THE CORRELATION OF JOINT SPACE WIDTH WITH SYNOVIAL FLUID CARTILAGE OLIGOMERIC MATRIX PROTEIN LEVEL IN KNEE OSTEOARTHRITIS PATIENTS

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ABSTRACT

Background Osteoarthritis (OA) was a degenerative joint disease associated with joint cartilage damage, where the most commonly affected joints are vertebrae, pelvis, knee, and ankle. Radiology examination was the most common method used to monitor the progression of OA but can not show changes in knee OA except in the advanced phase of the disease. Conventional radiology can estimate the thickness of the cartilage through measurement joint space width (JSW) . One alternative method that can detect changes in the joint at an early stage of the disease is a measurement of the synthesis and degradation markers of the tissue. Cartilage oligomeric matrix protein (COMP) was one of the cartilage destruction markers of non-aggrecan and non-collagen groups, found in cartilage and other tissues. **Aims** This study aimed to assess the correlation between JSW and synovial fluid COMP levels in knee OA subjects. **Methods** The study was a descriptive-analytic method with a cross-sectional design in 69 knee OA subjects. It was conducted in the rheumatology outpatient clinic of Wahidin Sudirohusodo Hospital Makassar and its networks on March-June 2015. **Results** The correlation analysis between JSW and synovial fluid COMP levels showed a significant negative correlation ($p< 0.001$) and its correlation is included in the strong correlation category ($r>-0.887$). **Conclusion** There was a correlation between JSW and synovial fluid COMP levels, where synovial fluid COMP levels were higher in knee OA subjects with more severe JSW narrowing.

Keywords : cartilage oligomeric matrix protein, joint space width, osteoarthritis

ABSTRAK

Latar belakang Osteoartritis (OA) merupakan penyakit sendi degeneratif yang berkaitan dengan kerusakan rawan sendi, dimana sendi yang paling sering terkena OA adalah vertebra, panggul, lutut dan pergelangan kaki. Radiologi konvensional dapat memperkirakan ketebalan rawan sendi melalui pengukuran lebar celah sendi atau *joint space width* (JSW). Salah satu metode alternatif yang dapat mendeteksi perubahan sendi pada stadium dini penyakit adalah dengan pemeriksaan petanda sintesis dan degradasi jaringan. Cartilage oligomeric matrix protein (COMP) merupakan salah satu petanda destruksi rawan sendi dari golongan non-agrekan dan non-kolagen, terdapat pada rawan sendi dan jaringan lainnya. **Tujuan** Penelitian ini bertujuan untuk menilai hubungan antara lebar celah sendi dengan kadar COMP cairan sendi pada subyek OA lutut. **Metode** Penelitian ini meupakan deskriptif analitik dengan pendekatan *cross sectional* pada 69 subyek OA lutut yang berobat jalan di poliklinik reumatologi RS Wahidin Sudirohusodo Makassar dan RS Jejaring Pendidikan, Maret-Juni 2015. **Hasil** Dari analisis korelasi antara lebar celah sendi (JSW) dan kadar COMP cairan sendi menunjukkan korelasi negatif signifikan ($p< 0.001$) dan termasuk kategori korelasi kuat ($r>-0.887$). **Kesimpulan** Penelitian ini menunjukkan adanya hubungan antara lebar celah sendi (JSW) dengan kadar COMP cairan sendi, dimana semakin sempit JSW, semakin tinggi pula kadar COMP cairan sendi.

Kata kunci : cartilage oligomeric matrix protein, joint space width, osteoartritis

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease associated with cartilage damage, where the joints most commonly affected by OA are the vertebrae, hips, knees, and ankles.[1] OA is the most common joint disease in the world and one of the most frequent diagnoses in clinical practice.[2] The incidence and prevalence of OA increase with age. In developing countries, in the population aged 65 years and older, it is estimated that OA will increase up to 71% by 2020.[3] In Indonesia up until now, there has been no comprehensive report on the prevalence of OA. The radiological prevalence of knee OA is quite high, reaching 15.5% in

men and 12.7% in women.[1] Outpatients' data from the Rheumatology Polyclinic at Dr. Wahidin Sudirohusodo Hospital Makassar in 2011, showed 55.7% of patients suffering from OA, of which 43.5% is men and 56.5% is women.[4] OA is a major cause of disability.[5]

The pathomechanism of OA includes a variety of etiologies that play a role in the balance of synthesis and destruction of articular cartilage.[6] Older age and obesity are the most important risk factors for OA.[7] Older age is associated with changes in the capacity of the joint tissue to adapt and the influence of biomechanics that promotes the development of OA.[8] As for the obesity risk factors, OA can occur due to trauma towards the joint cartilage tissue that is affected by body weight and inflammatory factors.[9, 10] OA manifestations are the result of morphological, biochemical, molecular, and biomechanical changes of chondrocyte and matrix cells that result in softening, fibrillation, ulceration, and thinning of joint cartilage, sclerosis, subchondral bone eburnation, osteophytes and subchondral cysts. OA is clinically characterized by pain in the joint(s), motion pain, limitation of movement, crepitus, occasionally effusion, and various degrees of inflammation that could be found without systemic symptoms.[11]

The diagnosis of OA was established based on the criteria of the American College of Rheumatology (ACR) 1986, which consisted of clinical symptoms, radiological features, and/or laboratory tests on synovial fluid to rule out infectious causes.[7,12] Conventional radiological examination is the most frequent, simple and economical method of joint imaging in monitoring the progression of OA. Radiographs clearly show bone abnormalities such as osteophytes, subchondral sclerosis, subchondral cysts that accompany OA but can only estimate the thickness of articular cartilage by measuring the distance between bones or *joint space width* (JSW).[13] Radiological examination would not be able to show changes in the knee due to OA until the advanced phase of the disease.[14] The JSW measurement is more sensitive to disability effect caused by knee OA compared to the Kellgren Lawrence classification system.[15]

To prevent disability due to OA, it is necessary to have an early diagnosis and an accurate assessment of the severity of joint changes.[5] Therefore, we need a sensitive diagnostic tool that can diagnose OA in the early phase before abnormalities are visible on radiographs.[16] One alternative method to detect joint changes at an early stage of the disease is by examining markers of tissue synthesis and degradation.[17] Cartilage oligomeric matrix protein (COMP) is one of the markers of cartilage destruction from non-aggressive and non-collagenous groups that can be found in joint cartilage and other tissues, such as ligaments, meniscus, synovial membranes, and tendons. This protein can be identified in the form of a complete molecule or fragments from joint cartilage, synovial fluid, and serum from OA patients.[16, 17] This COMP protein is an important marker in early OA studies.[18]

There have been many studies regarding the relationship between COMP levels both in serum and in synovial fluid. A study by Vilim et al, 2002, has reported an association between COMP in the serum and radiographic progression of knee OA patients.[19] Then a study by Darweesh H et al, in 2010, also reported that COMP levels both in serum and in the synovial fluid were associated with the destruction of joint cartilage.[20]

Based on the description above, the researchers wanted to find out whether there is a relationship between the width of the joint space and the COMP level from the synovial fluid as a sign of joint cartilage destruction.

MATERIALS AND METHODS

Place and Time

This research was conducted at the Rheumatology Polyclinic, Dr. Wahidin Sudirohusodo Hospital, Makassar and other teaching hospitals within our network, from March-June 2015.

Research Design and Variables

This research was descriptive analytic with cross sectional approach. The research variables consisted of related variables, namely *joint space width* (JSW), independent variables, namely levels of cartillage oligomeric matrix protein (COMP) in synovial fluid, and confounding variables were age and obesity.

Population and Sample

The population of our study were all patients at the Rheumatology Polyclinic, Dr. Wahidin Sudirohusodo Hospital who visited the medical examination at Dr. Wahidin Sudirohusodo Hospital Makassar and other teaching hospitals. The subject was knee OA patients who met the inclusion criteria, until the required number of samples was reached. The total sample in this study was 69 patients with knee OA.

Methods of Data Collection

All knee OA patients at the polyclinic were given an explanation of their disease and if they agreed to participate in the study they would be given and signed an informed consent form. All knee OA patients who are willing to participate in the study will be subjected to a physical examination, knee joint radiographs, measurement of JSW, synovial fluid aspiration, COMP level examination, and synovial fluid analysis.

The procedure for collecting synovial fluid samples was starting from the preparation of materials and tools (10 cc syringe, needle 22G x 1 1/2) for arthrocentesis, then marking the insertion area (lower midpoint of the patella), disinfection of the insertion area with povidone iodine and 70% alcohol, could use local anesthesia (ethyl chloride spray/procaine injection), aspiration of knee synovial fluid, synovial fluid obtained is collected in a sterile glass tube, then closed and stored at room temperature □ 1 hour. The synovial fluid was then centrifuged for 10 minutes then the supernatant was taken and stored in a sterile tube and stored at minus 80 oC.

Quantitative synovial fluid COMP levels was measured using COMP enzyme immunoassay or ELISA kit (DRG Diagnostics, Marburg, Germany). Absorbance of 450 nm was measured using an ELISA plate microtiter reader (Tecan, Salzburg, Austria). The standard curve was made by plotting the absorbance graph of each reference standard based on the concentration (ng/ml). COMP levels in each joint fluid sample were determined by relating the absorbance value to the standard curve value above, and multiplied by 5 according to the COMP solubility above (1:5).

Measuring the joint space width (JSW); radiologic examination of the knee was performed in the AP position (weight bearing position), where the patient was standing on both feet, with both legs fully extended. Subsequently, X-rays of the AP genu were interpreted by radiologists and rheumatologists. The width of the joint space was expressed in millimeters. A vertical line was drawn from midfemoral of the medial condyle and the lateral condyle to the tibial plane, then the value was taken at the narrowest point. The joint space width category was divided into 4 degrees, namely: grade 0 (joint space width 5 mm), grade 1 (joint space width 3.5 - 4.9 mm), grade 2 (joint space width 2 - 3.4 mm), and grade 3 (joint space width < 2 mm).

Data Analysis Technique

We analyse the data using SPSS version 22 computer statistics program. Analysis of the relationship between joint space width/JSW and synovial fluid COMP levels was using the statistical *Spearman's Correlation, Kruskal-Wallis and Mann-Whitney tests*. Statistical test results are considered significant if the p value <0.05. The data is presented in the form of a narrative and clarified by displaying tables and figures.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the ethical committees of Faculty of Medicine, Hasanuddin University, Indonesia (ref: no.0298/H4.8.4.5.31/PP36-KOMETIK/2015) for study sites in Makassar districts and all participants provided written informed consent.

RESULTS

Sixty nine patients with knee joint OA were included in the study consisted of 40 female patients (58.0%) and 29 male patients (42.0%). There were 29 patients within the age category of 50-59 years (42.0%), 25 patients within the age category of 60-69 years (36.2%), 11 people within the age category of 70-79 years (15.9%), and 4 patients with age more than 80 years (5.8%).

Based on BMI, the number of patients in the BMI category of underweight was only 1 patient (1.4%), the normal BMI category and the overweight BMI category were 11 patients (15.9%), the obese I BMI category was 27 patients (39.1%), and the of obesity II BMI category as many as 19 patients (27.5%). From the JSW measurements, it was found that the most JSW categories were grade 3 (50.7%), while JSW categories of grades 2, 1 and 0 were 26.1%, 14.5%, and 8.7%, respectively. The characteristics of the sample are shown in table 1.

Table 1. Characteristics of Research Subject

	Frequency (n)	%
Gender		
Male	29	42
Female	40	58
Age (year)		
50-59	29	42
60-69	25	36,2
70-79	11	15,9
≥ 80	4	5,8
BMI (Kg/m^2)		
Less	1	1,4
Normal	11	15,9
More	11	15,9
Obese 1	27	39,1
Obese 2	19	27,5
JSW (mm)		
Degree 3	35	50,7
Degree 2	18	26,1
Degree 1	10	14,5
Degree 0	6	8,7
Total	69	100

The patients were at least 50 years old and the oldest was 86 years old, the average age was 61.9±9.1 years. As for the BMI, the lowest value was 16.7 kg/m2 and the highest value was 42.9 kg/m2, the mean BMI was 27.2 ± 4.4 kg/m2. Measurement of synovial fluid COMP levels obtaining the lowest value of 4714.2 ng/ml and the highest value of 19003.9 ng/ml, the

average COMP level was 14265.0±3331.7 ng/ml. From the JSW measurement, the lowest value was 1.0 mm and the highest value was 8.9 mm, the mean of JSW was 2.6±1.7 mm, (Table 2).

Table 2. Statistical Description of Research Variabel

Variabel	n	Minimum	Maximum	Average	SD
Age (year)	69	50	86	61,9	9,1
BMI (Kg/m^2)	69	16,7	42,9	27,2	4.4
COMP (ng/ml)	69	471,2	19003,9	14265,0	3331.7
JSW (mm)	69	1,0	8,9	2.6	1,7

COMP= Cartilage Oligomeric Matrix Protein, SD= Standar Deviation,
JSW= Joint Space Width, Kruskal-Wallis Test

The results of the correlation analysis between JSW and synovial fluid COMP levels showed a significant negative correlation ($p < 0.001$). The narrower the joint space width, the higher the COMP level in the synovial fluid, and *vice versa* the wider the joint space, the lower the synovial fluid COMP level was obtained. The close correlation between JSW and synovial fluid COMP levels is included in the strong correlation category (R>-0.887), shown in Figure 1. From this correlation test, it is possible to estimate the COMP level of synovial fluid based on the JSW by using the formula $y = (1{,}88.10^4 – 1{,}72.10^3)\ x$, for example at 2 mm JSW, the estimated COMP level of synovial fluid is 15360 ng/ml.

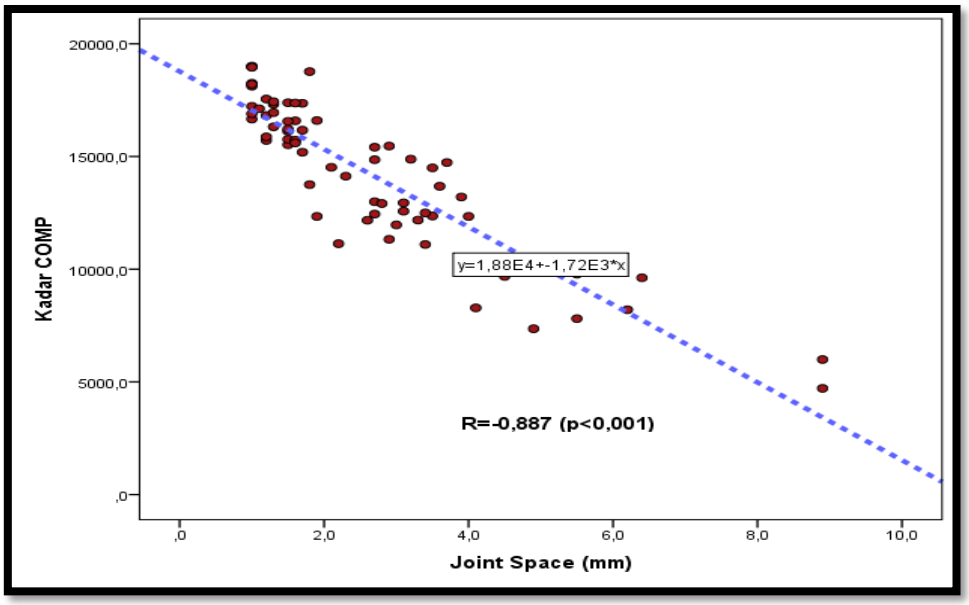

Figure 1. Correlation between joint space width (JSW) and synovial fluid COMP levels

The comparison of the mean synovial fluid COMP level by JSW category is shown in Table 3. The table shows that there is a significant difference between the mean COMP levels of synovial fluid according to the JSW category, $p < 0.001$. The higher the degree of JSW narrowing, the higher the mean synovial fluid COMP level obtained. The results of this comparison can be seen more clearly in Figure 2.

Table 3. Comparison between JSW Categories and Average Synovial Fluid COMP Level

JSW Category	n	COMP Average (ng/ml)	SD	P
Degree 3	35	16574,2	1405,5	
Degree 2	18	13082,4	1443,4	<0,001
Degree 1	10	11629,8	2602,2	
Degree 0	6	7685,6	2005,3	

COMP= Cartilage Oligomeric Matrix Protein, SD= Standar Deviation, JSW= Joint Space Width, Kruskal-Willis Test

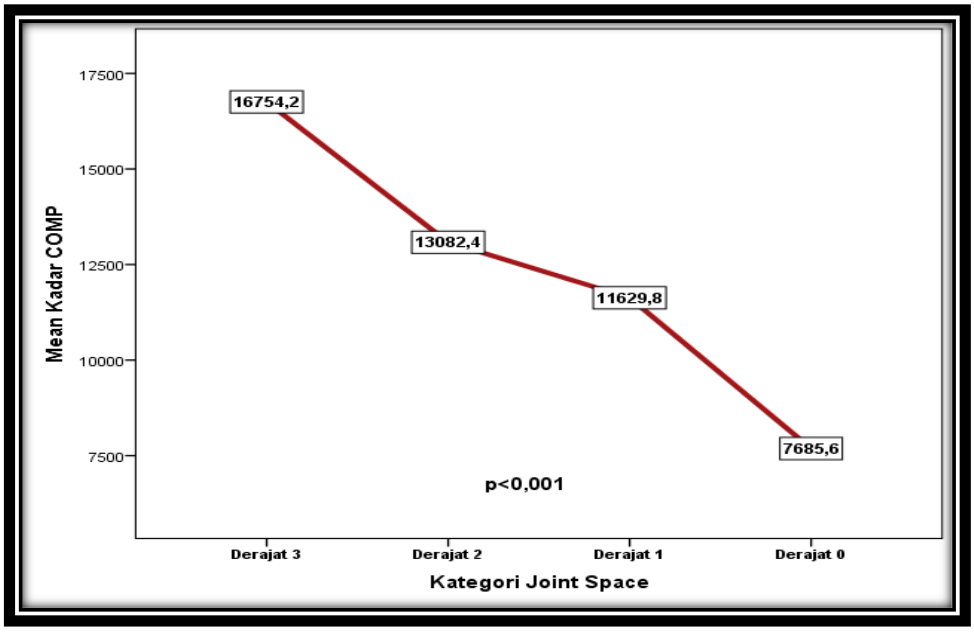

Figure 2. Correlation between Joint Space Width (JSW) Category and Average Synovial Fluid COMP Level

The results of the role analysis of confounding factors (age and obesity determined by BMI) on the mean JSW and mean COMP levels of synovial fluid are shown in tables (table not shown), *Kruskal-Wallis test*. The tables shows that there is no significant difference in mean JSW and mean Synovial fluid COMP levels according to age category (p> 0.05) and also, there is no significant difference between the mean JSW and the mean Synovial fluid COMP levels according to BMI category (p> 0.05). So the confounding factors did not have a significant role on JSW or on COMP levels of synovial fluid.

DISCUSSION

This study involved 69 OA patients with majority were females (40 patients, 58%), and 29 males (42%). Soeroso et al. mentioned that women are more often affected by knee OA, while men are more often affected by hip, wrist and neck OA. In addition to gender, age also affects the incidence of OA. At the age under 45 years, the frequency of OA in both sexes is the same, but at the age above 50 years it is more common in women.[21]

The increasing incidence of OA in postmenopausal women has led to many studies regarding the relationship between hormonal factors and OA, but the results are contradictory. Several studies have shown that hormone replacement therapy is associated with a lower radiographic prevalence of knee and hip OA, but not showing any preventive effect on joint symptoms.[8] The opposite result was reported by Srikanth et al. in 2005, in a systematic review

involving 17 studies, that there was no clear association between sex hormones and hand, knee or hip OA in women, although a single analysis of these studies was not possible due to the heterogeneity of the studies.[22]

In this study, 29 knee OA patients were within the age category of 50-59 years (42.0 %), 25 patients were within the age category of 60-69 years (36.2 %), 11 patients were within the age category of 70-79 years (15 ,9 %), and 4 patients were more than 80 years old (5.8 %). The association between age and risk of OA is multifactorial and may be due to multiple individual factors involving oxidative damage, thinning of joint cartilage, muscle weakness, and proprioceptive reduction. The basic cellular mechanisms that maintain tissue homeostasis also decline with age, leading to an inadequate response to stress or joint damage and resulting in destruction and loss of joint tissue.[22]

Based on the BMI values in this study, most patients were obese 1 and obese 2 (39.1% and 27.5%, respectively) Obesity is known to be a risk factor for OA. The risk of knee OA increases progressively with increasing BMI. The prospective study in 2007 by Reijman M et al., showing that weight gain plays a role in the development of radiological features of knee OA.[9, 23]

Data from the National Health and Nutrition Examination Survey (NHANES I) period of 1971-1975, show that obese women are 4 times more likely to develop knee OA compared to non-obese women and obese men are 4.8 times higher compared to non-obese men.[10] In a meta-analysis, it was found that being overweight or obese was 2.96 times higher in the risk of knee OA compared with normal weight. The effect of obesity on OA may be through mechanical effects and systemic effects (metabolic or inflammatory). New research shows that total body fat as measured by DXA is accompanied by a decrease in the thickness of the cartilage. Adipose tissue is also known to be metabolically active, secreting adipokines such as adiponectin, leptin, and resistin, but their role in the incidence of OA remains unclear.[2]

In this study, it was also found that the most JSW category groups were grade 3 (50.7%), compared to grade 2, 1 and 0 (26.1%, 14.5%, and 8.7% respectively). These data may suggest that OA patients presenting to the clinic are mostly accompanied with severe joint space narrowing. The value of JSW correlates with cartilage thickness, and previous studies have evaluated and reported that JSW loss is considered a substitute for cartilage loss.[24] This result is different from the percentage of OA according to the JSW category obtained in the study of Gossec L et al. in 2008, where the degrees 3, degrees 2, and degrees 0-1, was obtained 17%, 31%, and 52% respectively.

New markers continue to be a concern in musculoskeletal diseases so that they can be diagnosed early and can determine the prognostic process of cartilage destruction. One of the markers of cartilage destruction is COMP, which increases in serum and synovial fluid in patients with RA and OA.[20] COMP was a non-collagenous extracellular matrix (ECM) glycoprotein belonging to the thrombospondin family (TSP), also known as TSP-5. Primarily, COMP was found in the human skeletal system (joint cartilage, meniscus, ligaments, tendons, and synovium). COMP was also found in the heart, vitreous of the eye, and vascular smooth muscle cells. Its fragments were also present in body fluids. Serum and joint fluid COMP levels in the normal population were approximately 5.93 ± 1.95 g/mL and 33 ± 10 g/mL, respectively.[25]

Several studies have shown increased COMP levels in serum and joint fluid. Among them research Lohmander LS et al. 1994. The study found an increasing release of aggreacan and COMP fragments into synovial fluid and serum after joint injury and in early stage osteoarthritis. It was also found that the average level of COMP fragments in synovial fluid in a group of 6 athletes with healthy knees was 47 ug/ml (reference value 10-109 ug/ml). The study also found that serum COMP levels were positively correlated with synovial fluid COMP levels (r=0.52).[26] The COMP levels were found in high concentrations in synovial fluid and

can reach up to 250 ug/ml.[27] And then research by Daweesh H et al. in 2010, found that synovial fluid COMP levels were higher than serum COMP levels in the two groups, where the mean synovial fluid COMP levels in RA and OA were 14.3±5.19 ug/ml and 9.26±2.42 ug/ml respectively (conversion: 14300±5190 ng/ml and 9260±2420 ng/ml), $p< 0.01$.[20] Our results were consistent with those obtained in that study, where the minimum synovial fluid COMP levels was 4714.2 ng/ml and the maximum value was 19003.9 ng/ml (mean 14265.0 ± 3331.7 ng/ml) in knee OA patients (Table 2).

The recent study by Li XY et al. 2022, who conducted a study on 59 knee OA patients admitted to the hospital in 2018-2020. From this study, it was found that the levels of osteopontin (OPN) and COMP of joint fluid increased in knee OA patients and they increase with the increase of Kellgren Lawrence grade. It was also found that OPN and COMP of joint fluid were independent risk factors that affected the degree of K-L in knee OA patients, and they have high AUC, sensitivity and specificity in predicting of K-L4 knee OA, and can be used to evaluate the progression of knee OA disease.[28]

High levels of synovial fluid COMP that are examined in the early stages may be a result of the degradation of joint cartilage.[20] High levels of synovial fluid COMP have been reported in various joint diseases that examined with polyclonal antisera, including COMP derived from diseased synovial fibroblasts, not only COMP released by degrading joint cartilage. This explains why high levels of COMP in synovial fluid or serum was found in patients with RA and early stages of OA where radiological changes have not been seen. Specific antibodies to COMP fibroblasts are required, which are different from antibodies to COMP from articular cartilage degradation, so that it can be distinguished between articular cartilage degeneration and disease activity in the synovium.[26]

The increase in synovial fluid COMP in this study supports the theory that COMP is released in response to the breakdown of the cartilage matrix. This may result from destabilization of the extracellular matrix which increases protease activity against COMP in the affected joint. It can also be due to increased synthesis of new COMP as repair efforts by chondrocytes or synovium. There are also new data that in arthritis cases, synovial cell COMP production is triggered by proinflammatory cytokines as transforming growth factor β.[20]

In this study, it was found that the lowest JSW value was 1.0 mm and the highest value was 8.9 mm, with an average joint space width (JSW) was 2.6±1.7 mm, which is shown in Table 2. The results are almost the same as the study by Piperno M et al. in 1998, who found a mean JSW value was 3.5±1.5 mm on the medial side of knee OA by conventional AP examination.[13, 29] The rate of joint space narrowing among cohort studies of knee OA varies. This may be due to different causes, for example due to changes in the characteristics and clinical status of the patient over time, different knee position during serial radiographic examinations, and other technical factors.[30] Although the JSW examination only assesses the thickness of the cartilage, it is considered as a new method to assess the progression of knee OA.[15]

The relationship between JSW and synovial fluid COMP levels was assessed by the *Spearman* correlation test (r>-0.887; p<0.001), which means that there is a significant negative correlation that is very strongly related between JSW and synovial fluid COMP levels. So the narrower the JSW, the higher the synovial fluid COMP levels, or vice versa, the wider the JSW, the lower the synovial fluid COMP levels was obtained, as shown in Figures 1 and Table 2.

Elevated COMP levels of synovial fluid in radiographically progressive OA patients have been reported in previous studies. Darweesh H et al. in 2010, found that in the OA group, COMP levels in serum and synovial fluid were significantly negatively correlated with cartilage thickness ($p< 0.001$) and concluded that COMP in synovial fluid was considered as a marker of disease activity and cartilage destruction in OA patients.[20] Research by El Arman

MM et al. in 2010, also found that elevated COMP and aggrecan, in serum and synovial fluid, were positively correlated with radiological joint damage.[31]

In Table 3 and Figure 2 it can be seen that the mean synovial fluid COMP levels was highest in the 3rd degree JSW category, value $p<0.001$. Similar results were found by Azab NI et al. in 2012, where there was an increase in serum COMP and YKL-40 in OA patients, compared to control group ($p< 0.001$). Both were highly significantly positively correlated with the severity of radiological abnormalities according to KL, but the opposite correlated with JSW ($p< 0.001$). The similar result was also found by Garnero et al. 2001, Vilim et al. 2002 and Jung et al. in 2006, who found that hyaluronic acid and COMP levels were higher in more severe OA cases than in milder OA cases, using knee ultrasound examination.[32]

The most recently by Li XY et al., 2022. it was found that the levels of osteopontin (OPN) and COMP of joint fluid increased in knee OA patients and they increase with the increase of Kellgren Lawrence grade. [28]

Several previous studies have also proven an association between elevated serum COMP levels and OA progression which is monitored by radiological examination. However, all of these studies used serum COMP levels (not synovial fluid COMP levels), for example the study by Sharif et al. 1995, demonstrated a significantly elevated serum COMP level in patients with clinical knee OA and demonstrated joint space narrowing or requiring knee surgery within 5 years of *follow-up*. Study by Conrozier et al. in 1998, also saw a correlation between the severity of hip OA and COMP level in serum and found a significant correlation between COMP level in serum and JSW, $r= 0.40$, $p= 0.001$.[33, 34]

The study by Hao HQ et al., 2019, found that serum COMP and urinary CTX-II can distinguish between knee or hip OA patients and control subjects. Serum COMP is effective in predicting the progression of OA.[35] Hao, HQ, 2019 And study by Hussain et al., 2022, found that both sCOMP and serum C-terminal cross-linked telopeptide of type I collagen (sCTX-I) are very effective in distinguishing between healthy adults and those affected by knee OA. But sCOMP failed to distinguish between K–L grades.[36]

The mean JSW and COMP levels of synovial fluid were not significantly different by age group ($p> 0.05$) and to BMI group ($p> 0.05$). (data not shown) These results are inline with study from Lanyon P et al. in 1998, which showed that radiographs of the normal knee, the minimum JSW (mJSW) varied according to sex, but did not decrease with age.[37] Clark A et al. in 1999, also reported no significant difference in COMP levels in serum by gender and obesity, but COMP level in serum was found to be increased in the age group of ≥ 65 year (mean serum COMP value 1301±496 ng/ml, $p= 0.0001$).[38]

Measurement of joint fluid COMP levels is more difficult to apply than serum COMP levels, which is a limitation of this study.

CONCLUSIONS AND RECOMMENDATIONS

There was a relationship between joint space width and COMP levels of synovial fluid in which caused the narrower the joint space width, the higher the synovial fluid COMP level. This relationship, however, was not influenced by age and obesity. In conclusion, the width of the joint space is related to COMP levels can be used as a marker of joint cartilage destruction in osteoarthritis.

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