Age and Knee Osteoarthritis Severity Relationship in Indonesian Secondary Referral Hospital

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ABSTRACT

Osteoarthritis is a chronic joint disease that causes pain, disability, and loss of function. More than 80% of cases of osteoarthritis affect the knee joint. The exact cause of knee osteoarthritis is still unknown, but it is generally associated with aging and obesity. This study aimed to determine the relationship between age and the severity of knee osteoarthritis. This research used a cross-sectional study involving patients who suffered from knee osteoarthritis. Data on gender and the severity of osteoarthritis was collected from medical records. The severity of knee osteoarthritis was assessed using the Kellgren-Lawrence system. The data was analyzed using the Spearman correlation. There were 3 patients (8.1%) in the category of late adulthood, 7 patients (18.9%) in the middle-aged category, 13 patients (35.1%) in the early-onset elderly category, and 14 patients (37.8%) in the elderly. Seven patients (23.7%) suffered from osteoarthritis grade 1, 13 patients (35.1%) had grade 2, 16 patients (43.2%) had grade 3, and one patient had grade 4. The Spearman test showed that there was no significant relationship ($p>0.05$) between age and the severity of knee osteoarthritis. According to the study's findings, there was no correlation between age and the severity of knee osteoarthritis in women and men patients at Baptis Hospital, Batu City.

Keywords: Age, degree of severity, Kellgren-Lawrence, osteoarthritis

INTRODUCTION

Osteoarthritis (OA) is a chronic joint disease that is extremely common and causes pain, disability, and loss of function.[1] This disease is followed by changes in subarticular bone, osteophyte formation, weakening of ligaments and particular muscles, inflammation of the synovial fluid, and limited joint space.[2] Osteoarthritis is characterized by the abrasion of joint cartilage and irregular new bone formation.[3] Patients with this disease also experience excruciating pain and impairment, which interfere with day-to-day activities. As a result, 25% of individuals with osteoarthritis cannot do daily activities, and up to 80% have movement restrictions.[4]

WHO lists osteoarthritis as one of four muscle and bone conditions that burden individuals, the health system, and the social care system. Furthermore, osteoarthritis necessitates a significant financial investment, with a ratio of 9.6% in men and 18% in women [5]

Osteoarthritis is believed to be the result of biomechanical and molecular changes in the joints caused by injury, joint malalignment, obesity, aging, and inflammation. Osteoarthritis is classified as idiopathic or secondary to anatomic abnormalities, trauma, or arthritis.[6] According to the WHO, 151.4 million people worldwide suffer from osteoarthritis, including 27.4 million in Southeast Asia.[7] According to data from 2018, the prevalence of osteoarthritis in Indonesia is still high, at 8.5% for women and 6.1% for men.[8] According to estimates, osteoarthritis disables 2 million elderly individuals in Indonesia. Based on research conducted in Malang, the prevalence of osteoarthritis in people between the ages of 49 and 60 reached 21.7%, with 6.2% of men and 15.5% of women affected.[9]

All of the body's joints are susceptible to osteoarthritis, particularly weight-bearing joints, including the hips, knees, and spine.[10] The knee is the most frequently affected joint, followed by the hand and the hip.[1] More than 80% of cases of osteoarthritis affect the knee joint. The exact cause of knee osteoarthritis is still unknown, but it is generally associated with aging and obesity.[10]

Primary osteoarthritis and secondary osteoarthritis are the two categories into which knee osteoarthritis is divided based on the cause. Primary osteoarthritis is idiopathic aging-related osteoarthritis. In younger people, secondary osteoarthritis develops as a result of diseases like diabetes, avascular necrosis, or obesity that put them at risk for systemic osteoarthritis.[5]

An aging process affects the physiology and anatomy of the body, resulting in reduced joint protection mechanisms and increased joint instability. Osteoarthritis is the most common feature found on radiographic examination at 65–70 years old. At the age of 60, more than 50% of people have a picture of the joint narrowing on radiographic examination, and almost all people over 65 have a similar picture.[11]

It has only recently become apparent that age-related changes in tissues other than articular cartilage may play a role in the onset of osteoarthritis. The absence of nerve supply in articular cartilage is the cause of this, and osteoarthritis-related alterations in joint tissues such as the meniscus, ligaments, synovium, bone (including osteophytes), joint capsule, and bone can also cause knee discomfort. In the early phases of osteoarthritis, these tissues may be crucial. As a result, osteoarthritis is characterized as a disease affecting the entire joint.[12]

With age, the incidence of osteoarthritis has increased. More than 30 million adults in the United States have been diagnosed with osteoarthritis. In the age range between 65 and 74 years, osteoarthritis increases to 39% in men and 3% in women. At the age of more than 75, both men and women have symptoms of osteoarthritis.[3] The aging population and the increase in obesity seen at all ages are estimated to double by 2030 to 67 million, with more than 50% of osteoarthritis cases occurring in the group aged 65 and over.[13]

The number of people with osteoarthritis in Indonesia is mostly over 50 years old; 85% describe osteoarthritis on X-ray images, and 35–50% only experience symptoms of osteoarthritis. The prevalence of osteoarthritis under the age of 45 years is more common in men, while the most common is found in women at the age of 55 years. Several studies have shown that the increase in the occurrence of osteoarthritis is also influenced by obesity and genetics. For example, a woman who suffers from osteoarthritis will have a 2-3 times greater tendency to pass the disease on to their daughters compared to a woman who does not suffer from osteoarthritis.[5]

Research conducted by Peters et al.[14] showed that with increasing age there was a strong correlation between a decrease in cartilage shear storage modulus (G') and a moderate correlation with an increase in subchondral bone elastic modulus E using overall joint means. However, there was no significant correlation between increasing age and trabecular bone elastic modulus. These findings provide direct support for the conceptual representation of cartilage and subchondral bone as a single functional unit. Based on Rita's (2014) research, it appears that osteoarthritis occurs mostly in nurses aged 51–60 years, affecting as many as 14 people (56%). Based on gender, the highest number was found among women; there were 23 people (92%). Based on the degree of knee pain, most of them experienced mild pain—as many as 19 people (76%).

The diagnosis of OA includes three symptoms and three indicators, according to the European League Against Rheumatism. Constant pain, morning stiffness, and diminished joint function are three symptoms. Crepitus, a decreased range of motion, and the development of osteophytes are the three indicators of osteoarthritis.[15] The study most frequently used to assess the severity of osteoarthritis is the Kellgren and Lawrence (K&L) system, which is classified into 4 grades (0–4) based on the presence of steoaphytic features, joint space narrowing, sclerosis, and cysts. WHO adopted these criteria as the standard for epidemiological studies of osteoarthritis.[16]

Reduced bone tension and decreased cartilage growth are caused by the quality of the proteoglycans, collagen, and nutritional supply in the joints of the elderly. Depending on the disease's severity, this occurs. So osteoarthritis can hinder the majority of regular activities. Eleven percent of senior people require help with self-care, and 14% require help with necessities. One of the top five medical conditions that disable older people is osteoarthritis.[17]

Based on the description above, the purpose of this study was to see if there was a relationship between age and the severity of osteoarthritis in men and women patients with

knee osteoarthritis at Baptis Hospital in Batu City.

METHOD

A cross-sectional study was conducted for this research from April to July 2020. The population used in this study was osteoarthritis control patients at Baptist Hospital, Batu City. Samples are patients who meet the inclusion and exclusion criteria to be selected. Patients with knee osteoarthritis who have complete medical records and radiographic confirmation of their condition are eligible for inclusion criteria. Patients with pain in the knees caused by a disease other than osteoarthritis were excluded from this study, as were patients with no or incomplete medical records. Sampling in this study was conducted using a consecutive sampling technique, including non-probability sampling, where the research subjects were selected based on the researcher's decision. Based on the sample formula, the number of samples used is a minimum of 27 people.

The dependent variable in this study was the severity of knee osteoarthritis based on Kellgren & Lawrence, which was obtained from the diagnosis and radiographic examination of the patient's medical record. On radiographic examination, the assessment of severity is based on osteophyte formation, joint space narrowing, sclerosis, and cysts. The Kellgren-Lawrence system includes four grades: 0–4 (none, doubtful, minimal, moderate, and severe). No osteophyte development or joint narrowing in Grade 0; Grade 1: possible joint space narrowing and osteophyte lip; Grade 2: a few osteophytes and suspected joint space narrowing; Grade 3 includes rather severe osteophytes, noticeable joint space narrowing, sclerosis, and abnormalities at the ends of the bones. Grade 4 includes severe osteophytes, severe joint space constriction, and severe sclerosis.[18] The age of the patients in this study was the independent variable. This study uses an ordinal age classification of 4 groups based on the Ministry of Health (2009), including late adulthood (36–45 years), middle age (46–55 years), early elderly (56–65 years), and the elderly (> 65 years). The instrument used is an interview formula followed by checking the patient's medical record data. The data in this study were analyzed using Spearman correlation to determine the relationship between two variables based on the Kallgren-Lawrence system with a $p<0.05$ significance level. This study hypothesizes that there is a relationship between age and the severity of knee osteoarthritis in general and by gender. The ethical committee from the Faculty of Medicine at Universitas Brawijaya reviewed and approved this study proposal, as stated in the ethical clearance certificate No. 73/EC/KEPK/03/2020.

RESULT AND DISCUSSION

The total number of respondents obtained was 49, but only 37 of them complied with the inclusion and exclusion criteria.

Table 1. General characteristics of patients

Characteristics	n	%
Age		
36-45	3	8.1
46-55	7	18.9
56-65	13	35.1
>65	14	37.8
Gender		
Men	10	27
Women	27	73
Grade of osteoarthritis		
1	7	18.9
2	13	35.1
3	16	43.2
4	1	2.7

Table 1 shows that three (8.1%) of the 37 patients with knee osteoarthritis were in late adulthood, seven (18.9%) were in middle age, 13 (35.1%) were in early elderly, and 14 (37.8%) were elderly. The results showed that the group of patients with the greatest distribution was the elderly (age >65 years). The mean age of the patients in this study was 62.40 years. Several studies conducted in Indonesia found similar results in the age distribution of osteoarthritis patients. Research conducted by Ahmad [19] at RS. dr. Soetomo, Surabaya, shows that the highest distribution is in the age range of 60–69 years, with an average age of 59.08 years. The youngest age is 40 years, while the oldest age is 71 years. In another study conducted at PKU Muhammadiyah Hospital, it was stated that those aged >60 years had the highest incidence of osteoarthritis at 49% and the least at age <50, which was 24%.[20] The age group >65 years is the most common age group in this study, which is similar to the study in America, which states that osteoarthritis affects many elderly people over 65 years with a prevalence of 33.6%, or more than 12.4 million people.[15] The three studies prove that the highest prevalence of patients is found in those over 60 years of age.

The elderly often suffer from osteoarthritis because the degeneration process in the joints increases with age. Weakening of muscle strength, thinning of joint cartilage, and reduced proprioceptive abilities are also consequences of increasing age, which can lead to osteoarthritis.[16] Several aging mechanisms that can cause osteoarthritis include cellular aging by senescence-associated secretory phenotype (SASP), dysfunction of energy metabolism due to reduced activity of 5'-AMP-activated protein kinase associated with decreased autophagy, and changes in the extracellular signaling matrix.[13] Although old age is the greatest risk factor for osteoarthritis, the joints affected and the severity of the disease are more associated with other risk factors. These factors include a history of trauma, obesity, genetics, and anatomical factors that affect the joint mechanism.[21]

When other osteoarthritis risk factors are also present, aging alters the cells and extracellular matrix of joint tissue, making older persons more susceptible to the disease. Aging contributes to the imbalance between catabolic and anabolic activity in the joints that characterizes osteoarthritis. Aged chondrocytes are unable to keep articular cartilage in a state of homeostasis because they respond poorly to growth factor stimulation. These alterations will then produce a protracted inflammatory environment that prevents the joints from healing on their own, which results in osteoarthritis.[22]

Based on gender, in this study, there were 10 patients (27% men) and 27 patients (73% women) (Table 1). The findings of this study are consistent with those of Laksmitasari et al. (23), which revealed that women were more likely to have both severe (grades 3-4) and mild (grades 1-2) conditions. The findings of this study demonstrate that women experience osteoarthritis more frequently than men do, which can be brought on by hormones. Osteoarthritis, which is related to a decrease in estrogen levels after menopause, is more common in postmenopausal women in particular. Estrogen receptors in articular cartilage point to a possible connection between estrogen and the health of the cartilage.[23] Another study demonstrated that postmenopausal women taking estrogen replacement therapy had a lower chance of developing radiographic evidence of knee osteoarthritis. In addition, the protective effect of estrogen replacement therapy increases with the duration of therapy.[24] It is well known that estrogen can increase the production of proteoglycans and that articular chondrocytes have functional estrogen receptors. Various studies, however, have found no relationship between exposure to women's sex hormones and osteoarthritis.[22] A decrease in the hormone estrogen acts as a protective effect on the pathogenesis of the disease. This protective effect is caused by chondrocyte cells having estrogen receptors that increase the synthesis and production of proteoglycans associated with the disease process, where women's hormones affect the cartilage cushions between the joints to allow smoother joint movement. Although estrogen protects cartilage from inflammation, women will lose this protection after menopause when estrogen levels decrease.[25] After menopause, elevated levels of IL-1, IL-6, TNF-, and other inflammatory factors in serum and synovial fluid can aggravate and worsen osteoarthritis. The causes of the different progression of osteoarthritis between men and women may be multifactorial and include anatomical differences, previous trauma, and genetic problems. The anatomical differences between men and women that may play a role include a narrower femur, a thinner patella, a larger quadriceps angle, and differences in tibial condyle size.[26]

Seven (18.9%) of the 37 patients had grade 1 osteoarthritis, 13 (35.1%) had grade 2, 16 (43.2%) had grade 3, and one had grade 4

(Table 1). Generally, the prevalence of osteoarthritis will increase at the age of 50–55 years, but people as young as 30–40 years old can suffer from early osteoarthritis. Patients with early osteoarthritis have other risk factors, such as a history of injury, obesity, or malignancy of the extremities.[27] People with a history of anterior cruciate ligament (ACL) injury may develop osteoarthritis before the age of 40.[28] Excluding the age group of 45 years, experimental data analysis revealed that age had a significant relationship with the severity of osteoarthritis.

The Spearman Rank test was used to assess the relationship between age and the severity of osteoarthritis in patients, with a P-value of 0.189 indicating that the probability value was greater than the significant value (α). According to these findings, there is no significant relationship between age and the severity of knee osteoarthritis patients at Baptis Hospital in Batu City (Table 2). The results of research by Sibarani et al.[29] showed similar results: there was no correlation between age and the degree of osteoarthritis based on the Kellgren-Lawrence classification system. This indicates that other factors influence the degree of knee joint osteoarthritis. In theory, the results of this study could be caused by multifactorial risk factors. Risk factors in the development of

osteoarthritis are divided into individual-level and joint-level risk factors. At the individual level, there are age, gender, obesity, genetics, and diet. Meanwhile, at the joint level, there is a history of injury and abnormal joint loading.[16] Occupational factors also affect the occurrence of osteoarthritis. Patients who work or engage in strenuous physical activities are often found to suffer from osteoarthritis.[30]

Several similar studies in Indonesia produced contradictory results, such as the study conducted at the Al-Islam Hospital in Bandung and the Dr. Sudirohusodo Hospital in Makassar, which found no significant relationship between age and the severity of osteoarthritis.[20,21] However, PHC Hospital research found a significant relationship with a low correlation between age and the severity of osteoarthritis.[33] Differences in the results of these studies can be influenced by several factors, such as the total number of samples. Research conducted at PHC Hospital, Surabaya, used a sample of >100 patients, while other studies, including this study, used a sample of <60 patients. In addition, it can also be influenced by the proportion of elderly patients at the Baptist Hospital, where patients with osteoarthritis are very numerous and the population is limited.

Table 2. Descriptive results between age and severity of osteoarthritis

Age	Grade of osteoarthritis								Total		P-value
	Grade 1		Grade 2		Grade 3		Grade 4				
	n	%	n	%	n	%	n	%	n	%	
Late adulthood (36-45)	0	0	1	2.7	2	5.4	0	0	3	8.1	
Middle age (46-55)	3	8.1	1	2.7	3	8.1	0	0	7	18.9	0.189
Early elderly (56-65)	4	10.8	6	16.2	2	5.4	1	2.7	13	35.1	
Elderly (>65)	0	0	5	13.5	9	24.3	0	0	14	37.8	
Total	7	18.9	13	35.1	16	43.2	1	2.7	37	100	

According to Table 2, patients with grades 1 and 2 osteoarthritides are frequently found in the early elderly (56–65), patients with grades 3 are commonly found in the elderly (>65), and patients with grade 4 are found in the early elderly (56–65). The results of this study follow those of Laksmitasari et al.[25], who discovered that individuals with grade 3–4 osteoarthritis experienced higher pain than people over the age of 60 (62.5%). Patients

under the age of 60 were more likely to have grade 1-2 osteoarthritis (89.5%). Osteoarthritis is a degenerative condition that develops with age and is frequently referred to as a chronic disease and considered an inevitable part of aging. The aging process generates an imbalance in chondrocyte signaling.[34], thus creating a lower ability of chondrocytes to respond to growth factor stimulation in senior people, and osteoarthritis cartilage is less

susceptible to converting TGF-β and insulin-like growth factor-1. Eventually, the joint space thins due to cartilage thinning, and subchondral cysts occur. In the meantime, the cartilage becomes loose due to synovial inflammation, which is followed by the development of new bone osteophytes.[34,35]

Patient characteristics in terms of socioeconomic status also influence the incidence and progression of knee osteoarthritis. Patients living in rural areas have a 1.14 higher risk of developing knee osteoarthritis compared to patients living in urban areas. This can be caused by several factors, such as information and access to health services.[36] Thus, age cannot be the only risk factor in the diagnosis of knee osteoarthritis severity.

The exact cause of osteoarthritis is still a question. According to several recent studies, osteoarthritis has several causes. Age, women's gender, obesity, physical activity, genetic variables, joint trauma, race, and chondrocalcinosis are the main risk factors.[22] This shows a correlation between risk factors for osteoarthritis; therefore, for further research, it can be associated with two risk factors such as age with comorbidities and physical activity, as well as other factors.

There is a substantial correlation between osteoarthritis and age, gender, nutritional status, family background of osteoarthritis, type of labor, length of work, work position, and land location, according to research by Afifa et al.[37] on risk factors for knee osteoarthritis in farmers.

This study demonstrates how the risk variables affect the likelihood of developing knee osteoarthritis. In addition, the number of samples in further research can be expanded to be able to represent the total population. Because this research was conducted during the COVID-19 pandemic, there are limitations in the number of samples that may affect the results of the study. Nonetheless, this study has advantages because it can be used as a reference for future research. This is because there has never been any research on the relationship between osteoarthritis and age at Baptis Hospital. This study can also be used as a reference for osteoarthritis care and diagnosis.

CONCLUSION

According to the findings of this study, there was no significant relationship between age and the severity of knee osteoarthritis in men and women patients at Baptis Hospital in Batu City.

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