

CLINICAL SCIENCE

The association of anthropometric measures and osteoarthritis knee in non-obese subjects: a cross sectional study

Divya Sanghi,¹ Rajeshwar Nath Srivastava,¹ Ajai Singh,¹ Reema Kumari,² Rachna Mishra,³ Abhishek Mishra¹

¹Department of Orthopaedic Surgery, Erstwhile KG Medical College, CSM Medical University, Lucknow, India. ²Department of Social and Preventive Medicine, Erstwhile KG Medical College, CSM Medical University, Lucknow, India. ³Department of Nutrition, IT College; Lucknow, India.

OBJECTIVE: Body mass index (BMI) and knee osteoarthritis have a strong association, but other anthropometric measures lack such associations. To date, no study has evaluated non-obese knee osteoarthritis to negate the systemic and metabolic effects of obesity. This study examines the validity of the contention that BMI and other anthropometric measures have a significant relationship with knee osteoarthritis.

METHODS: In total, 180 subjects with a diagnosis of knee osteoarthritis were recruited and classified according to Kellgren-Lawrence (KL) grades. Body mass index, mid-upper arm circumference, waist-hip ratio and triceps-skinfold thickness were recorded by standard procedures. Osteoarthritis outcome scores (WOMAC) were evaluated.

RESULTS: (1) In both genders, the BMI was significantly higher for KL grade 4 than for grade 2; triceps-skinfold thickness was positively correlated with the joint space width of the tibial medial compartment. (2) In males, triceps-skinfold thickness significantly increased as the KL grades moved from 2 to 4; the significantly higher BMI found in varus aligned knees was positively correlated with WOMAC scores. (3) In females, the waist-hip ratio was significantly higher for KL grade 4 than for grade 2; a significant correlation was found between BMI and WOMAC scores. The waist-hip ratio was significantly associated with varus aligned knees and it positively correlated with WOMAC scores and with the joint space width of the tibial medial compartment. The mid-upper arm circumference demonstrated no correlation with knee osteoarthritis.

CONCLUSION: This study validates the contention that BMI and other anthropometric measures have a significant association with knee osteoarthritis. Contrary to common belief, the triceps-skinfold thickness (peripheral fat) in males and the waist-hip ratio (central fat) in females were more strongly associated with knee osteoarthritis than BMI.

KEYWORDS: Osteoarthritis; Knee; Obesity; Anthropometric measures; BMI.

Sanghi D, Srivastava RN, Singh A, Kumari R, Mishra R, Mishra A. The association of anthropometric measures and osteoarthritis knee in non-obese subjects: a cross sectional study. Clinics. 2011;66(2):275-279.

Received for publication on September 17, 2010; First review completed on October 20, 2010; Accepted for publication on November 8, 2010

E-mail: divyasanghi_14@rediffmail.com

Tel.: 91-522-2257515

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease of multifactorial origin.¹ Estimated population prevalence varies from 4-30% depending on the age, sex and disease definition.² Risk factors include obesity, previous knee injury, selected physical activities, the presence of hand OA (Heberden's nodes) and the family history of the disease.^{3,4} Of all the risk factors known, obesity is most strongly associated with development and progression⁵⁻⁹ of KOA. Two major theories have been proposed to explain this association: biomechanical

and systemic/metabolic mechanisms.¹⁰ The biomechanical theory suggests that obesity increases axial loading (local effect) with consequent degeneration of articular cartilage, whereas metabolic theory proposes that some metabolic factors adversely affect cartilage and obesity acts indirectly to increase the risk of KOA.¹¹

Anthropometry is the study of the measurement of the human body in terms of the dimension of bone, muscle and adipose tissue. Literature shows that muscle mass or muscle strength is protective for the development of Osteoarthritis.¹²⁻¹⁴ Because BMI is a measure of both fat and lean mass, the relative contribution of adipose tissue and muscle mass, and their contribution to muscle strength cannot be disaggregated.¹⁵ Anthropometric measurements such as BMI, skin fold thickness and mid upper arm circumferences will allow cross-sectional analysis of the relationship between obesity and risk of disease.

The purpose of the present study was to examine the validity of the contention that BMI and other anthropometric measures have a significant relationship with the severity of Osteoarthritis knee in non-obese subjects.

METHODOLOGY

Study sample

Six hundred sixty seven individuals attending Orthopaedic OPD with knee pain underwent a physician lead clinical and radiological examination to verify their eligibility for inclusion as per guidelines of American College of Rheumatology (ACR)¹⁶. Individuals with any evidence of secondary OA, inflammatory arthritis and those with neurological conditions were excluded. Also excluded were obese individuals having BMI >30. 180 cases of primary Osteoarthritis knee (KOA) could be enrolled for the study. Ethical approval for the study was granted by the institutional ethics committee. The voluntary written consent was taken from all the subjects for participation in the study. Demographic data for all subjects were obtained by self report.

Outcome variable

Osteoarthritis knee. Weight bearing antero-posterior and recumbent lateral knee radiographs were taken by standard procedures. All the radiographs were evaluated by at least two readers with a third consensus reader for the presence of KOA defined by the Kellgren-Lawrence (KL) grade.¹⁷ OA was defined as the presence of at least one knee with a grade 2 or higher. Joint space width of tibial medial compartment (TMC) and tibial lateral compartment (TLC) were measured¹⁸ in mm and Tibio-femoral alignment was measured¹⁹ as either >180 or <180 depending on valgus or varus malalignment.

Clinical scores. Clinical assessment was done by - Visual analogue scale (VAS) for knee pain and Western Ontario McMaster Universities Osteoarthritis (WOMAC)²⁰ Index for knee pain and knee related disability.

Exposure variable

Anthropometric measures. Measurements were taken at the time of diagnosis. The patients were weighed with a calibrated balance beam scale to the nearest 0.1 kg in possible minimum clothing and standing height was measured with Stadiometer in centimeters (cms). Mid upper arm circumference, Triceps skin fold thickness and Waist hip ratio was measured by standard procedure at standard location.²¹ Physical activity scores were calculated by Framingham physical activity index.²⁸

Statistical analysis

The descriptive statistics of the subjects were calculated (mean \pm SD). The One way analysis of variance (ANOVA) was used to estimate the significant difference between/ among various anthropometric measures and severity of Osteoarthritis knee in terms of KL grades and LSD pair-wise test was applied in case of any variable found to be significant in ANOVA. Difference of mean values of anthropometric measurements was analyzed by non-paired t-test between dichotomous variables of KL grade, whereas Pearson product correlation was used for continuous variable of KL grades and anthropometric measures. Data

was analyzed using Statistical Package of Social Sciences (SPSS) version 11.5.

RESULTS

The age of the subjects varied from 40 to 72 years (mean 54.11 years). Out of total number of 180 subjects, 57 were males and 123 females. 99 (55%) were overweight with male female ratio being 28:71 and 81 (45%) were normal in a ratio of 29:52. 9 males and 13 females were in KL grade 2, 32 males and 71 females in KL grade 3 and 16 males and 39 females in KL grade 4.

Age was not associated with severity of KOA. Physical activity scores were significantly associated, as KL grade 2 had higher score (33.91 ± 4.20 , 32.88 ± 3.50) in comparison to KL grade 3 (33.40 ± 4.71 , 31.56 ± 2.80) and 4 (31.31 ± 4.90 , 30.59 ± 3.10) in males and females respectively (Table 1).

In both the genders BMI was not significantly different amongst 3 KL grades studied together, however pair-wise comparison showed that difference was significant between KL grade 2 and 4 in males and in females ($p=0.048$, $p=0.046$). TSFT, in males was significantly higher in KL grade 4 (13.95 ± 1.36) in comparison to KL grade 3 (12.83 ± 1.90) and KL grade 2 (12.22 ± 2.11). Such an association of TSFT was not found in females. WHR, in females was marginally significant amongst all 3 grades, however pairwise comparison showed a significant higher WHR in KL grade 4 (0.86 ± 0.10) in comparison to KL grade 2 (0.82 ± 0.09) (Table 1). No significant difference was found for MUAC in either gender.

Anthropometric measures under study were further correlated with individual radiological features of KL grade. Similarly, clinical evaluation of disease severity by VAS and WOMAC index were correlated with anthropometric measures (Table 2).

No significant difference was found between anthropometric measures and osteophytes in either compartment in both the gender. In tibio-femoral mal-alignment (varus), there was significant higher mean of BMI (25.95 ± 2.45 , 24.53 ± 2.72 , $p=0.04$) in males and higher WHR (0.84 ± 0.09 , 0.81 ± 0.09 , $p=0.04$) in females. Joint space width (JSW) of TLC was not correlated with any of the anthropometric measures in either gender. However, JSW of TMC in males was significantly negatively correlated with two anthropometric measures- BMI ($r=-0.32$, $p=0.01$) and TSFT ($r=-0.37$, $p=0.01$). In females, significant decrease of TMC was defined by WHR ($r=-0.21$, $p=0.02$) and TSFT ($r=-0.17$, $p=0.04$). VAS was not significantly correlated with any of the anthropometric measures in either group. WOMAC scores were positively correlated with BMI both in males ($r=0.23$, $p=0.04$) and in females ($r=0.24$, $p=0.01$). Additionally it was also defined by WHR ($r=0.25$, $p=0.01$) in females (Table 2).

DISCUSSION

The purpose of the present study was to examine the validity of the contention that BMI and other anthropometric measurements have a significant relationship with osteoarthritis knee in non-obese subjects. Non obese subjects were taken for study to negate the systemic and metabolic effects of obesity.

Several studies have shown that body weight rather than body fat distribution is independently associated with KOA^{22,23} Davis MA suggests that body fat distribution also

Table 1 - KL grades and anthropometry measures between males and females.

Variables	KL grades				p-value†	Total (n=123)	Grade 2 (n=13)	Grade 3 (n=71)	Grade 4 (n=39)	p-value†	Females
	Total (n=57)	Grade 2 (n=9)	Grade 3 (n=32)	Grade 4 (n=16)							
Age	57.89±8.75	56.00±9.67	58.22±8.51	58.31±9.14	0.78	52.35±8.74	52.46±10.28	51.68±8.81	53.54±8.15	0.57	
Physical activity scores	32.87±4.60	33.91±4.20	33.40±4.71	31.31±4.90	0.02	31.67±3.13	32.88±3.50	31.56±2.80	30.59±3.10	0.046	
Height (cm)	163.66±5.87	161.27±7.01	164.02±5.77	164.31±5.40	0.40	154.70±4.15	153.54±4.35	155.09±4.30	154.36±3.79	0.39	
Weight (kg)	67.69±8.30	62.64±5.96	67.66±8.56	70.59±7.88	0.07	60.44±7.07	58.30±6.56	60.04±7.46	61.87±6.33	0.22	
BMI	25.23±2.67	24.07±1.92	25.14±2.91	26.26±2.51	0.13	25.23±2.55	24.70±2.19	24.93±2.66	25.95±2.33	0.10	
MUAC	33.01±3.44	33.06±3.04	33.08±3.59	32.84±3.53	0.98	32.19±3.36	31.42±3.44	32.84±2.87	33.37±3.04	0.32	
WHR	0.97±0.12	0.96±0.14	0.97±0.06	0.98±0.10	0.93	0.83±0.10	0.82±0.09	0.86±0.09	0.86±0.10	0.05	
TSFT	12.80±2.01	12.22±2.11	12.83±1.90	13.95±1.36	0.02	17.61±3.34	17.44±3.50	17.81±3.38	17.92±2.25	0.80	

Values given in Mean ± SD; † By ANOVA test

Table 2 - Individual radiological features of KOA and anthropometric measurements between males and females.

Radiological features	Male				Height	Weight	BMI	MUAC	WHR	TSFT	Female
	Height	Weight	BMI	MUAC							
Osteophyte lateral present	164.33±4.16	69.67±6.80	25.75±1.65	34.17±3.75	1.01±0.27	13.33±1.32	154.81±4.19	60.28±7.27	25.57±2.54	32.58±2.87	0.81±0.09
Osteophyte lateral absent	163.46±5.91	67.57±8.49	25.24±2.73	32.99±3.46	0.96±0.11	12.81±2.05	153.16±3.18	60.0±6.32	25.12±2.64	32.19±3.40	0.84±0.10
Osteophyte medial p value	0.80	0.68	0.74	0.57	0.52	0.66	0.35	0.93	0.69	0.78	0.55
Osteophyte medial present	164.33±4.16	69.67±6.80	25.76±1.65	34.17±3.75	1.01±0.27	13.33±1.32	153.17±3.19	60.00±6.32	25.67±2.54	32.58±2.87	0.81±0.10
Osteophyte medial absent	163.46±5.19	67.57±8.50	25.42±2.73	32.99±3.46	0.97±0.11	12.81±2.05	154.80±4.19	60.28±7.28	25.12±2.61	32.19±3.40	0.84±0.10
Tibio-femoral – alignment p value	0.80	0.68	0.75	0.65	0.80	0.62	0.35	0.93	0.69	0.78	0.55
Tibio-femoral – alignment Varus	164.26±5.82	70.09±6.71	25.95±2.45	33.33±3.57	0.99±0.12	13.15±1.94	154.78±3.62	61.01±7.48	25.49±2.57	32.60±3.40	0.84±0.09
Valgus p value	163.46±5.91	65.37±9.10	24.53±2.72	32.69±3.34	0.94±0.10	12.46±2.04	154.64±4.47	59.31±6.76	24.75±2.70	31.54±3.22	0.81±0.09
Lateral*	0.45	0.31	0.04	0.48	0.20	0.20	0.89	0.21	0.14	0.09	0.04
Medial*	0.09, 0.50	-0.03, 0.83	-0.02, 0.89	0.14, 0.29	0.12, 0.38	-0.15, 0.26	-0.05, 0.58	-0.01, 0.94	0.02, 0.85	-0.05, 0.62	-0.13, 0.13
Joint space*	0.02, 0.89	-0.26, 0.05	-0.32, 0.01	-0.07, 0.60	0.01, 0.95	-0.37, 0.01	-0.01, 0.93	-0.15, 0.11	-0.16, 0.07	-0.12, 0.20	-0.21, 0.02
Clinical Scores											
VAS*	0.08, 0.53	0.04, 0.79	0.11, 0.41	0.13, 0.34	0.29, 0.26	0.11, 0.42	0.01, 0.99	0.08, 0.37	0.09, 0.30	0.37, 0.69	0.12, 0.90
WOMAC*	-0.05, 0.71	0.08, 0.53	0.23, 0.04	0.21, 0.11	0.15, 0.26	0.32, 0.05	-0.12, 0.20	0.14, 0.11	0.24, 0.01	0.20, 0.05	0.25, 0.01

Values given in Mean ± SD; t-test; *r, p-value, Pearson correlation

play a significant role in KOA.²² Lauren M Abbathe²³ found that body composition measurements from DXA and fat distribution by MRI were not strongly associated with KOA and concluded that such measurements offer no advantage over the simpler measures of BMI or weight in assessment of KOA. After extensive literature search we focused our study on the anthropometric measures which were simple to document and have evidence for their role in obesity – BMI is a heuristic measure of body weight based on a person's weight and height. Though it does not actually measure the percentage of body fat, it is used to estimate a healthy body weight based on a person's height. MUAC is a major determinant of arm muscle and subcutaneous fat, TSFT determine peripheral fat distribution and WHR central fat distribution.

On analysis of the effects of anthropometric measures on KOA, in all the subjects taken together, only BMI was found to have a significant effect. However when data was bifurcated according to genders, BMI and TSFT were associated with disease in males and the association was stronger for TSFT. In females BMI and WHR were significant and WHR was more strongly associated.

On analysis of individual radiological features, Joint space width of TMC in relation to BMI and TSFT was found negatively correlated as in previous studies¹⁸, but when data was divided gender wise, in males decrease of TMC was defined by BMI and TSFT, however in females decrease of TMC was defined by WHR and TSFT.

David T Felson⁸ postulated that the risk of progression of KOA increased significantly with an increase in weight. However this progression was not present in all, but limited to knees from limbs that were moderately mal-aligned. In neutrally aligned limbs on one end of the spectrum and severely malaligned limbs on the other had no effect on risk of KOA progression. Leena Sharma²⁴ et al found a relationship between BMI and radiographic KOA with varus deformity but not in those with valgus knee. BMI correlated with the severity of varus mal-alignment. The authors were unable to account whether the association precedes or follows the onset of disease. This dilemma has persisted for too long and has been reported by others also. In this study, when all subjects taken together were divided according to tibio-femoral alignment (varus/valgus), as expected we found BMI was associated with varus. However, when data was bifurcated according to genders, the association of BMI and varus was found only in males and in females it was associated with WHR.

Osteophytosis is the first and the cardinal feature in diagnosis of KOA, but we found that inspite of high prevalence BMI and all other anthropometric measures were inconsistently associated with osteophyte formation. These results provide direct evidence that increasing weight (BMI) may not induce osteophyte formation.

In relation to association of knee pain and anthropometric measures BMI was positively correlated to WOMAC index. Our findings were consistent with those of Jinks C²⁵, Rogers MW²⁶ and Marks R.²⁷ On gender based analysis, WHR also emerged a significant factor in females.

This study has a number of limitations. Measurement error may influence results, however, a positive interrelation of anthropometric measures and high reproducibility of radiological measures suggest that this is unlikely. Secondly this study was cross sectional in design and cannot comment on causal directions, thus longitudinal data will

be required to confirm these results. Finally there may be confounding factors for which our analysis has been unable to account. Such influences might include for example the use of medication, occupation, physical activities and other health problems like cardio vascular disease. This is a true representation of KOA of idiopathic variety and finding a significant association is meaningful and a justifiable evidence.

CONCLUSION

This study validates the contention that BMI and other anthropometric measures have a significant association with KOA. Contrary to common belief, peripheral fat in males and central fat in females were more strongly associated with KOA in comparison to heuristic body weight. Subcutaneous fat has no correlation with KOA. Clinicians and therapists may augment and formulate a need based physical therapy accordingly.

ACKNOWLEDGEMENTS

Sources of funding: The study was supported financially by Council of Science and Technology, UP, Govt. of Uttar Pradesh, Lucknow, India

REFERENCES

1. Felson DT, Lawrence RC, Dieppe PA, Helmick CG, Jordan JM, Kington RS, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med.* 2000;133:635-46.
2. Lanyon P, O'Reilly S, Jones A, Doherty M. Radiographic assessment of symptomatic knee osteoarthritis in the community: definitions and normal joint space. *Ann Rheum Dis.* 1998;57:595-601, doi: 10.1136/ard.57.10.595.
3. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman B, Aliabadi P, et al. Risk factors for incident radiographic knee osteoarthritis in the elderly: the Framingham Study. *Arthritis Rheum.* 1997;40:728-33, doi: 10.1002/art.1780400420.
4. Lau EC, Copper C, Lam D, Chan VNH, Tsang KK, Sham A. Factors associated with osteoarthritis of the hip and knee in Hong Kong Chinese: obesity, joint injury, and occupational activities. *American Journal of Epidemiology* 2000;152:855-62, doi: 10.1093/aje/152.9.855.
5. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and Knee Osteoarthritis The Framingham Study. *Annals of internal medicine.* 1988;109:18-24.
6. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Body mass index in young men and the risk of subsequent knee and hip osteoarthritis *Am J Med.* 1999;107:542-8.
7. Cooper C, Snow S, McAlindon TE, Kellingray S, Stuart B, Coggon D, et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. *Arthritis and Rheumatism.* 2000;43:5:995-1000, doi: 10.1002/1529-0131(200005)43:5<995::AID-ANR6>3.0.CO;2-1.
8. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis in dependent on alignment. *Arthritis and Rheumatism.* 2004;50:3904-9, doi: 10.1002/art.20726.
9. Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: An epidemiological study in the general population with 10 years follow-up. *BMC Musculoskeletal Disorders.* 2008;9:132, doi: 10.1186/1471-2474-9-132.
10. Van Saase JL, Vandebroucke JP, van Romunde LK, Valkenburg HA. Osteoarthritis and obesity in the general population: a relationship calling for an explanation. *J Rheumatol.* 1988;15:1152-8.
11. Hartz AJ, Fischer ME, Bril G, Kelber S, Rupley D Jr, Oken B, et al. The association of obesity with joint pain and osteoarthritis in the HANES data. *J Chronic Dis.* 1986;39:311-9, doi: 10.1016/0021-9681(86)90053-6.
12. Toda Y, Segal N, Toda T, Kato A, Toda F. A decline in lower extremity lean body mass per body weight is characteristic of women with early phase osteoarthritis of the knee. *J Rheumatol.* 2000;27:2449-54.
13. Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, et al. Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med.* 1997;127:97-104.
14. Slemenda C, Heilman DK, Brandt KD, Katz BP, Mazzuca SA, Braunstein EM, et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? *Arthritis Rheum.* 1998;41:1951-9, doi: 10.1002/1529-0131(199811)41:11<1951::AID-ART9>3.0.CO;2-9.
15. Sowers MF, Yosef M, Jamadar D, Jacobson J, Karvonen-Gutierrez C, Jaffe M. BMI vs. body composition and radiographically-defined

- osteoarthritis of the knee in women: a 4-year follow-up study. *Osteoarthritis Cartilage*. 2008;16:367-72, doi: 10.1016/j.joca.2007.07.016.
16. Altamn R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. Criteria for classification and reporting of Osteoarthritis knee. *Arthritis Rheum*. 1986;29:1039-49, doi: 10.1002/art.1780290816.
 17. Kellgren JH, Lawrence JS. Atlas of Standard Radiographs of Arthritis. II. Philadelphia, PA: F.A. Davis. The epidemiology of chronic rheumatism 1963.
 18. Cimen OB, Incel NA, Yapici Y, Apaydin D, Erdogan C. Obesity Related Measurements and Joint Space Width in Patients with Knee Osteoarthritis. *Upsala J Med Sci*. 2004;109:159-64, doi: 10.3109/2000-1967-105.
 19. Colebatch AN, Hart DJ, Zhai G, Williams FM, Spector TD, Arden NK. Effective measurement of knee alignment using AP knee radiographs. *The Knee*. 2009;16:42-5, doi: 10.1016/j.knee.2008.07.007.
 20. Bellamy N, WOMAC Osteoarthritis Index. A Users Guide. London, ON: University of western Ontario 1996.
 21. Timby BK. Fundamental's nursing skills and concepts. (adapted from Jelliffe, DB. 1986. The assessment of nutritional status of community. World health Organization monograph No.53. Geneva World Health organization.
 22. Davis MA, Neuhaus JM, Ettinger WH, Mueller WH. Body fat distribution and osteoarthritis. *Am J Epidemiol*. 1990;132:701-7.
 23. Abbate LM, Stevens J, Schwartz TA, Renner JB, Helmick CG, Jordan JM. Anthropometric Measures, Body Composition, Body Fat Distribution, and Knee Osteoarthritis in Women. *Obesity*. 2006;14:1274-81, doi: 10.1038/oby.2006.145.
 24. Sharma L, Lou C, Cahue S, Dunlop DD. The mechanism of the effect of obesity in knee Osteoarthritis. *Arthritis & Rheumatism*. 2000;43:568-75, doi: 10.1002/1529-0131(200003)43:3<568::AID-ANR13>3.0.CO;2-E.
 25. Jinks C, Jordan K, Croft P. Disabling knee pain- another consequence of obesity: results from a prospective cohort study. *BMC public health*. 2006;6:258, doi: 10.1186/1471-2458-6-258.
 26. Rogers MW, Wilder JV. The association of BMI and knee pain among persons with radiographic knee osteoarthritis: A cross-sectional study. *BMC Musculoskeletal Disorders*. 2008;9:163, doi: 10.1186/1471-2474-9-163.
 27. Marks R. Obesity profiles with knee osteoarthritis: correlation with pain, disability, disease progression. *Obesity*. 2007;15:1867-74, doi: 10.1038/oby.2007.221.
 28. Mc Alindon TE, Felson DT, Zhang Y, Hannan MT, Aliabadi P, Weissman B, et al. Relation of dietary intake and serum levels of vitamins D to progression of osteoarthritis of the knee among participant in framingham study. *Ann Intern med*. 1996;125:353-9.