ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 9, Issue, 8(D), pp. 28549-28554, August, 2018

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

IS ARTICULAR CARTILAGE VOLUME A POTENTIAL TOOL IN DEFINING NORMAL, PRE-ARTHRITIS AND OSTEOARTHRITIS KNEE? A CROSS - SECTIONAL STUDY

Sudeepti Ratan Srivastava[1]., Rajeshwar Nath Srivastava[2]*., Amar Chandra Sharma[3]., Anit Parihar[4] ., Wahid Ali[5] and Lavini Raj[6]

[1,2,3]Department of Orthopedic Surgery, King George's Medical University, Lucknow, U.P., India
[4]Department of Radio- diagnosis, King George's Medical University, Lucknow, U.P., India
[5]Department of Pathology, King George's Medical University, Lucknow, U.P., India
[6]Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, U.P., India

DOI: http://dx.doi.org/10.24327/ijrsr.2018.0908.2479

ARTICLE INFO

Article History:
Received 6th May, 2018
Received in revised form 10th June, 2018
Accepted 24th July, 2018
Published online 28th August, 2018

Key Words:

Knee Osteoarthritis, Articular cartilage volume, Magnetic Resonance Imaging

ABSTRACT

Introduction: Knee Osteoarthritis (KOA) is a persistent debilitating disease characterized by loss of articular cartilage and proliferative reaction of subchondral bone. This study aimed to determine and compare articular cartilage volume (ACV) in healthy and osteoarthritis knee. Further, the ACV was correlated with age, body mass index and clinico- radiological severity in knee osteoarthritis subjects.

Method: Sixty KOA subjects (cases) and thirty-one age-sex matched individuals with healthy knees (controls) were recruited. MRI of the selected knees was performed to measure ACV. The self-reported pain, stiffness and physical function were assessed using the Western Ontario and McMaster Universities index. Visual Analogue Scale score for knee pain and radiological severity by Kellgren- Lawrence grade were also recorded in cases.

Results: The mean ACV of controls in our population was almost similar to other populations. The ACV in controls was significantly higher than cases. With age, a statistically significant inverse correlation of ACV was found both in controls and cases. Height, weight and body mass index were independent of ACV in controls; however, in cases, a significant positive correlation of ACV was observed with height only. A significant inverse correlation of ACV was found with Western Ontario and McMaster Universities scores in cases.

Conclusion: This study makes an attempt to set a cut-off value of ACV between a normal healthy knee and an osteoarthritis knee to identify at risk or "pre-arthritis" status in individuals. ACV is also being proposed to be an ideal tool for prediction and early diagnosis of knee osteoarthritis.

INTRODUCTION

Knee Osteoarthritis (KOA) is a quotidian ailment of synovial joints with a complex pathogeny. It is marked by structural and functional changes in the joint, the core component being the progressive erosion and subsequent loss of articular cartilage. This results in a persistent debilitating disease associated with severe pain and disability and becomes a frequent cause for joint replacement. It has a tremendous medical, psychological and socioeconomic impact on our aging society. Epidemiological studies define OA on the basis of radiological findings[1] and knee pain on most of the days.[2] Conventional radiography (X- ray) has been the keystone of KOA to identify the pathological processes and has been widely used due to its cost effectiveness and easy availability. Although the X-Ray technique has been upgraded with computer- assisted methods and new imaging protocols, it has shown to have less sensitivity.[3] Assessment of joint space narrowing (JSN) is an indirect measure of cartilage damage as radiographs allow the articular cartilage to be evaluated only in one anatomic plane although cartilage loss occurs all around the joint.[4,5] Moreover, X- ray imaging is unable to identify the short term changes and is not sensitive for mild to moderate changes[4] in the cartilage as the disease progresses. Finally, quantitative assessment of damage is not possible with X-rays.

A three- dimensional magnetic resonance imaging (MRI) technique has revolutionized the field of clinical research in OA[6] as it overcomes the limitations of conventional

Corresponding author:* **Rajeshwar Nath Srivastava
Dept. of Orthopedic Surgery, King George's Medical University, Lucknow, U.P., India,

radiography with advantage of soft tissue evaluation such as cartilage. It additionally permits to obtain quantitative measures of relevant tissue structures and their changes over time. Quantitative measures of cartilage morphology (i.e., thickness and volume) represent potentially powerful surrogate endpoints in OA. These can be used to identify risk factors of structural disease progression and can facilitate the clinical efficacy testing of disease modifying drugs in OA. However, the use of MRI in routine management of OA is still controversial because of the costs involved and optimized examination protocols not being available[7].

As said earlier, the course of the disease is progressive resulting into inexorable loss of cartilage and subsequent joint damage. Therefore, measurement of articular cartilage volume (ACV) to monitor disease progression and to develop therapeutic approaches that provide symptomatic relief, may exhibit the potential to slow down or stop the structural changes involved in OA[9]. Despite the growing concern for the use of ACV as an outcome measure in OA researches, it is still unclear what components of cartilage will be most useful as markers of structure in the tri-compartmental knee joint. A limitation of measuring cartilage morphology is that cartilage loss rarely involves the entire joint surface homogeneously, but starts and progresses only at specific locations and this rate of cartilage loss is highly variable between individuals.[8]

Different researchers have evaluated different regions of ACV in their studies. To identify the most useful and efficient component of knee cartilage, Cicuttini *et al* (2001) compared the changes that occur in femoral and tibial ACV both in normal and osteoarthritis knees. A strong correlation between femoral and tibial cartilage was observed in both medial and lateral tibio- femoral joints in normal and OA subjects using coronal sequences. They thereby suggested that either femoral or tibial cartilage could be used for measurement as both the components yielded similar information.[10]

This study was designed to compare ACV in healthy adult knee with osteoarthritis knee in our population and to correlate ACV with age, body mass index (BMI) and clinico- radiological severity in KOA subjects.

METHODS

The present study was a cross-sectional study with level of evidence III. The study was conducted in the Department of Orthopaedic Surgery in collaboration with Dept. of Radio-diagnosis, King George's Medical University (KGMU). The study protocol was approved by Institutional Ethics Committee of KGMU. This study consisted of subjects of either sex with KOA as cases and age- sex matched individuals with healthy knee as controls. Informed consent was obtained from all the participants. KOA subjects were recruited from the outpatient clinic of the Department of Orthopaedic Surgery, KGMU using American College of Rheumatology criteria for KOA diagnosis. It comprised knee pain persisting for more than six months with Kellgren0 & Lawrence (KL) grades- 2, 3 or 4 on radiograph (X-ray). The exclusion criteria were evidence of secondary OA such as gout, infection, trauma, congenital & developmental disorders affecting knee joint and contraindications to MRI (metal implant, claustrophobia, pregnancy). Inclusion criteria for recruitment of controls was age- sex matched individuals without knee pain attending Orthopaedic outpatient clinic for other reasons (not related to knee joints) or some systemic disease involving any joint in the body.

A total of ninety-one subjects were recruited, sixty as cases and thirty-one as controls. During the initial phase, 87 subjects with knee pain underwent radiological examinations for confirming KOA. 21 subjects with evidence of secondary OA and 6 subjects who did not undergo MRI were excluded. Finally, 60 primary KOA were available to participate in the study. 31 controls were enrolled after ensuring that they had no problems related to knees.

In cases with bilateral KOA and controls, left knee was chosen for analysis and termed as reference knee. Radiological imaging (weight bearing antero-posterior view) of the reference knee was performed. In unilateral KOA cases, the knee with clinical symptoms was similarly imaged. Radiographs were evaluated for severity by KL grading system. Each subject had MRI of the same knee for which X- ray was performed. Knees were imaged on 1.5 Tesla whole body magnetic resonance unit using a commercial transmit- receive extremity coil. The parameters used for imaging by 3D FSPGR sequence were as follows: flip angle- 90^{o}, repetition time- 40ms, echo time- 82.7ms, field of view- 16x16cm, in- plane resolution- 352x256 pixels, one acquisition time- 2min30sec, partition thickness- 4mm, band width- 31.2kHz. ACV was measured manually by means of image processing on an independent workstation using semi-automated machine GE Signa Excite Advance 4.5. The self-reported pain, stiffness and physical function were assessed using subscales of the Western Ontario and McMaster Universities (WOMAC) index along with total WOMAC scores in subjects with KOA. Visual Analogue Scale (VAS) score was also used for pain assessment in cases.

***Statistical Analysis*:** Data were represented as mean+standard deviation (SD) with 95% confidence interval (CI) at 5% level of significance. Two independent groups were compared by Student's t- test and categorical variables were compared using Chi- square test. Pearson's correlation coefficient was used to correlate the variables. One- way Analysis of Variance (ANOVA) was used for comparison between more than two groups. The analyses were performed using statistical software package SPSS version 16.0. The power of study was 80%.

RESULTS

The general characteristics of cases and controls are given in Table-1.

Table 1 General characteristics of controls and cases

Characteristics	Control (n=31)	Case (n=60)	95% CI	p- value
Age (years)	45+8.54	50.38+12.08	-9.67 to 0.00	0.0502[a]
Gender				
Male	20 (64.51%)	26 (43.33%)	-0.38 to 1.17	0.090[b]
Female	11 (35.48%)	34 (56.66%)		
Height (meter)	1.61+0.09	1.58+0.10	-0.01 to 0.07	0.164[a]
Weight (kg)	67.74+11.96	68.31+13.63	-6.32 to 5.18	0.845[a]
BMI	25.62+3.26	27.51+4.75	-4.07 to 0.29	0.089[a]

BMI- Body Mass Index.

ACV in Healthy Adult Knee and its Comparison with Osteoarthritis knee

Mean ACV in healthy adult knee was 7.46+0.63cm^3 in comparison to osteoarthritis knee where it was 4.41+1.49cm^3.

This diminution was statistically significant (p<0.001). ACV was significantly higher in males with healthy knees (p=0.024) whereas in osteoarthritis knee this gender difference was insignificant (p= 0.312) (Table-2).

Table 2 Genderwise distribution of ACV in controls and cases

Gender	Controls			Cases		
	ACV (cm^3) (Mean+SD)	95% CI	p-value[1]	ACV (cm^3) (Mean+SD)	95% CI	p-value[1]
Male	7.650+0.52	0.074 to 0.982	0.024*	4.639+1.67	-0.381 to 1.172	0.312
Female	7.122+0.69			4.243+1.33		

ACV- Articular Cartilage Volume.
Values are represented as mean+ SD (standard deviation). Means were compared using Student's unpaired t- test; * p<0.05 considered as statistically significant

With age, a statistically significant inverse correlation of ACV was found in healthy knees (p= 0.033) and also in osteoarthritis knees (p= 0.0006). Height, weight and BMI were independent of ACV in healthy adult knee. In KOA subjects, a significant positive correlation of ACV was observed with height (p=0.010) whereas no correlation was observed with weight and BMI (Table-3).

Table 3 Correlation of ACV with variables in controls and cases

ACV	Variables	Pearson's correlation coefficient (r)	p- value
Controls 7.46+0.63 cm^3	Age	-0.382	0.033*
	Height	0.102	0.708
	Weight	0.100	0.591
	BMI	0.226	0.311
Cases 4.41+1.49 cm^3	Age	-0.426	0.0006*
	Height	0.356	0.010*
	Weight	-0.069	0.609
	BMI	-0.101	0.442
	WOMAC	-0.267	0.039*
	VAS	-0.223	0.091

ACV- Articular Cartilage Volume, BMI- Body Mass Index, WOMAC- Western Ontario and McMaster Universities Arthritis Index, VAS- Visual Analogue Scale.
Pearson's correlation coefficient (r) was used to correlate ACV with variables, * p<0.05 considered as statistically significant

ACV in osteoarthritis knee (KOA subjects)

A significant inverse correlation of ACV was observed with WOMAC scores (p= 0.039).The statistical difference in ACV between the two categories of WOMAC scores (<32 and >32) was significant (p=0.023). The association of ACV, thereafter, was also studied with sub- scales of WOMAC index (pain, stiffness and physical function) and significant difference was found with all the sub- scales (p<0.001) (Table-4).

Table 4 Association of ACV with WOMAC sub- scales in cases

Cartilage Volume (cm^3)	WOMAC sub-scales	95% CI	p-value[1]
4.415+1.49	Pain (7.616+2.23 cm^3)	-3.887 to -2.514	<0.001*
	Physical function (24.516+8.94 cm^3)	-22.418 to -17.783	<0.001*
	Stiffness (1.716+1.35 cm^3)	2.183 to 3.213	<0.001*

ACV- Articular Cartilage Volume, WOMAC- Western Ontario and McMaster Universities Arthritis Index.
Values are represented as mean+ SD (standard deviation). Means were compared using Student's unpaired t- test; * p<0.05 considered as statistically significant

A post hoc analysis was performed for inner and in between comparison of ACV in different radiological grades of severity. The results of these multiple comparisons showed statistically significant differences among ACV of various grades (p<0.001). When radiological severity was analyzed genderwise, a significant difference was found (p=0.01) in ACV in early KOA (KL grade-2) with females dominating males. This difference became statistically insignificant (p= 0.363 and p= 0.241 respectively) in later stages of the disease (KL grades 3 and 4). Notwithstanding with ACV, when total WOMAC scores and sub- scale scores were analyzed and compared genderwise, females were found to be more severely affected than males experiencing more pain (p=0.001) and functional difficulties (p<0.001) (Table-5).

Table 5 Genderwise association of WOMAC subscales and total WOMAC scores in cases

WOMAC sub- scales	Male (Mean+SD)	Female (Mean+SD)	p-value[1]
Pain	6.58+2.12	8.41+2.00	0.001*
Physical function	19.46+9.02	28.38+6.77	<0.001*
Stiffness	1.46+1.39	1.91+1.3	0.204
Total WOMAC	27.54+11.10	38.71+8.77	<0.001*

ACV- Articular Cartilage Volume, WOMAC- Western Ontario and McMaster Universities Arthritis Index.
Values are represented as mean+ SD (standard deviation). Means were compared using Student's unpaired t- test; * p<0.05 considered as statistically significant

DISCUSSION

Knee Osteoarthritis (KOA) is one of the commonest diseases of the elderly and the most common reason for knee replacement surgery contributing to a substantial socio- economic burden. Deterioration of articular cartilage is regarded as the initial defect in KOA and its early recognition would be the most ideal tool for an early diagnosis and timely intervention to prevent progression. Cartilage being radiolucent, its assessment on X-rays is only possible by JSN, which is an indirect measure of cartilage damage. MRI is a viable technique of ACV determination and is reproducible with coefficient of variations of about 2%. They are less observer dependent and more objective, hence, overcome all the limitations of radiological grading.

One of the objectives of this study was to report ACV of healthy individuals in our population and its comparison with ACV reported in other populations. For this, we evaluated mean tibio-femoral ACV of healthy adults and found it to be 7.46+0.63cm^3. Our findings were almost similar to that of the Australian population[11] where it was 7.08+0.54cm^3 and 7.74+0.84 cm^3. A study conducted on patellofemoral cartilage volume in Japanese healthy population reported the mean ACV as 7.6+1.6cm^3.[12] The upper and lower values of ACV in all these populations were 7.426cm^3 and 6.50cm^3 respectively.

Although the body structure of the three mentioned populations are quite varying and in fact at extremes, the mean ACV is nearly the same. One possible explanation for this could be that ACV is independent of BMI and bone size as reported by Cicuttini *et al*.[13] Similarly, in our study ACV was independent of BMI (r= 0.226, p= 0.311). Genderwise assessment of ACV by Cicuttini *et al*[13] showed that males had more cartilage volume than females and the same was found in our study;

significantly larger ACV in males as compared to females (p=0.024, 95% CI: 0.074 to 0.982). If ACV is independent of BMI and bone size then why the same is not found on gender differentiation. The role of hormonal factors may be the possible explanation. Both estrogen and testosterone seem to influence ACV. Loss of articular cartilage due to decrease in estrogen levels in postmenopausal women[14] and 10% more ACV in women on hormone replacement therapy[15]has already been reported. Similarly, testosterone levels both in females[16] and males[17] seem to influence cartilage loss.

As of now, there is no evidence that at which particular ACV level, the damage characteristic of KOA begins. Since we found that ACV in healthy adult knees was almost similar in all the studied populations, we propose to set a cut off point at the mean of lower values as the normal ACV (6.50 cm^3). This may make it easy to label people whose ACV lies above this value as *"normal"* and those below as *"cartilage deficient"*. Similarly by defining the cutoffs for diagnosing KOA, we also propose a new category of "borderline KOA" or *"pre-KOA"* based on normal ACV levels and levels underneath of those at risk of developing KOA. Such a terminology of *"pre-arthritis"* with timely intervention may not go on to develop into full-fledged KOA. A consensus on this enthusiastic statement will only ensue once this is validated and accepted by other researchers.

The other objective of this study was to correlate ACV with age, BMI and clinical (WOMAC index and VAS) severity in KOA subjects. Age is a well-known risk factor for knee OA and this relationship has been the most striking feature in various epidemiological studies.[18,19] A significant negative correlation of ACV was established with age in the present study in controls (p= 0.033) and cases (p<0.001). Supportive evidences of such negative correlation are also available in post-menopausal women, a mixed gender group of 92 subjects with and without OA and in a study of men only.[15]

BMI exhibited a non- significant negative correlation (r= -0.101, p= 0.442) with ACV. Although BMI is a known risk factor for KOA, little is known about its relationship to ACV.[20-22] BMI has not been consistently demonstrated as a significant determinant of ACV when assessed by MRI, despite it being associated with JSN on radiographs.[23] Our finding also reaffirms that ACV is independent of BMI.

Amongst the clinical scoring systems for KOA, we have earlier reported that WOMAC has advantage over others (like VAS and Lequesne Index) in being more precise and was most significantly associated with disease severity.[24] With respect to ACV, in a study by Hunter *et al*[4] cartilage volume in tibio-femoral compartment did not show significant association with pain and a significant association existed between changes in patella volume and WOMAC pain score. On this basis it was suggested that patella cartilage volume should be included as another individual feature in KOA MRI assessment. This may not be always required as when we investigated our findings with the three sub- sets of WOMAC (pain, stiffness and physical function), it was found that each correlated significantly with tibio- femoral cartilage volume and so did the total WOMAC scores (p<0.0001). Pain was assessed on 0-10 point VAS scale in addition to WOMAC. A negative correlation of ACV was observed with VAS score. Unlike WOMAC, the correlation was not significant (p=0.091).

As the cartilage is devoid of nociceptive nerve fibers, the emergence of pain in early stage is presently unidentified. It is being argued that cartilage loss exposes the subchondral bone which is rich in neurovascular supply.[4] Any movement producing friction on the opposing subchondral surfaces may produce pain and other symptoms and these worsen on altered biomechanical loading in KOA.[25] It is also likely that other joint structures, such as bone, synovial tissue, capsule, ligaments, and menisci, may be the source of pain in patients with OA especially in later stage.

ACV may have a say on the debate on which radiological feature correlates best with pain and other clinical features of KOA. We have earlier reported that discordance between radiological and clinical KOA found by many researchers was because they had studied only four radiological features of KL grades, whereas there are many other radiological aberrations occurring in KOA.[25]Amongst all radiological features studied, the diminution of ACV was most significantly associated with each and every individual clinical feature. Not only this, it also correlates best with every KL grade, reiterating our assumption that ACV is the true determinant of KOA at every stage of the disease. Measurement of ACV is simple, anatomical and reproducible. It is being proposed as a telltale sign of predicting and diagnosing KOA and its severity. A strong correlation of ACV with knee pain once again makes it one the best tools for early diagnosis of KOA.

In our study a significant difference was observed between male and female subjects with KOA regarding pain (p=0.001) and physical function (<0.0001) with females experiencing more pain and disability. It has been observed that symptomatic KOA is more commonly reported in women as compared to men.[26]Felson *et al*[27] reported the prevalence of KOA to be 4-10 times more in females. Although not to this extent, we also found women were more commonly affected in our study in the ratio of 56.66% (females) vs 43.33% (males). Likewise, Wluka *et al*[22] and Cicuttini *et al*[28] mentioned the prevalence of knee OA in females vs males in their population as 57%vs 43% and 54% vs 46% respectively. Sex differences in pain perception and pronounced prevalence of chronic pain in women are the result of numerous factors. Gender bias in rearing and upbringing of boys and girls in developing countries, exposure to different risks and distinguished occupational and social roles performed by either sex support the evidence that women are more sensitive to painful stimuli than men[29] and regard pain as serious and attend to pain sooner.[30]

If KOA is much more common in females, then why is this gender preponderance not seen in total knee replacement (TKR), where the prevalence in both is almost the same? While exploring the answer of this, we came across an incidental finding in our study. Mean ACV was significantly higher in males in healthy knee (controls) and in early KOA (KL grade 2 subjects); whereas in moderate and late osteoarthritis knee (KL grade 3 & 4), this gender difference in ACV became insignificant, suggesting rapid cartilage loss in males in comparison to females, once KOA sets in. This rapid deterioration could be related to occupation or lifestyle of the male gender. Therefore, our observation is that in females KOA occurs at an early age and progresses slowly whereas in males it occurs late and progresses rapidly accounting for less

gender disparity when TKR is considered an endpoint (KL grade 4)

It has been suggested that TKR is underutilized in both the genders and this underutilization is three times greater in women.[31] Is it because of the economics in the male dominant society, sacrificing nature of the weaker gender or some pathophysiology hidden underneath? Without any evidence, we suggest it may be due to low pain threshold in females because of which they reach hospitals earlier and get treated delaying the progression of the disease.

CONCLUSION

This study concluded that ACV is significantly lower in osteoarthritis knee as compared to healthy adult knee. Mean ACV was significantly higher in males in healthy knee and in early KOA (KL grade 2 subjects), whereas in moderate and late osteoarthritis knee (KL grade 3 & 4), this gender difference in ACV became insignificant suggesting rapid cartilage loss in males in comparison to females, once KOA sets in. This finding is being reported for the first time. This study also found that KOA in females occurs at an early age and progresses slowly whereas in males occurs late and progresses rapidly accounting for less gender disparity when TKR is considered an endpoint. Although an indirect indicator of knee pain, ACV may become one of the tools for early diagnosis of KOA. Near similar ACV (7.47+0.90cm^3) in healthy knee of any population could probably be a landmark in establishing normal or cut-off ACV values in human beings.

Acknowledgement- The authors are thankful to Dr. S. S. Sarkar, Consultant Radiologist, Lucknow, Uttar Pradesh for his guidance in sequencing and interpretation of MR images.

Conflict of interest- The authors declare that they have no conflict of interest.

References

1. Kellgren JH, Lawrence JS. Osteoarthritis and disk degeneration in an urban population. *Ann Rheum Dis* 1958; 17:388-97.
2. Altman R, Asch E, Bloch D, *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; 29:1039-49.
3. Guermazi A, Burstein D, Conaghan P, *et al*. Imaging in osteoarthritis. *Rheum Dis Clin North Am* 2008;34:645–87.
4. Hunter DJ, March L, Sambrook PN. The association of cartilage volume with knee pain. *Osteoarthritis Cartilage* 2003; 11:725–729.
5. Raynauld JP, Martel-Pelletier J, Berthiaume MJ,*et al*. Long term evaluation of disease progression through the quantitative magnetic resonance imaging of symptomatic knee osteoarthritis patients: correlation with clinical symptoms and radiographic changes. *Arthritis ResTher* 2006;8:R21.
6. Augat P, Eckstein F. Quantitative imaging of musculoskeletal tissue. *Annu Rev Biomed Eng* 2008; 10:369-390.
7. Maataouia A, Gurunga J, Ackermann H, *et al*. Facilitating cartilage volume measurement using MRI. *Eur J Radiol* https://doi:10.1016/j.ejrad.2009.05.005.
8. Wolfe F, Lane NE. The long term outcome of osteoarthritis: rates and predictors of joint space narrowing in symptomatic patients with knee osteoarthritis. *J Rheumatol* 2002;29(1):139-46.
9. Beary JF III. Joint structure modification in osteoarthritis: development of SMOAD drugs. *CurrRheumatol Rep* 2001;3:506-512.
10. Cicuttini FM, Wluka AE, Stuckey SL. Tibial and femoral cartilage changes in knee osteoarthritis. *Ann Rheum Dis* 2001;60:977–980
11. Wluka AE, Wolfe R, Davis SR, *et al*. Tibial cartilage volume change in healthy postmenopausal women: a longitudinal study. *Ann Rheum Dis* 2004;63:444-449.
12. Nishimura K, Tanabe T, Kimura M, *et al*. Measurement of articular cartilage volumes in the normal knee by magnetic resonance imaging: can cartilage volumes be estimated from physical characteristics? *J Orthop Sci* 2005;10(3):246-52.
13. Cicuttini F, Forbes A, Morris K, *et al*. Gender differences in knee cartilage volume as measured by magnetic resonance imaging. *Osteoarthritis Cartilage*1999;7:265-71.
14. Sowers MF, Hochberg M, Crabbe JP, *et al*. Association of bone mineral density and sex hormone levels with osteoarthritis of the hand and knee in premenopausal women. *Am J Epidemiol* 1996;143:38-47.
15. Wluka AE, Davis SR, Bailey M, *et al*. Users of oestrogen replacement therapy have more knee cartilage than non-users. *Ann Rheum Dis* 2001;60:332-3.
16. Ben-Hur H, Thole HH, Mashiah A, *et al*. Estrogen, progesterone and testosterone receptors in human fetal cartilaginous tissue: immune histochemical studies. *Calcif Tissue Int* 1997;60:520-6.
17. Cicuttini FM., Wluka A, Bailey M, *et al*. Factors affecting knee cartilage volume in healthy men. *Rheumatology* 2003;42:258-2624.
18. Felson DT, Brandt KD, Doherty M, Lohmander LS. Epidemiology of osteoarthritis. In: Osteoarthritis, 2nd edn. Oxford University Press, Oxford, UK, 2003;pp 9–16.
19. Davis MA, Ettinger WH, Neuhaus JM, Mallon KP. Knee osteoarthritis and physical functioning: evidence from the NHANES I epidemiologic follow-up study. *J Rheumatol* 1991;18(4):591–598.
20. Felson DT, Anderson JJ, Naimark A, *et al*. Obesity and knee osteoarthritis: The Framingham Study. *Ann Intern Med*1988; 109:18–24.
21. Davis MA, Ettinger WH, Neuhaus JM, Hauck WW. Sex differences in osteoarthritis of the knee: The role of obesity. *Am J Epidemiol* 1988; 127:1019–30.
22. HartDJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population. The Chingford Study. *J Rheumatol* 1993;20:331–5.

23. Ding C, Cicuttini F, Scott F, *et al*. *Obesity Res* 2005c; 13:350-61.
24. Avasthi S, Sanghi D, Singh A, *et al*. Significance of clinical parameters and role of clinical scoring systems in predicting severity of primary osteoarthritis knee. *The Internet Journal of Orthopedic Surgery* 2008;13(1).
25. Sanghi D, Avasthi S, Mishra A, *et al*. Is radiology a determinant of pain, stiffness and functional disability in knee osteoarthritis? A cross- sectional study. *J Orthop Sci*https://doi 10.1007/s00776-011-0147-y
26. Cubukcu D, Sarsan A, Alkan H. Relationships between Pain, Function and Radiographic Findings in Osteoarthritis of the Knee: A Cross-Sectional Study. *Arthritis*http://dx.doi.org/10.1155/2012/984060
27. Felson DT, Naimark A, Anderson J, *et al*. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum*1987; 30:914-8.
28. Cicuttini F, Hankin J, Jones G, Wluka A. Comparison of conventional standing knee radiographs and magnetic resonance imaging in assessing progression of tibiofemoral joint osteoarthritis. *Osteoarthritis Cartilage* 2005; 13:722-727.
29. Berkley KJ. Sex differences in pain. *Behav Brain Sci*1997; 20:371-380.
30. Dao T TT. Gender Differences in Pain. *J OrofacPain* 2000; 14:169-184.
31. Hawker GA, Wright JG, Coyte PC, *et al*. Differences between men and women in the rate of use of hip and knee arthroplasty. *N Engl J Med* 2000;342:1016-22.

How to cite this article:

Sudeepti Ratan Srivastava *et al.,*2018, Is articular Cartilage volume a Potential tool in Defining Normal, pre-arthritis and Osteoarthritis knee? A cross - Sectional study. *Int J Recent Sci Res.* 9(8), pp.28549-28554.
DOI: http://dx.doi.org/10.24327/ijrsr.2018.0908.2479

****