.3)	30 (10.0)	154 (13.9)	
TUG (n, [%])					0.7694
Normal physical function	2978 (84.4)	1713 (82.3)	299 (87.9)	966 (87.3)	
Decreased physical function	549 (15.6)	368 (17.7)	41 (12.1)	140 (12.7)	

Notes: The data are expressed as n (%). Statistically significant P-values (P-value < 0.05) are shown in bold.

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis; OA, osteoarthritis; KL, Kellgren-Lawrence; CESD-10, Center of Epidemiologic Studies Depression Scale-10; TUG, Timed Up and Go Test.

Table 2 Association Between CESD-10 and Knee Pain

	CESD-10:		p-value
	No Depression	Depression	
Knee pain:			<0.0001
No pain	386 (90.0)	43 (10.0)	
Mild pain	372 (87.1)	55 (12.9)	
Moderate pain	128 (80.5)	31 (19.5)	
Severe pain	66 (72.5)	25 (27.5)	

Notes: The data are expressed as n (%). Statistically significant P-values (P-value < 0.05) are shown in bold.

Abbreviations: CESD-10, Center of Epidemiologic Studies Depression Scale-10.

Univariate Analysis: Association Between TUG Score and Confounders

We found significant associations with TUG score in subjects' age 65–74 years (OR, 2.76; 95% CI, 1.33–5.69), age ≥ 75 years (OR, 11.88; 95% CI, 8.82–24.24), moderate knee pain (OR, 2.81; 95% CI, 1.66–4.76), severe knee pain (OR, 4.90; 95% CI, 2.77–8.67), KL grade 3 (OR, 4.38; 95% CI, 1.32–14.50), KL grade 4 (OR, 17.45; 95% CI, 5.12–59.53), and depression (OR, 2.73; 95% CI, 1.79–4.15) in univariate analysis (Table 3).

Multivariate Analysis: Association Between TUG Score and Confounders

We summarized the relationships between TUG score and confounders (age, gender, BMI, knee pain, KOA category, and CESD-10) in Table 4. Compared to subjects aged <65 years, the OR was 2.13 times higher in those aged 65–74 years (95% CI, 1.00–4.52) and 8.93 times higher in subjects ≥ 75 years old (95% CI, 4.18–19.05). Significant associations with decreased physical function were found in severe pain (OR, 2.13; 95% CI, 1.08–4.21). Depression was also significantly associated with decreased physical function (OR, 2.64; 95% CI, 1.61–4.33). Only KL grade 4 was significantly associated with decreased physical function in the radiographic KOA severity (OR 6.58, 95% CI 1.75–24.68).

Table 3 Univariate Analysis of TUG

Decreased Physical Function	Univariate Analysis	
	OR (95% CI)	p-value
Age, yrs:		
<65	Ref.	–
65–74	2.76 (1.33–5.69)	0.0062
≥ 75	11.88 (8.82–24.24)	<0.0001
Gender:		
Male	Ref.	–
Female	1.41 (0.97–2.05)	0.068
BMI:		
<18.5	2.04 (0.81–5.16)	0.1325
18.5–24.9	Ref.	–
25.0–29.9	1.28 (0.87–1.88)	0.2043
≥ 30	1.61 (0.69–3.76)	0.2704
Knee pain:		
None	Ref.	–
Mild	1.47 (0.93–2.33)	0.1009
Moderate	2.81 (1.66–4.76)	0.0001
Severe	4.90 (2.77–8.67)	<0.0001
Radiographic KOA severity:		
KL grade 0	Ref.	–
KL grade 1	2.38 (0.70–8.03)	0.1637
KL grade 2	3.14 (0.94–10.51)	0.0639
KL grade 3	4.38 (1.32–14.50)	0.0157
KL grade 4	17.45 (5.12–59.53)	<0.0001
CESD-10:		
No depression	Ref.	–
Depression	2.73 (1.79–4.15)	<0.0001

Notes: In the present univariate analyses, logistic regression analysis was performed with age, gender, BMI, knee pain, radiographic KOA severity, and CESD-10. OR and P-values of variables that showed statistically significant (P-value < 0.05) are shown in bold.

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis; OA, osteoarthritis; KL, Kellgren-Lawrence; CESD-10, Center of Epidemiologic Studies Depression Scale-10.

Table 4 Multivariate Analysis of TUG

Decreased Physical Function	Multivariate Analysis		
	OR (95% CI)	p-value	VIF
Age, yrs:			
<65	Ref.	–	1.13
65–74	2.13 (1.00–4.52)	0.0491	
≥75	8.93 (4.18–19.05)	<0.0001	
Gender:			
Male	Ref.	–	1.09
Female	1.08 (0.70–1.67)	0.7245	
BMI:			
<18.5	2.02 (0.70–5.85)	0.1948	1.07
18.5–24.9	Ref.	–	
25.0–29.9	1.19 (0.77–1.83)	0.4368	
≥30	1.24 (0.46–3.31)	0.6689	
Knee pain:			
None	Ref.	–	1.13
Mild	1.09 (0.66–1.80)	0.7294	
Moderate	1.78 (0.97–3.25)	0.0605	
Severe	2.13 (1.08–4.21)	0.0284	
Radiographic KOA severity:			
KL grade 0	Ref.	–	1.30
KL grade 1	2.11 (0.60–7.39)	0.2425	
KL grade 2	2.41 (0.69–8.37)	0.1679	
KL grade 3	2.39 (0.68–8.40)	0.1730	
KL grade 4	6.58 (1.75–24.68)	0.0053	
CESD-10:			
No depression	Ref.	–	1.03
Depression	2.64 (1.61–4.33)	0.0001	

Notes: In the present multivariate analysis, logistic regression analysis was performed with age, gender, BMI, knee pain, radiographic KOA severity, and CESD-10 as covariates. OR and P-values of variables that showed statistically significant (P-value < 0.05) are shown in bold.

Abbreviations: VIF, variance inflation factor; BMI, body mass index; KOA, knee osteoarthritis; OA, osteoarthritis, KL, Kellgren-Lawrence; CESD-10, Center of Epidemiologic Studies Depression Scale-10.

Physical function was independently associated with age, knee pain and depression, but not with the radiographic KOA severity except for KL grade 4. We determined that there was no multicollinearity between confounders in this study because the VIF of each confounder was quite low.

Discussion

The results of our multivariate analyses demonstrated that age, severe knee pain, and depression were significantly associated with decreased physical function, while radiographic KOA severity was not significantly associated with decreased physical function except for KL grade 4.

Symptomatic KOA has been thought to cause decreased physical function and a decline in ADLs.¹⁴ Depression affects decreased physical function,²³ but there are a few quantitative evaluation reports.²⁴ In addition, depression is closely related to knee pain in KOA.^{20–22} We analyzed the association of knee pain, a common symptom of KOA, radiographic KOA severity, and depression with decreased physical function. To the best of our knowledge, this investigation is the first to analyze the impact of KOA severity based on imaging findings and degree of knee pain on

decreased physical function, taking psychological factors into account. Our results corroborate and extend the findings of previous studies.

Our analyses indicated that age ≥ 65 years was significantly associated with decreased mobility. Prior research found that increasing age is associated with decreased physical function,³⁹ which is consistent with our results. Lower extremity muscle strength and one's usual and maximum walking speeds are age-dependent mobility abilities.⁴⁰ A decrease in physical function with age is plausible, and prevention and countermeasures are necessary. Identifying factors other than age that are associated with decreased physical function is important.

Our analyses revealed that decreased physical function was significantly associated with severe knee pain. Among the elderly, knee pain is considered a major cause of physical disability, including physical function and ADL impairment,⁴¹ and the present results are consistent with this understanding. Pain associated with OA causes reduced use of the affected limb or joint, muscle weakness, and gradual develop joint mobility disorders,⁴² resulting in decreased physical function.⁴³ Accurate knee pain assessment is necessary as an indicator of physical function in KOA.

Our analyses also demonstrated an interesting significant association between depression and decreased mobility. Depression has been shown to affect motor limitations and accelerate physical disability,²³ which is consistent with our results. This may be explained by the effects of depression itself, since psychological distress leads to the avoidance of daily activities, resulting in muscle weakness,⁴⁴ hence, the association between knee pain and depression. Depression has been reported to be a modifier of knee pain and is strongly related to knee pain.⁴⁵ The present χ^2 analysis also identified a significant association between depression and knee pain. We speculate that knee pain may be an intermediate factor between depression and decreased mobility. Rather than depression directly decreasing mobility, it may exacerbate knee pain, resulting in the avoidance of daily activities and decreased physical function. The assessment of depression in KOA in clinical practice has received little attention, but the results of this study indicate that it is an important indicator of physical function.

Our present finding that radiographic KOA severity except for KL grade 4 was not significantly associated with decreased physical function directly. A positive correlation between TUG scores and radiographic KOA severity had previously been reported.²⁶ On the other hand, another investigation found no significant differences in TUG scores among subgroups of patients classified based on their radiographic KOA severity, although the patients with the most severe KOA (KL-4) tended to exhibit the worst performance.²⁵ Both studies performed univariate analyses of KL grade and TUG score and did not consider the influence of knee pain or psychological factors. In other words, the association between severe OA on imaging findings and decreased physical function may be confounded by other factors. Patients with KOA included in KL grade 4 have been shown to have poorer physical function due to restricted limited joint range of motion, altered lower extremity alignment, and more severe synovitis, compared to patients with less severe KOA.^{46,47} In KL grade 4, the morphological changes have an impact on decreased physical function, as suggested by the present study. However, the radiographic KOA severity below KL-3 was not significantly associated with decreased physical function in this study, which limits the ability to assess decreased physical function based on the radiographic severity alone. National Institute for Health and Care Excellence (NICE) guidelines recommended that imaging should not be routinely used to diagnose osteoarthritis unless some atypical features or features suggest an alternative or additional diagnosis.⁴⁸ The severity of imaging findings is only one indicator, and it is important to assess clinical symptoms and physical findings correctly.

One of the diagnostic criteria for KOA in clinical practice is its severity on imaging findings, but knee pain and psychological factors related to decreased physical function must also be assessed. Our present findings demonstrate the limitations of assessing physical function solely on the radiographic KOA severity, which tends to be the focus of clinical attention. When assessing the decreased physical function, it is necessary to take into account the patient's knee pain and psychological factors, rather than being restricted to radiographic KOA severity. In addition, future intervention studies on knee pain and psychological factors are needed to validate these findings.

We must address several study limitations. (i) As this study was a cross-sectional analysis, a causal relationship cannot be definitively determined. (ii) There may have been a measurement error in measuring TUG times. Previous studies have reported a measurement error of 0.22 seconds.⁴⁹ The measurement error in a TUG assessment is greater in frail older adults, and the longer it takes to perform the TUG test, the greater the variability.⁵⁰ (iii) In our analyses, we

were unable to include low socioeconomic status, comorbidities, or physiological factors (ie, inflammation or vitamin D deficiency), each of which is commonly considered a risk factor for decreased mobility.⁵¹ (iv) Plain radiographs of the knee were optional, which may have resulted in a high number of symptomatic subjects participating, possibly biasing in the study.

Conclusions

In conclusion, our findings demonstrate that age ≥ 65 years, severe knee pain, and depression were significantly associated with decreased mobility, but not radiographic KOA severity except for KL grade 4. The limitations of using radiographic KOA severity alone as the indicator of assessment for physical function were suggested. When assessing decreased physical function, the clinical focus tends to be on radiographic KOA severity, but it is important to consider the patient's knee pain and psychological factors.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments

We thank the Japanese Orthopaedic Association (JOA-Subsidized Science Project Research 2022-1). We would like to thank the staff of the Tadami and Minamiaizu Town Office, and Institute for Health Outcomes and Process Evaluation Research for their help with participant recruitment and data acquisition. The authors also thank all of the subjects who agreed to participate in this study.

Funding

This research did not receive any specific grant.

Disclosure

The author reports no conflicts of interest in this work. This paper has a shared database with another paper published in BMC at: <https://bmcmusculoskeletaldisord.biomedcentral.com/articles/10.1186/s12891-024-07421-1>. This paper has been uploaded to Research Square as a preprint: <https://www.researchsquare.com/article/rs-4010731/v1>.

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