

Correlation Between Symptomatic Knee Osteoarthritis and Serological Examination: A Longitudinal Study in China

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Abstract: *Background:* The correlation between symptomatic knee osteoarthritis (OA) and whole blood cell count (CBC) has not been well studied based on large-scale population. The purpose of this study was to analyze its correlation with serological examination, especially with CBC tests. *Methods:* Samples in our study was derived from China Health and Retirement Longitudinal Study (CHARLS), wave 3. Blood samples from 13,420 participants were collected. We define a subject as symptomatic knee OA patient if both questions (Individuals were asked whether they were troubled with knee pain and had a doctor-diagnosed arthritis) were responded positively. A total of 12,952 individuals were classified into four groups. Post hoc multiple comparisons were conducted then. The criterion of significance is $p < 0.05$. *Results:* Among the 20967 people included in the analysis, 19692 answered the diagnosis questions. Our results showed that the prevalence of symptomatic knee OA was 9.18%. The level of hemoglobin (Hgb) (13.34 ± 1.80 g/dl) in patients with symptomatic knee OA was significantly lower than that in other individuals. The HCT level of symptomatic knee OA individuals ($40.53 \pm 5.32\%$) was significantly lower than that of other individuals. Patients with arthritis but without ongoing knee pain had the lowest PLT level ($199.09 \pm 76.88 \times 10^9/L$) when compared with other groups. *Conclusion:* symptomatic knee osteoarthritis is common in China. Patients with symptomatic knee OA showed a downward trend in the serological results of hemoglobin and hematocrit compared with other populations. More research on symptomatic knee osteoarthritis needs to be carried out.

Keywords: Symptomatic Knee Osteoarthritis, Prevalence, Peripheral Blood, Correlation

1. Introduction

Osteoarthritis (OA) is a common chronic disease affecting the health of elder people, which was regarded as a main reason of pain and disability [1], has caused a serious economic burden worldwide [2]. An estimation of the National Health Interview Survey reported that over 14 million people in the US suffer from the symptomatic knee OA [3]. According to the data of China Health and Retirement Longitudinal Study (CHARLS) in 2011, the prevalence of symptomatic knee osteoarthritis in China was 8.1%, indicating that there are more than 100 million knee OA

patients troubled with knee pain in China [4].

The essence of osteoarthritis is chronic inflammatory response. Studies have shown that neutrophils, monocytes and lymphocytes play an important role in local cartilage injury of knee joint [5]. More and more studies have shown that there is a strong correlation between the level of peripheral blood indicators and the occurrence and development of osteoarthritis [6].

Symptomatic knee OA is defined as knee OA patients with knee pain symptoms. There is still lack of relevant researches on serological examination of people with or without knee pain and knee OA. There are currently few large sample analyses of

blood routine test results in osteoarthritis, and no studies have figured the influence of the pain symptoms on blood routine results. Our study aims to report the prevalence of symptomatic knee OA based on the data of CHARLS study in the year 2015, and analyze the correlation between symptomatic knee OA and complete blood count (CBC) results.

2. Methods

2.1. Study Population

CHARLS is a national representative longitudinal survey of Chinese middle-aged and elderly people. The national baseline survey (wave 1) was implemented in 2011. A follow-up wave (wave 2) was conducted in 2013, Wave 3 was then mainly finished in 2015 [7], this included the second wave of blood tests collection. The CHARLS national sample contains respondents in 150 counties/districts which are randomly picked from 30 provincial administrative units (excluding Macao and Hongkong Special Administrative Regions, Taiwan Province, Tibet Autonomous Region), 450

villages/urban communities were obtained from the whole country. A detailed description the CHARLS has previously been published [8].

2.2. Clinical Data Collection

This study used the data from the first wave 3, in which 21,100 residents were interviewed through a face-to-face computer-assisted personal interview (CAPI). Participants were asked whether they were often troubled with pain, and they'll point out the parts of the body experiencing ongoing pain. Also, each participant was asked if he or she had a doctor-diagnosed arthritis. Symptomatic knee OA were defined when a subject responded both questions positively.

The venous blood samples tested for CBC were analyzed at local county health centers, including white blood cell count (WBC), hemoglobin (HGB), hematocrit (HCT), platelet counts (PLT) and mean corpuscular volume (MCV) [7]. The individuals in CHARLS wave 3 who took the blood samples were targets of our study. A total of 13,420 blood samples were collected then.

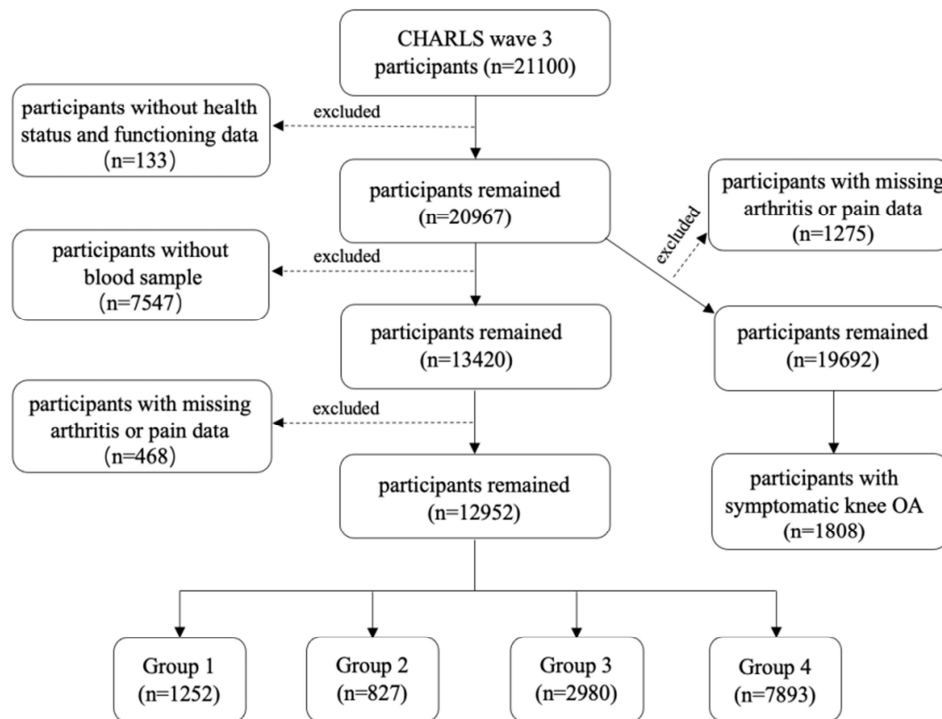


Figure 1. The flow chart of this study.

- (1) Group 1: participants with symptomatic knee OA;
- (2) Group 2: participants who has ongoing knee pain but have no arthritis;
- (3) Group 3: participants who are diagnosed with arthritis but have no ongoing knee pain;
- (4) Group 4: participants without arthritis and ongoing knee pain.

2.3. Study Process

Among the 20,967 individuals with health status and functioning data included in the analysis, a total of 19,692 individuals answered both the knee pain and the doctor-diagnosed arthritis question. Among those 20,967

individuals, 13,420 individuals with blood samples were remained, after participants with missing arthritis or pain data were excluded, 12,952 individuals were taken into analysis eventually.

The 12,952 participants were categorized into four groups (Figure 1):

- (1) Group 1: participants with symptomatic knee OA;
- (2) Group 2: participants who has ongoing knee pain but have no arthritis;
- (3) Group 3: participants who are diagnosed with arthritis but have no ongoing knee pain;
- (4) Group 4: participants without arthritis and ongoing knee pain.

2.4. Statistical Analysis

Statistical analysis was finished using the SPSS (IBM, 25.0, CA, USA), the prevalence of symptomatic knee OA based on the data in the CHARLS study was calculated by narrative statistics. Post hoc multiple comparisons were conducted to analyze the CBC level among four groups. The criterion of

significance is defined as $p < 0.05$.

3. Results

Among all the 21,100 residents participated in the CHARLS wave 3 survey, 20,967 participants were contained in the analysis. And 19,692 (93.33%) answered the questions of the knee pain and the doctor-diagnosed arthritis, while 1808 subjects responded both questions positively, indicating that the symptomatic knee OA prevalence was 9.18% in the year 2015. The response rate of blood sample taken was 63.60%. The response rate of women was 3.77% higher than that of men (65.95% versus 62.18%).

Table 1. The CBC level (WBC, HGB, HCT, MCV, PLT) of four groups.

	Group 1		Group 2		Group 3		Group 4	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
WBC ($10^9/L$)	6.06	1.93	6.00	4.21	5.93	1.83	6.01	1.78
HGB (g/dL)	13.34	1.80	13.51	1.98	13.62	2.03	13.82	1.92
HCT (%)	40.53	5.32	40.64	5.84	41.23	5.83	41.79	5.62
MCV (fL)	91.26	7.56	90.80	7.87	91.48	7.86	91.37	7.74
PLT ($10^9/L$)	203.84	74.05	208.20	81.03	199.09	76.88	207.33	74.81

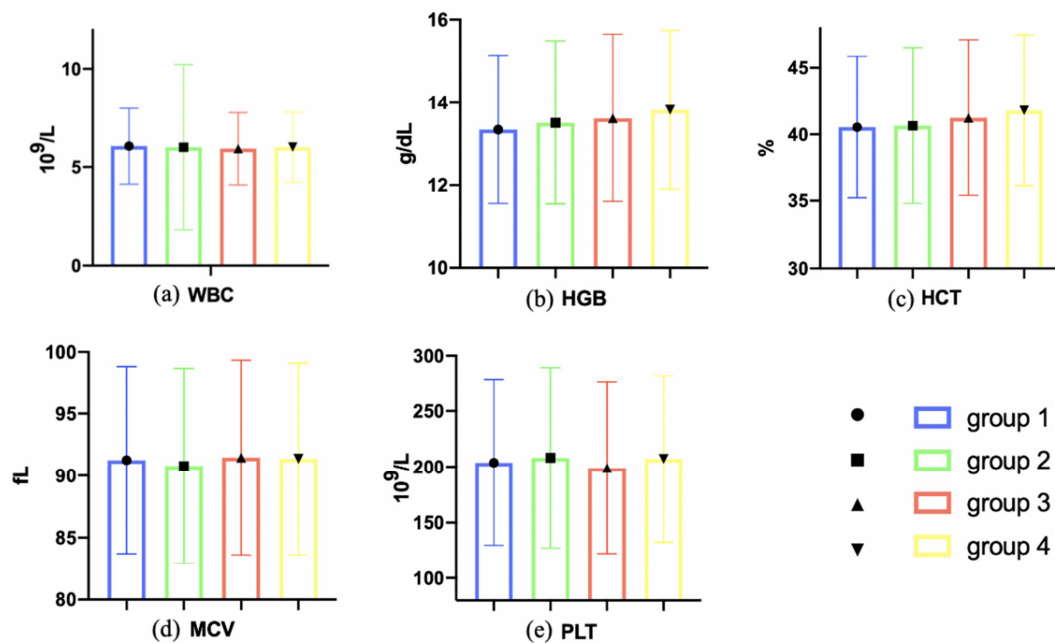


Figure 2. The CBC level (WBC, HGB, HCT, MCV, PLT) of four groups.

After grouping, 1,252 participants who have symptomatic knee OA were assigned to group 1, 827 individuals who have ongoing knee pain but have no arthritis were assigned to group 2, 2,980 participants who are diagnosed with arthritis but have no ongoing knee pain were assigned to group 3, and 7,893 participants who don't have arthritis and knee pain were assigned to group 4. The CBC level of the four groups was revealed in Table 1 and Figure 2. The significance between CBC level in the four groups was revealed in Table 2.

The WBC level of the four groups were (6.06 ± 1.93 , 6.00 ± 4.21 , 5.93 ± 1.83 , 6.01 ± 1.78) $\times 10^9/L$, respectively. There

were no prominent differences in the assessment of WBC levels between the four groups.

Table 2. The significance between CBC level in four groups.

	Group 2	Group 3	Group 4
Group 1		* †	* †
Group 2		† ‡	* †
Group 3			* † ‡

*: significance in HGB ($p < 0.5$)

†: significance in HCT ($p < 0.5$)

‡: significance in PLT ($p < 0.5$)

The HGB level of the four groups were (13.34 ± 1.80 , 13.51 ± 1.98 , 13.62 ± 2.03 , 13.82 ± 1.92) g/dL, respectively. The level of HGB in the group without arthritis and knee pain (group 4) was markedly higher than the rest of groups. HGB level in group 3 was markedly higher than that in group 2.

The HCT level of the four groups were (40.53 ± 5.32 , 40.64 ± 5.84 , 41.23 ± 5.83 , 41.79 ± 5.62) %, respectively. Obviously, about the HCT level, group 4 was markedly higher than the rest of groups. In addition, the HCT level of group 3 was markedly higher than the HCT level of group 2 and group 1.

The MCV level of the four groups were (91.26 ± 7.56 , 90.80 ± 7.87 , 91.48 ± 7.86 , 91.37 ± 7.74) fL, respectively. There were no prominent differences in the assessment the MCV level between the four groups.

The PLT level of the four groups were (203.84 ± 74.05 , 208.20 ± 81.03 , 199.09 ± 76.88 , 207.33 ± 74.81) $\times 10^9/L$, respectively. The group 2 and group 4 was markedly higher than group 3 in regard to the PLT level.

4. Discussion

From the data obtained from the CHARLS study, a national population-based survey, we found the phenomenon that symptomatic knee OA remained common among the adults in China. The prevalence of symptomatic knee OA in 2015 is 9.18%, which is 1.08% higher than that in 2011, the age and gender distribution of the two waves represent similarity. Indicating that the occurrence and development of symptomatic knee is still a serious problem in China, and the control level still needs to be improved.

It is generally believed that the level of neutrophils in blood is closely related to various inflammatory related cytokines, chemokines and proteolytic enzymes produced by chronic inflammatory reaction. Studies have clearly shown that low grade inflammation exists in OA joint tissues, where it may conduce to disease pathogenesis [9, 10]. In our study, although group 1 showed the highest levels of white blood cell among the four groups, there was no statistically prominent correlation between the level of white blood cell and knee pain/ knee OA. A study by Ishihara indicated that there were no striking discrepancy between OA and healthy controls on blood polymorphonuclear leukocytes with nitro-blue tetrazolium (NBT) test values [11], showing that the function of peripheral white blood cells in knee OA patients is as same as normal people, which is similar to our results. A study reported by Attur M identified that the increase of inflammatory gene (IL-1, TNF α or COX-2) in peripheral blood leukocytes predicted the imaging progression of patients with symptomatic knee OA, suggesting that inflammatory events in the joint tissues of patients with symptomatic knee OA have been reported in peripheral blood [12]. Considering our findings together with those of others, the white blood cell in the peripheral blood is not the clinical feature of most patients with symptomatic knee OA or knee pain. Though the

inflammatory events cannot be prognosed by white blood cells, they still exist in the peripheral blood.

The HGB level of symptomatic knee OA is prominently lower than that in the normal population as well as individuals diagnosed with arthritis but without the symptom of ongoing knee pain. We speculate that there is a correlation between symptomatic osteoarthritis and decreased hemoglobin levels, knee pain may have a greater impact on the decline in hemoglobin levels in peripheral blood than osteoarthritis itself. Studies have shown that OA is related to new-onset anemia [13]. Low hemoglobin levels are associated with the occurrence of many adverse events such as stroke, renal failure, heart attack which may lead to higher mortality [14, 15]. These results suggest that when treating pain symptoms of OA patients, attention should be paid to the level of hemoglobin and guided interventions should be given if necessary.

HCT refers to the percentage of red blood cells (RBCs) to the whole blood volume. Decreased HCT is frequently connected with anemia, chronic disease states, etc. The trend of HCT level in our study is similar to the results of HGB level, individuals with symptomatic knee represented the lowest level of HCT, while normal individuals represented the highest level of HCT. There are studies reporting that when compared to normal people, there was no meaning of the width of red cell volume distribution in the peripheral blood of OA patients, suggesting that the anemia in OA patients is a homogeneous anemia [16]. Based on this theory, the HCV variation basically reflects the level of RBCs, showing that patients with symptomatic knee OA or knee pain tends to have relatively decreased nutritional levels.

The MCV level of the four groups showed no significance. Showing that the mean size of RBCs was not significance among symptomatic knee OA patients, individuals with knee pain/OA and normal individuals. Interestingly, we found that the PLT level of individuals diagnosed with OA but have no ongoing knee pain is the lowest among the four groups, while individuals with knee pain but have no OA is the highest. These findings indicate that OA is frequently accompanied by a decrease in platelet levels, knee pain may be accompanied by a mild increase in platelet levels, although the data did not show statistical differences.

There's no doubt that our study also have some imperfections and limitations. First of all, the participants in the CHARLS study were not evaluated radiographically so that the radiographic osteoarthritis prevalence couldn't be derived, thus the diagnosis of symptomatic knee OA prevalence obtained in this study was based on self-reported knee pain along with physician diagnosis arthritis. Secondly, white blood cell count couldn't accurately reflect OA activity, instead, high sensitivity C-reactive protein (hs CRP) levels, erythrocyte sedimentation rate (ESR) levels may be relatively more sensitive and accurate. Thirdly, the combination of RBCs, HGB, and HCT provides a more accurate assessment of the anemia related status, while our study lacked RBCs related data.

5. Conclusion

Among the middle-aged and elderly Chinese people, there exists a high prevalence of symptomatic knee OA, and the trend is continuously increasing. There were strong correlations between symptomatic knee OA and HGB/HCT levels. Patients with symptomatic knee OA showed a downward trend in the serological results of hemoglobin and hematocrit compared with other populations. Attention should be paid to blood routine examination when treating symptomatic knee OA patients, guided interventions should be given when necessary. Besides, subsequent studies need to focus on the methods of prevention, powerful management and effective treatment of symptomatic knee OA.

Abbreviations

OA: osteoarthritis; CBC: complete blood count; CHARLS: China Health and Retirement Longitudinal Study; HGB: hemoglobin; HCT: hematocrit; WBC: white blood cell count; PLT: platelet counts; MCV: mean corpuscular volume; CAPI: computer-assisted personal interview; NBT: nitro-blue tetrazolium; RBCs: red blood cells; hsCRP: high sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate.

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