



Association Of Radiographic Grading With Functional Status And Quality Of Life In Primary Knee Osteoarthritis

¹Dr. Mohammad Kaleem Ul Haque, Senior Resident Department of Physical Medicine and Rehabilitation, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, India

²Dr. Tufail Muzaffar, Assistant Professor, Department of Physical Medicine and Rehabilitation, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, India

³Dr. Chand Mohamed Ikram Malik, Senior Resident, Department of Physical Medicine and Rehabilitation, National Institute for Locomotor Disabilities, Kolkata, India

Citation of this Article: Dr. Mohammad Kaleem Ul Haque, Dr. Tufail Muzaffar, Dr. Chand Mohamed Ikram Malik, “Association Of Radiographic Grading With Functional Status And Quality Of Life In Primary Knee Osteoarthritis”, IJMSAR – March – 2021, Vol. – 4, Issue - 3, P. No.21-36.

Copyright: © 2021, Dr. Chand Mohamed Ikram Malik, et al. This is an open access journal and article distributed under the terms of the creative commons attribution noncommercial License. This allows others to remix, tweak, and build upon the work non commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Corresponding Author: Dr. Chand Mohamed Ikram Malik, Senior Resident, Department of Physical Medicine and Rehabilitation, National Institute for Locomotor Disabilities, Kolkata, India

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background

Osteoarthritis of the knee is a complex musculoskeletal disorder which not only is a degenerative disorder of articular cartilage but synovium and subchondral bone are also affected.¹ The prevalence of osteoarthritis in India has been estimated to be around 28.7% which has been calculated based on data from five Indian states.² It is graded radiographically using the classical Kellgren-Lawrence scale, functionally with WOMAC score and QoL with SF-36. Some discrepancies have been seen in some patients of OA between the radiographic grade of OA and functional

status and QoL. The purpose of this study is to help the healthcare professionals better understand the limitations brought by OA to functional status and QoL in concordance with radiographic grading.

Objectives

To study the association of radiography and grading using Kellgren-Lawrence scale in primary knee unilateral or bilateral osteoarthritis using anteroposterior standing view with functional status using Western Ontario and McMaster Universities Osteoarthritis Index(WOMAC) and Health Related Quality of Life using Short Form 36 (SF-36) in the age group of 35 to 70 years.

Methods

Study Site and Populations

The patients with primary knee OA visiting the outpatient department of NILD, Kolkata as per the inclusion and exclusion criteria.

Study Design and Sampling Strategy

It is an observational, cross-sectional and descriptive study over a period of one year after getting Institutional ethical committee clearance. Total number of patients selected for the study were 194 with primary knee OA meeting the inclusion criteria. Each patient was stratified on KL scale for OA grading using stress radiographs. Both WOMAC and SF-36 for functional status and QoL assessment respectively were done for each patient. Statistical analysis was performed using SPSS-18, Epi-info, and Graphpad Prism.

Results

A total of 194 patients with OA knees with different grades of radiographic changes were analysed using Pearsons correlation test. Positive correlation was found between radiography using KL grade and functional status using WOMAC score with statistical significance (p value <0.0001). Negative correlation was found between radiography and QoL using SF-36 and was statistically significant (p value < 0.0001).

Conclusions

There is concordance between radiographic grading and functional status of the patient with OA knee; and between radiographic grading and QoL of the patient with OA knee.

Keywords

Knee osteoarthritis, Functional status, Quality of life, WOMAC Score, SF-36, Kellgren-Lawrence,

Introduction

Overview

Osteoarthritis of the knee is one of the leading cause

of pain, loss of function and decreased quality of life among the rheumatic diseases in adults.¹ It represents a complex musculoskeletal disorder with multiple genetic, constitutional and biomechanical risk factors including the invasive knee procedures².

Prevalence

It is estimated that the cost of osteoarthritis accounted for 0.28% of the GNP in Asia³. The prevalence of osteoarthritis in India has been estimated to be around 28.7% which has been calculated based on data from five Indian states.⁴ Worldwide the prevalence of OA is estimated to be around 9.6% in men and 18% in women aged over 60 years of age.⁵ And 4 out of every 5 will have limitations in movement and 1/4 out of these will have issues performing their major daily activities.⁵ It is estimated that over 14 million people in the US are having symptomatic OA and 7 million among this group are having advanced OA.⁶ Women are having more burden of OA knees than men worldwide with an increased incidence after menopause.^{7,8}

Signs and Symptoms

Knee pain which is persistent along with limited morning stiffness are persistent features of OA as defined by ACR criteria.⁹ Pain in the knee and any three of; over 50 years of age, less than 30 minutes of morning stiffness, crepitus on active motion, bony tenderness, bony enlargement, no palpable warmth of synovium⁶. If radiology is included in the diagnosis of osteoarthritis then pain in knee along with any one of over 50 years of age, morning stiffness of less than 30 minutes and crepitus on active motion and osteophytes.¹⁰ Other complaints include noisy knee, giving way, locking and sometimes exacerbation in cold weather. Bony tenderness, bony enlargement, joint effusions are other findings seen in OA. Joint laxity, limitation of motion and malalignment occur after a long

time of knee OA. Genu varum and flexion contracture are usually seen in late stages of OA.

Investigations

OA knee is diagnosed with clinical and radiographic evidence. Plain radiography is cost effective and readily available.^{11,12} Kellgren and Lawrence (KL) in 1957 established the radiographic classification of knee osteoarthritis.¹³

Treatment

The goal of OA treatment is the alleviation of pain, improvement of function and improvement in QoL. Patients receive both pharmacologic and non-pharmacologic therapy.

Body weight reduction in patients who are overweight improves both function and symptoms in knee OA patients.¹⁵ ACR 2012 recommends muscle strengthening and low impact aerobic exercises.^{16,17}

Physical therapy (PT) has shown to improve both mobility and pain in knee OA using various PT programmes.^{18,19} Aquatic, Tai Chi, aerobic, hydrotherapy along with muscle strength training have been shown to increase the functional ability, joint stability and pain scores.²⁰ Isotonic, isometric and isokinetic exercises are commonly used but eccentric exercises have been shown to decrease pain levels in knee OA.^{20,21} Heat, cold, light, pressure,²² electromagnetic therapy^{23,24} has been used for improvement in pain and preservation of morphology of articular cartilage. Assistive devices and braces, walking aids have been shown to significantly decrease the pain^{25,26}

Acetaminophen has been found to be good for short term analgesia.²⁷ Capsaicin has 50% reduction in pain as compared to placebo.^{28,29} Intra-articular corticosteroids have shown short term relief in pain.^{30,31} Diacerein showed short term benefit for pain.³² Duloxetine is used

in chronic knee pain in OA.³³ Glucosamine showed mixed results in pain relief and physical function in studies.^{34,35} Hyaluronic acid (intra-articular) has small but significant effect on pain relief.^{30,36} Oral non-selective NSAIDs have effect in relief from pain. Topical NSAIDs are useful in knee OA pain.³⁷ Codeine has moderate benefit in knee OA pain, with oxycodone having small to moderate benefit and morphine with small benefit.³⁸ Tramadol has small but statistically significant benefit in pain relief.³⁹ Risedronate higher doses of 15mg per day reduces the level of marker of cartilage degradation (CTX-II) which helps in reduction of radiological progression of knee OA.⁴⁰ Rosehip has positive effect on pain.⁴¹

Arthroscopic surgery for knee OA has no significant additional benefit when compared with physical and medical therapy.⁴² Osteotomy is useful in knee OA patients with nonalignment like genu varum or bowleg deformity.^{43,44} Knee arthroplasty is performed after conservative treatment fails or are ineffective with improvement in pain and function.^{45,46} Joint fusion relieves pain at the cost of motion. Joint lavage has no relief either in pain or function.⁴⁷

Functional Ability

Functional ability of the knee declines with age. This disability is compounded by social, biological and psychological factors.⁴⁸ For assessing the functional status in these patients, WOMAC score is the most widely used scale.⁴⁹ The American College of Rheumatology notes that the test-retest reliability of the WOMAC varies for the pain, stiffness, and function subscales and generally meets the minimum standard." Reliability for the physical function scale "has been more consistent and the stiffness sub-scale has shown low test-retest reliability."⁵⁰

Quality of life

'WHO defines Quality of Life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.'⁵¹The health related quality of life most widely used is SF-36 developed by RAND US. RAND developed the 36-Item Short Form Health Survey (SF-36). SF-36 is a set of generic, coherent, and easily administered quality-of-life measures. These measures rely upon patient self-reporting and are now widely utilised by managed care organisations and by Medicare for routine monitoring and assessment of care outcomes in adult patients. The RAND 36-Item Health Survey (Version 1.0) taps eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions.

Purpose of the study

Some patients with low grade osteoarthritis may present with decreased levels of functional status and some patients with high grade osteoarthritis may present with good functional status. The discrepancy between pain and radiographic changes may be explained by the propensity of some OA patients to develop sensitised central nociceptive circuits that enhance pain during various states of peripheral tissue insult. It was to our understanding that only few cross-sectional studies have been done in Indian set up till date to look for association between radiographic grading with functional status and

QoL in patients with OA knees. So this study was done to have a better understanding of the association so that interventions to treat these patients can be done earlier.

Materials and Methods

The Study was conducted in outpatient Department in Tertiary Care Hospital in NILD, Kolkata. This study was cross-sectional, observational and descriptive study conducted from June 2018 to June 2019 (1 year). The sample size was 194 based on previous study showing prevalence of 28.7%.⁴

Inclusion criteria

- a. Primary knee osteoarthritis
- b. Age group 35-70 years
- c. Patients fulfilling the American college of Rheumatology criteria for osteoarthritis
- d. Patient willing to participate in the study

Exclusion criteria

- a. History of ligamentous injuries in the knee joint
- b. History of intra-articular injections in knee joint
- c. Fractures around the knee
- d. Infection in and around knee
- e. Myofacial pain
- f. Bursitis around the knee joint
- g. Secondary knee osteoarthritis

Methodology

Institutional scientific and ethical committee clearance was taken for the study. Patients were selected according to inclusion and exclusion criteria. A total of 194 patients were examined and selected meeting the criteria in the outpatient setting in National Institute for Locomotor Disabilities, Kolkata. Informed written consent was taken. Each participant was advised stress

radiograph of the knees to grade them into Kellgren-Lawrence Scale^{11,12,13,14} KL scale.

The instrument for measuring the functional status of knee OA patients was Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score.

The instrument for measuring QoL for the patients was Short Form (SF-36), which is a questionnaire based tool and contains 36 questions pertaining to health related QoL.

Statistical Analysis

For statistical analysis data was analysed by SPSS (version 24.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Correlation was calculated by Pearson correlation analysis. P -value ≤ 0.05 was considered for statistically significant.

Results and Observations

A total of 194 patients who came to NILD in out patient department were examined who met the inclusion criteria. Each patient was stratified on KL-scale, WOMAC score and SF-36. 7(3.6%) patients had 31-40 years of age, 46(23.7%) patients had 41-50 years of age, 81(41.8%) patients had 51-60 years of age and 60(30.9%) patients had 61-70 years of age. 117(60.3%) patients were female and 77(39.7%) patients were male. Standing radiographs showed 41(21.1%) patients had

KL-grade 1, 80(41.2%) patients had KL-grade 2, 54(27.8%) patients had KL-grade 3 and 19(9.8%) patients had KL-grade 4. The mean age (mean \pm s.d.) of the patients was 55.9330 ± 8.1254 years. The mean of Pain subscale of the patients was 8.2943 ± 2.3953 . The mean of Stiffness Subscale of the patients was 3.9881 ± 0.8377 . The mean of Function Subscale of the patients was 32.0161 ± 11.2827 . The mean of WOMAC (mean \pm s.d.) of the patients was 44.2977 ± 13.8904 . The mean physical function (mean \pm s.d.) of the patients was 26.0825 ± 20.8526 . The mean role limitation physical (mean \pm s.d.) of the patients was 12.2423 ± 30.0302 . The mean role limitation emotional (mean \pm s.d.) of the patients was 15.4691 ± 34.7573 . The mean energy fatigue (mean \pm s.d.) of the patients was 53.6856 ± 21.6172 . The mean energy fatigue well-being (mean \pm s.d.) of the patients was 61.2113 ± 18.5871 . The mean social function (mean \pm s.d.) of the patients was 53.5954 ± 20.7703 . The mean pain (mean \pm s.d.) of the patients was 51.6237 ± 22.3188 . The mean general health (mean \pm s.d.) of the patients was 43.0928 ± 20.2503 . The mean change in health (mean \pm s.d.) of the patients was 22.1503 ± 16.6822 .

		X-ray KL-grade	Remarks
Physical Function	Pearson Correlation Coefficient (r)	-.513**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
Role limitation Physical	Pearson Correlation Coefficient (r)	-.401**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
Role limitation emotional	Pearson Correlation Coefficient (r)	-.430**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
Energy fatigue	Pearson Correlation Coefficient (r)	-.267**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
Emotional Well-being	Pearson Correlation Coefficient (r)	-.012	Negative Correlation
	p-value	.867	Statistically not significant
	Number	194	
Social Function	Pearson Correlation Coefficient (r)	-.456**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
Pain	Pearson Correlation Coefficient (r)	-.285**	Negative Correlation
	p-value	<0.0001	Statistically significant
	Number	194	
General health	Pearson Correlation Coefficient (r)	-.117	Negative Correlation
	p-value	.105	Statistically not significant
	Number	194	
Change in Health	Pearson Correlation Coefficient (r)	-.236**	Negative Correlation
	p-value	.001	Statistically significant
	Number	194	

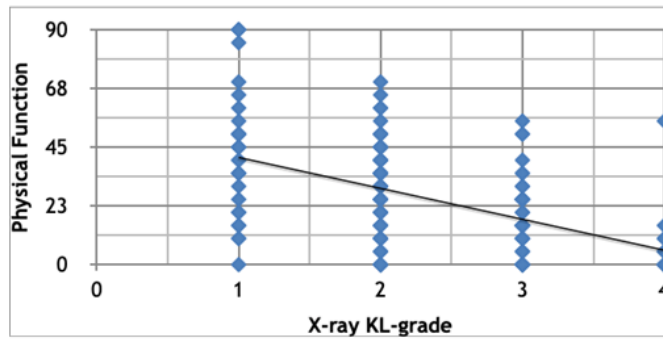
[Table/Fig 1] Correlation of Physical Function, Role limitation Physical, Role limitation emotional, Energy fatigue, Emotional Well-being, Social Function, pain, General health and Change in Health with X-ray KL-grade.

[Table/Fig 2] Negative correlation was found between Physical Function and X-ray KL-grade and it was statistically significant (p<0.0001). [Table/Fig 3] Negative correlation was found between Role limitation

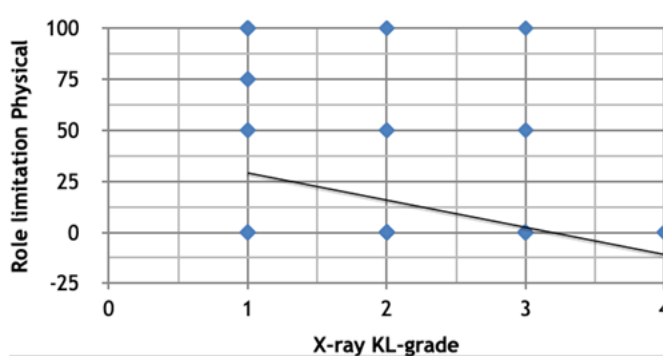
Physical and X-ray KL-grade and it was statistically significant (p<0.0001). [Table/Fig 4] Negative correlation was found between Role limitation emotional and X-ray KL-grade and it was statistically significant (p<0.0001). [Table/Fig 5] Negative correlation was found between Energy fatigue and X-ray KL-grade and it was statistically significant (p<0.0001). [Table/Fig 6] Negative correlation was found between Emotional Well-being and X-ray KL-grade and it was not

statistically significant ($p=.867$). [Table/Fig 7] Negative correlation was found between Social Function and X-ray KL-grade and it was statistically significant ($p<0.0001$). [Table/Fig 8] Negative correlation was found between Pain and X-ray KL-grade and it was statistically significant ($p<0.0001$). [Table/Fig 9]

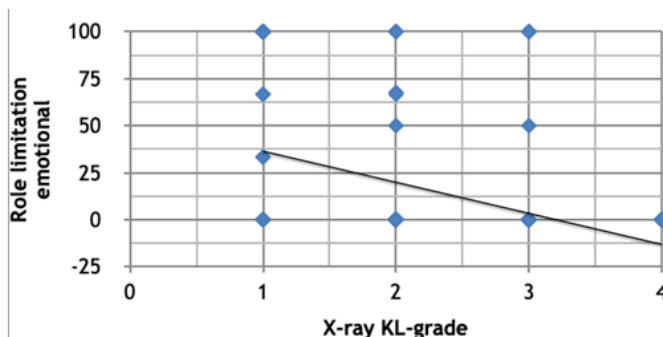
Negative correlation was found between General health and X-ray KL-grade and it was statistically significant ($p<0.0001$). [Table/Fig 10] Negative correlation was found between Change in Health and X-ray KL-grade and it was statistically significant ($p=.001$).



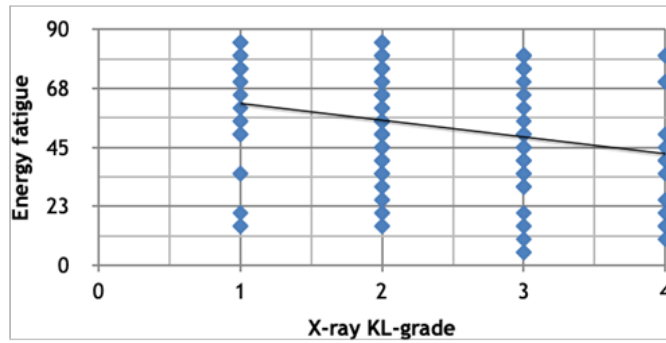
[Table/Fig 2] Correlation of Physical Function and Radiography



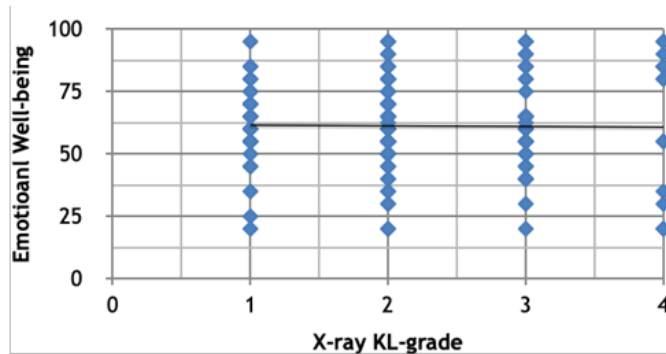
[Table/Fig 3] Correlation of Role Limitation physical and Radiography



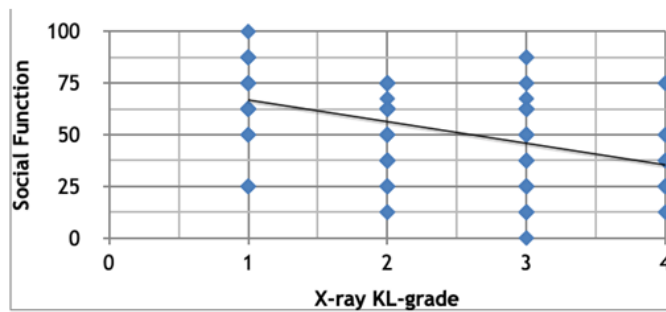
[Table/Fig 4] Correlation of Role Limitation emotional and Radiography



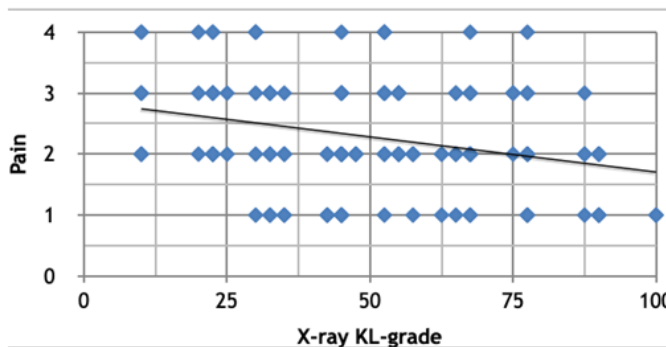
[Table/Fig 5] Correlation of Energy Fatigue and Radiography



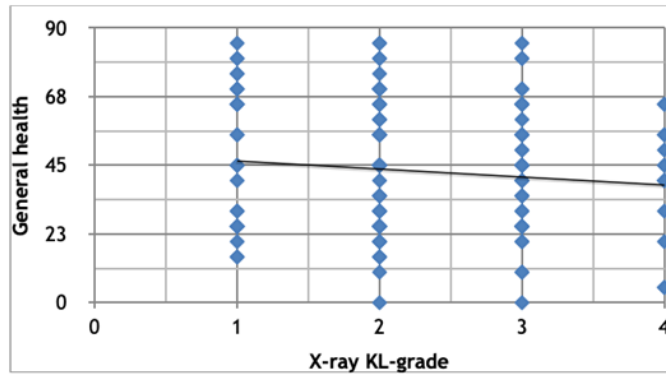
[Table/Fig 6] Correlation of Emotional Well-being and Radiography



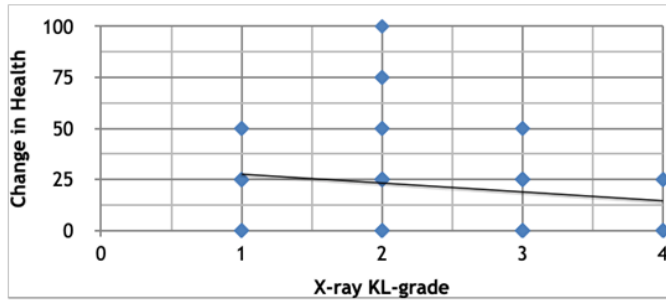
[Table/Fig 7] Correlation of Social Function and Radiography



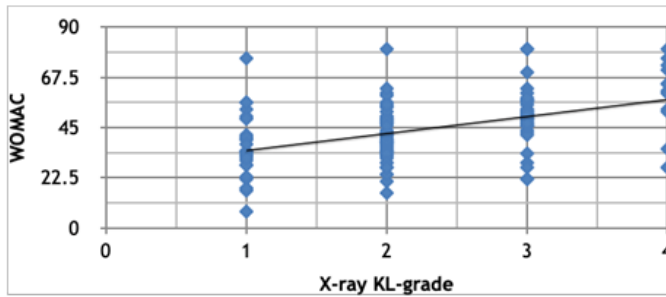
[Table/Fig 8] Correlation of Pain and Radiography



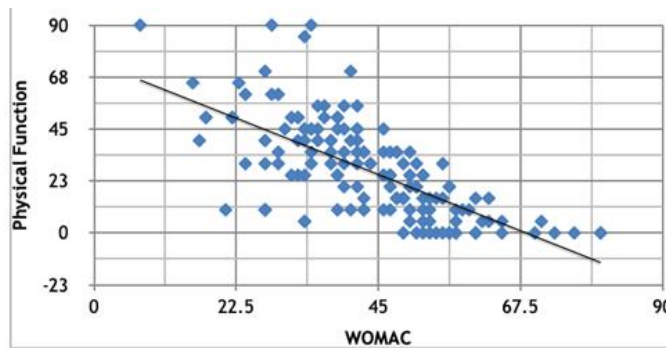
[Table/Fig 9] Correlation of General Health and Radiography



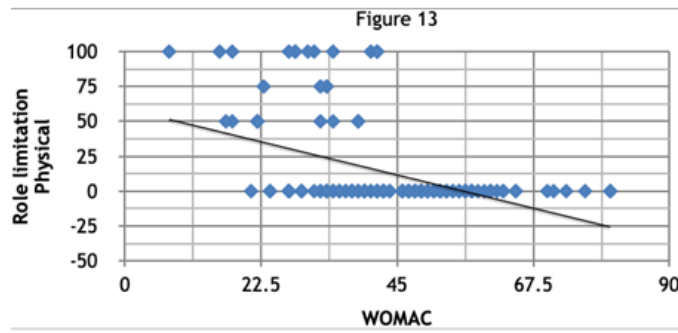
[Table/Fig 10] Correlation of Change in Health and Radiography



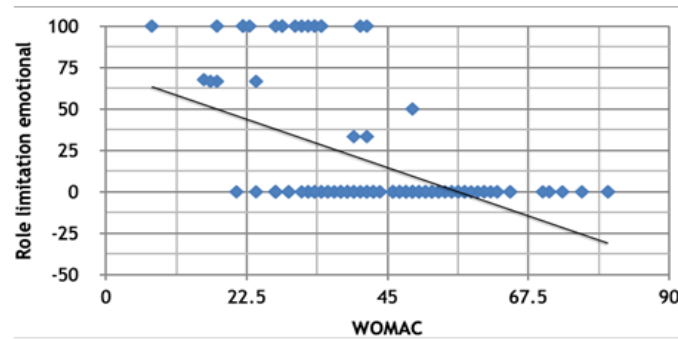
[Table/Fig 11] Correlation of WOMAC and Radiography



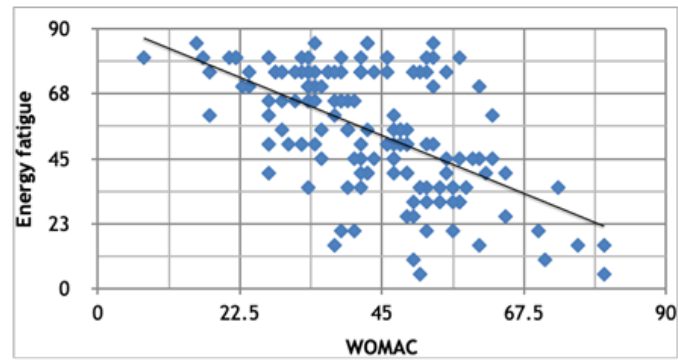
[Table/Fig 12] Correlation of Physical Function and WOMAC



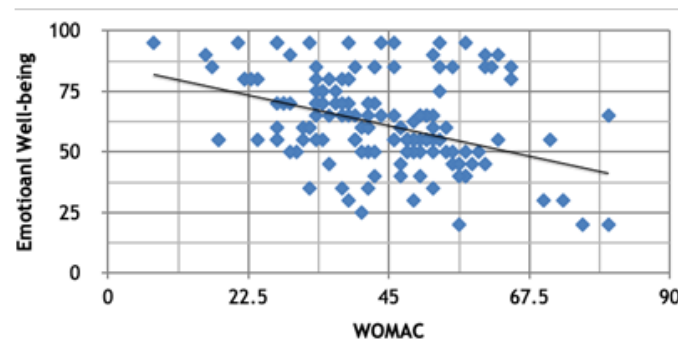
[Table/Fig 13] Correlation of Role Limitation Physical and WOMAC



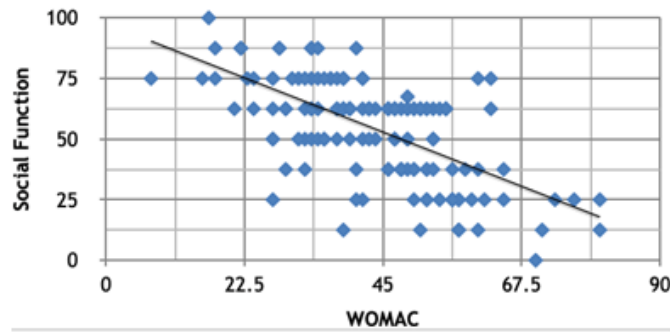
[Table/Fig 14] Correlation of Role Limitation Emotional and WOMAC



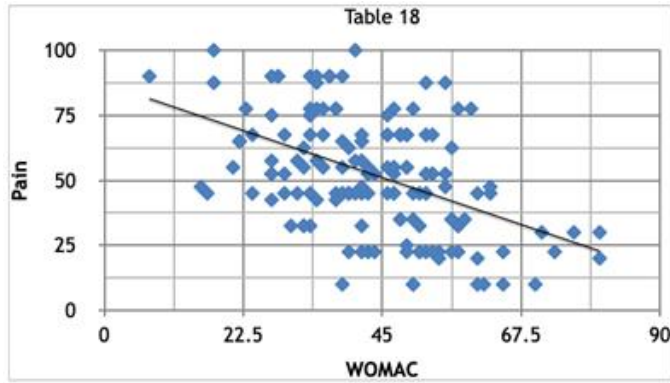
[Table/Fig 15] Correlation of Energy Fatigue and WOMAC



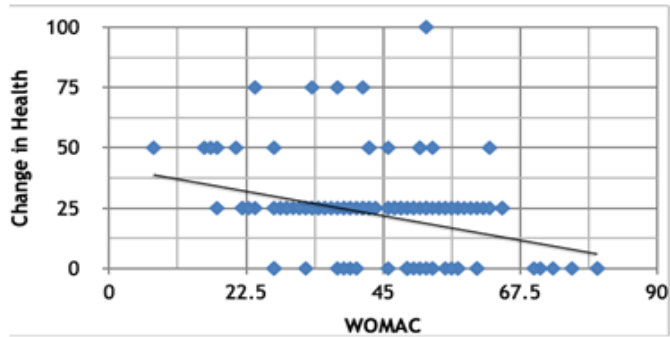
[Table/Fig 16] Correlation of Emotional Well-being and WOMAC



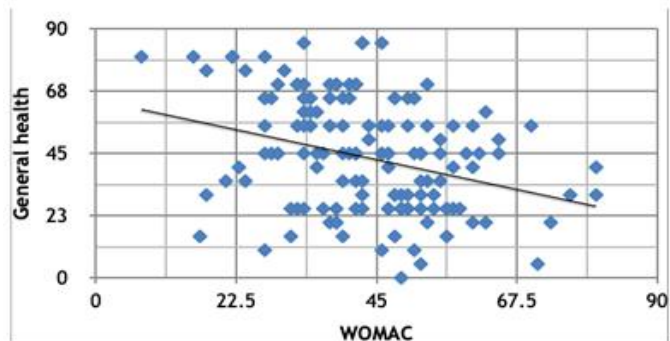
[Table/Fig 17] Correlation of Social Function and WOMAC



[Table/Fig 18] Correlation of Pain and WOMAC



[Table/Fig 19] Correlation of Change in Health and WOMAC



[Table/Fig 20] Correlation of General Health and WOMAC

Discussion

In this study we observed a significant positive correlation between WOMAC score and radiographic abnormality of knee in patients with OA. This finding was in concordance with the cross-sectional study done on the Indian population by J GeethaKalpana on 222 patients with OA in 2017 which showed a positive association between WOMAC and KL grading.⁵² The same finding was found by Sanghi D, et al in 2011⁵³ and Umar Abdul Aziz et al in 2019.⁵⁴

This study also showed a strong correlation between radiographic grading and QoL using SF-36. All parameters like physical functioning, role limitation due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain and general health were negatively correlated with radiographic findings and were statistically significant (p -value < 0.0001) except in case of emotional well-being which was not statistically significant (p value = 0.867). This finding was well corroborated from Kim IJ who did a prevalence study in 2011 on 514 Korean subjects and found that knee pain was substantially correlated with WOMAC score and negatively correlated with health related QoL using SF-36.⁵⁵ Wilson R et al did a cross-sectional study in 2018 to estimate the multi-dimensional health impact of radiographic OA and quantify the overall health related quality of life on 2895 from radiographic knee OA patients and 3202 for general population from National Health Measurement Study in New Zealand and found radiographic knee OA is significantly associated with worse health related QoL across most dimensions of health.⁵⁶ Helminen EE, et al. conducted a one year prospective RCT in 2016 on 111 patients with Kellgren-Lawrence grades of 2-4 to identify the determinants of pain and functioning using WOMAC score in knee

osteoarthritis and found that multiple psychological factors using RAND-36 health related QoL in people with knee osteoarthritis pain are associated with the development of disability and longer term worse pain.⁵⁷

Conclusion

A positive correlation was found between radiography grading using KL grade and WOMAC score with statistical significance. A negative correlation was found between radiography grading using KL grade and health related QoL using SF-36. There was statistical significance between all parameters of health related QoL (except emotional well-being) and KL grade.

No discordance was found between WOMAC score and health related QoL SF-36. There was a negative correlation between all parameters of health related QoL SF-36 and WOMAC score.

Therefore, it can be concluded that there is a correlation between the X-ray finding of patients with knee OA and functional status using WOMAC and health related QoL using SF-36. So, the null hypothesis is wrong, and the correlation is well established.

Limitations

There are several limitations of this study:

- This study was done only in one centre in National Institute for Locomotor Disabilities, Kolkata and therefore is a single centre study. The majority of the studies done on prevalence studies are multi-centric.
- The majority of the studies done on the correlation between radiographic finding and WOMAC score and health related QoL using SF-36 were done outside India and therefore the majority of the references were drawn from the international studies.

References

1. Song J, Chang RW, Dunlop D. Population impact of arthritis on disability in older adults. *Arthritis Rheum.* 2006;55:248–255.

2. Kraeutler MJ; Mitchell JJ; Chahla J; McCarty EC; Pascual-Garrido C. Intra-articular implantation of mesenchymal stem cells, Part 1: A review of the literature for prevention of postmeniscectomy osteoarthritis. *Orthop J Sports Med.* 2017; 5(1):1-7.
3. J. Woo, E. Lau, C. S. Lau et al., "Socioeconomic impact of osteoarthritis in Hong Kong: utilization of health and social services, and direct and indirect costs,". *Arthritis Care and Research.* 2003;49(4):526–534.
4. Chandra Prakash Pal, Pulkesh Singh, Sanjay Chaturvedi, Kaushal Kumar Pruthi, Ashok Vij. Epidemiology of knee osteoarthritis in India and related factors. *Indian J Orthop.* 2016 Sep; 50(5): 518–522.
5. WHO Department of Chronic Diseases and Health Promotion. Available at: <http://www.who.int/chp/topics/rheumatic/en/>.
6. Deshpande BR, Katz JN, Solomon DH, et al. Number of persons with symptomatic knee osteoarthritis in the US: Impact of race and ethnicity, age, sex, and obesity. *Arthritis Care Res (Hoboken)* 2016;68:1743–1750.
7. Bryan BD, Tosi L, et al. Sex Differences in osteoarthritis of the knee: *Journal of the American Academy of Orthopaedic Surgeons.* 2012; 20(10):668–669.
8. Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. *Semin Arthritis Rheum.* 1990; 20(3 Suppl 1):42- 50.
9. W Zhang, M Doherty, G Peat, M A Bierma-Zeinstra, N K Arden, B Bresnihan et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann of the rheu dis.* 2009; 69(3).
10. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum.* 1986;29(8):1039-49.
11. Recht MP, Kramer J, Marcelis S, Pathria MN, Trudell D, Haghighi P, et al. Abnormalities of articular cartilage in the knee: analysis of available MR techniques. *Radiology.* 1993 May; 187(2):473-8.
12. Keen HI, Wakefield RJ, Conaghan PG. A systematic review of ultrasonography in osteoarthritis. *Ann Rheum Dis.* 2009 May; 68(5):611-9.
13. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthritis. *Ann Rheum Dis.* 1957;16:494–502.
14. Wright RW. Osteoarthritis classification scales: interobserver reliability and arthroscopic correlation. *J Bone Joint Surg Am.* 2014;96:1145–1151.
15. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA.* 2013;310:1263–73.
16. Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. *J Am Acad Orthop Surg.* 2013;21:571–6.
17. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 2012;64:465–74.

18. Smink AJ, van den Ende CH, VlietVlieland TP. Beating osteoarthritis: Development of a stepped care strategy to optimize utilization and timing of non-surgical treatment modalities for patients with hip or knee osteoarthritis. *ClinRheumatol*. 2011;30:1623–9.
19. Kon E, Filardo G, Drobic M, Madry H, Jelic M, Dijk N, et al. Non-surgical management of early knee osteoarthritis. *Knee Surg Sports TraumatolArthrosc*. 2012;20:436–9.
20. Rogind H, Bibow-Nielsen B, Jensen B, Moller HC, Frimodt-Moller H, Bliddal H. The effects of a physical training program on patients with osteoarthritis of the knees. *Arch Phys Med Rehabil*. 1998;79:1421–7.
21. McQuade KJ, de Oliveira AS. Effects of progressive resistance strength training on knee biomechanics during single leg step-up in persons with mild knee osteoarthritis. *ClinBiomech (Bristol, Avon)* 2011;26:741–8.
22. Kozanoglu E, Basaran S, Guzel R, Uysal F. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. *Swiss Med Wkly*. 2003;133:333–8.
23. Ciombor DM, Aaron RK, Wang S, Simon B. Modification of osteoarthritis by pulsed electromagnetic field: A morphological study. *Osteoarthritis Cartilage*. 2003;11:455–62.
24. Fini M, Giavaresi G, Carpi A, Nicolini A, Setti S, Giardino R. Effects of pulsed electromagnetic fields on articular hyaline cartilage: Review of experimental and clinical studies. *Biomed Pharmacother*. 2005;59:388–94.
25. Goodman A. Knee Brace Reduces Damage, Pain in Osteoarthritis. *Medscape Medical News*. Available at <http://www.medscape.com/viewarticle/813572>. Accessed: May 3, 2019.
26. Kirkley A, Birmingham TB, Litchfield RB, Giffin JR, Willits KR, Wong CJ, et al. A randomised trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med*. 2008 Sep 11; 359(11):1097-107.
27. Bannuru RRDU, McAlindon TE. Reassessing the role of acetaminophen in osteoarthritis: systematic review and meta- analysis. *Osteoarthritis Research Society International World Congress*; 2010 Sep 23e26; Brussels, Belgium. *Osteoarthritis Cartilage* 2010;18(Suppl 2):S250.
28. Mason L, Moore RA, Derry S, Edwards JE, McQuay HJ. Systematic review of topical capsaicin for the treatment of chronic pain. *BMJ (Clinical Research Ed)* 2004;328(7446):991.
29. Kosuwon W, Sirichatiwapee W, Wisanuyotin T, Jeeravipoolvarn P, Laupattarakasem W. Efficacy of symptomatic control of knee osteoarthritis with 0.0125% of capsaicin versus placebo. *J Med Assoc Thai* 1/4 ChotmaiHetThangphaet 2010;93(10):1188-95.
30. Bannuru RR, Natov NS, Obadan IE, Price LL, Schmid CH, McAlindon TE. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Rheum* 2009;61(12):1704-11.
31. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev* 2006;(2):CD005328.
32. Bartels EM, Bliddal H, Schondorff PK, Altman RD, Zhang W, Christensen R. Symptomatic efficacy and safety of diacerein in the treatment of osteoarthritis: a meta-analysis of randomized placebo-controlled

- trials. Osteoarthritis and Cartilage/OARS. Osteoarthritis Research Society 2010;18(3):289-96.
33. Citrome L, Weiss-Citrome A. A systematic review of duloxetine for osteoarthritic pain: what is the number needed to treat, number needed to harm, and likelihood to be helped or harmed? *Postgrad Med* 2012;124(1):83-93.
34. Wandel S, Juni P, Tendal B, Nuesch E, Villiger PM, Welton NJ, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ (Clinical Research Ed)* 2010;341:c4675.
35. Towheed TE, Maxwell L, Anastassiades TP, Shea B, Houpt J, Robinson V, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database Syst Rev* 2005;(2):CD002946.
36. Rutjes AW, Juni P, da Costa BR, Trelle S, Nuesch E, Reichenbach S. Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med* 2012;157(3):180-91.
37. Chou R, McDonagh MS, Nakamoto E, Griffin J. Analgesics for osteoarthritis: An update of the 2006 comparative effectiveness review. Rockville MD 2011 Oct.
38. Nuesch E, Rutjes AW, Husni E, Welch V, Juni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev* 2009;(4):CD003115.
39. Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. *Cochrane database Syst Rev*. 2006;(3):CD005522.
40. Iwamoto J, Takeda T, Sato Y, Matsumoto H. Effects of risedronate on osteoarthritis of the knee. *Yonsei Med J*. 2010;51(2): 164-70.
41. Christensen R, Bartels EM, Altman RD, Astrup A, Bliddal H. Does the hip powder of *Rosa canina* (rosehip) reduce pain in osteoarthritis patients: a meta-analysis of randomized controlled trials. *Osteoarthritis and Cartilage/OARS, Osteoarthritis Research Society* 2008;16(9):965-72.
42. Kirkley A, Birmingham TB, Litchfield RB, Giffin JR, Willits KR, Wong CJ, et al. A randomised trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med*. 2008 Sep 11; 359(11):1097-107.
43. Pagenstert G, Knupp M, Valderrabano V, Hintermann B. Realignment surgery for valgus ankle osteoarthritis. *OperOrthopTraumatol*. 2009 Mar; 21(1):77-87.
44. Pipino G, Indelli PF, Tigani D, Maffei G, Vaccarisi D. Opening-wedge high tibial osteotomy: a seven to twelve year study. *Joints*. 2016 Jun 13; 4(1):6
45. Deirmengian CA, Lonner JH. What's new in adult reconstructive knee surgery. *J Bone Joint Surg Am*. 2008 Nov; 90(11):2556-65.
46. Lee K, Goodman SB. Current state and future of joint replacements in the hip and knee. *Expert Rev Med Devices*. 2008 May; 5(3):383-93.
47. Reichenbach S, Rutjes AW, Nuesch E, Trelle S, Juni P. Joint lavage for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2010 May 12; CD00.
48. Jiyeon Lee, Jung-Hee Kim, EunJung Chung, Byoung-Hee Lee. Functional state of knee arthritis patients and related factors. *J PhysTher Sci*. 2017 Feb; 29(2): 323–327.
49. "WOMAC Osteoarthritis Index". Retrieved 6 June 2012
50. American College of Rheumatology. "Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)--General Description". ACR. Retrieved 6 June 2012.

51. WHO | WHOQOL: Measuring Quality of Life. <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/>.
52. J.GeethaKalpana,P.Thirunavukkarasu,C.Ramesh,S hivanranjani.B, Padmanaban Srinivasan. A study to determinethe association between the Kellgren-Lawrence grade and WOMAC score in population with osteoarthritic knee. Stanley Medical Journal. 2017;4(1):64-67.
53. Divya Sanghi, Abhishek Mishra, Ajai Singh, Rajeshwar Nath Srivastava, SachinAvasthi, Sarita Agarwal. Is radiology a determinant of pain, stiffness, and functional disability in knee osteoarthritis? A cross-sectional study. J Orthop Sci. 2011;16(6):719–725.
54. S.Murak, H.Oka, T.Akune, A.Mabuchi, Y.Enyo, M.Yoshida, A.Saika, T.Suzuki, H.Yoshida, H.Ishibashi, S.Yamamoto, K.Nakamura, H.Kawaguchi, N.Yoshimura. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: The ROAD study. Osteoarthritis and Cartilage. 2009; 17(9):1137-1143.
55. Kim IJ, Kim HA, SeoYinsha, Song YW, Jeong JY, KIM DH. Prevalence of knee pain and its influence on quality of life and physical function in the Korean elderly population: a community based cross-sectional study. J Korean Med Sci. 2011; 26(9): 1140-6.
56. Umar AbdulAziz, Olufemi O Adelowo, Bello O Usman. Correlation between functional disability grade and radiographic severity among Nigerian patients with knee osteoarthritis. Jour of Med in the Tropics. 2019; 21(1):14-19.
57. Eeva-EerikaHelminen, Sanna H Sinikallio, Anna L Valjakka, Rauni H Väisänen-Rouvali, Jari PA Arokoski. Determinants of pain and functioning in knee osteoarthritis: a one-year prospective study. Clin Rehabil. 2016;30(9):890-900.