The Meaning of Serum CRP, ESR, Platelet Count and Mean Platelet Volume ratio (PC/MPV) and plasma Fibrinogen in the Diagnosis of Periprosthetic Joint Infection

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Research article

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Abstract

Background

The purpose of this study was to test the meaning of serum CRP, ESR, Platelet Count and Mean Platelet Volume ratio (PC/MPV) and plasma Fibrinogen in periprosthetic joint infection diagnosis.

Methods

Clinical data of 160 patients diagnosed with osteoarthritis (Group A), PJI (Group B) and aseptic loosening after joint arthroplasty (Group C) were retrospective studied. General data and preoperative serum CRP, ESR, Platelet count to Mean Platelet Volume ratio and plasma Fibrinogen level were recorded and compared.

Results

Serum CRP, ESR, PC/MPV and plasma Fibrinogen expression level in Group B are much higher than Group A and C. When PC/MPV>31.70 was set as the optimum threshold value for the diagnosis of PJI, the specificity of PC/MPV in PJI diagnosis was lower than CRP and ESR, whereas, the sensitivity of PC/MPV in PJI diagnosis was similar with CRP and ESR. When plasma Fibrinogen > 4.01 μg/mL was set as the optimum threshold value for the diagnosis of PJI, the specificity and sensitivity of plasma Fibrinogen in diagnosis of PJI was similar with CRP and ESR.

Conclusion

PC/MPV should not be used as the first screen marker for PJI diagnosis, whereas, the plasma Fibrinogen can be used as a new marker for PJI diagnosis.

Background

Periprosthetic joint infection (PJI) is still one of the most terrible complications for both patients who received and clinical surgeons who performed joint arthroplasty. Although one stage or two stage revision surgery combined with antibiotics treatment exert favorable clinical effect, it is still not easy to make an accurate PJI diagnosis in some situations. Until now, there is still no “gold standard” test for PJI diagnosis, which compels clinicians to rely on several tests to make an accurate PJI diagnosis. Despite serum CRP and ESR are the most commonly checked markers for PJI diagnosis[1], they do not work well in situations including chronic [2] and low virulence organism infections[3, 4]. Owing to the low-risk and rapidity of blood test, it is always selected by clinicians as the first option for PJI diagnosis. In the past a few years, the meaning of some new serological markers such as serum soluble intercellular adhesion molecule-1 (sICAM-1) [5], myeloid-related protein14 (MRP-14) [6], soluble urokinase plasminogen activation receptor (su-PAR) [7] and lipopolysaccharide-binding protein (LBP) [8, 9] were evaluated and demonstrated good performance in PJI diagnosis. However, due to high expense and limited clinical data, it is not easy to prevail them in clinical practice especially in primary hospitals in the near a few years. So,
it is emergent for us to explore some new convenient, quick and efficient serological markers for PJI diagnosis.

Coagulation and inflammation theory, which means excessive activation of coagulation could indicate the status of infection and inflammation, has been used in infection and inflammation diseases diagnosis for a long time [10, 11]. However, the relationship between PJI and coagulation is still unclear. In the past a few years, the sensitivity and specificity of several serum and plasma coagulation markers including serum D-Dimer [12, 13], Platelet Count and Mean Platelet Volume ratio [14] and plasma Fibrinogen [15] were compared with CRP and ESR in PJI diagnosis, and these data showed that these three coagulation markers can be used in PJI diagnosis. However, no subsequent studies were published thereafter. And whether these markers could be used for PJI diagnosis is still unclear. As these serological markers were commonly used in clinical practice, the diagnostic value of these markers in PJI diagnosis deserved our exploration.

In this study, we rechecked and evaluated the meaning of serum CRP, ESR, Platelet Count and Mean Platelet Volume ratio (PC/MPV) and plasma Fibrinogen in PJI diagnosis, and demonstrated that PC/MPV should not be selected as the first screening marker for PJI diagnosis, whereas, the plasma Fibrinogen can be used for as a new screening marker for PJI diagnosis.

**Methods**

Clinical data, for instance, gender, age, preoperative serum CRP, ESR, Platelet Count and Mean Platelet Volume ratio (PC/MPV) and plasma Fibrinogen level in patients presented with primary osteoarthritis, PJI, aseptic loosening in our department from July 2016 to December 2018 were retrospectively analyzed. Exclusion criterion can be seen in our previous published paper [16]. This retrospective study was approved by ethics board of Henan Provincial People’s Hospital.

**Definition of PJI and aseptic loosening**

PJI was defined using the MSIS criteria[1].

Aseptic loosening was defined using the criteria in our previous published paper [16].

**Statistical Analysis**

Quantitative data were recorded as mean ± standard deviation, single factor analysis of variance was selected for comparison difference among multiple groups and SNK test was selected for comparison between any two means. Chi-square test ($\chi^2$) was selected for comparison the counting data among groups. P value less than 0.05 was considered as significant difference. If the difference is significant, partition of chi-square is used for comparison between any two means and P value less than 0.017 was regarded as significant difference. All statistical analyses were carried out by IBM SPSS Statistics (version 19, IBM SPSS Software).
Results

Included population

160 patients were included in this study and grouped as: Group A: 52 patients (received primary arthroplasty); Group B: 58 PJI patients (received resection arthroplasty and antibiotic-cement spacer insertion surgery); Group C: 50 aseptic loosening patients (received revision surgery). Patient demographics are presented in Table 1 and there were no significant differences among the three groups.

Different expression of serum CRP, ESR, PC/MPV and plasma Fibrinogen level in patients from the three different groups

Serum CRP level in Group B (49.18 ± 57.14) mg/L is higher than in Group A (9.31 ± 19.04) mg/L and C (5.96 ± 10.58) mg/L. Serum ESR level in Group B (50.76 ± 28.81) mm/h is higher than in Group A (16.62 ± 14.39) mm/h and C (19.02 ± 16.24) mm/h. Serum PC/MPV in Group B (34.53 ± 17.89) is significantly higher than in Group A (26.21 ± 8.25) and C (24.87 ± 10.11). Plasma Fibrinogen in Group B (4.86 ± 1.42) g/L is higher than in Group A (3.30 ± 0.71) g/Land C (3.20 ± 0.79) g/L. All these data indicate that elevated serum CRP, ESR, PC/MPV and plasma Fibrinogen may predicate PJI.

PC/MPV does not do better than CRP, ESR and plasma Fibrinogen in PJI diagnosis

Although above results showed that elevated serum CRP, ESR, PC/MPV and plasma Fibrinogen may predicate PJI, and paper published by Li[15] and Paziuk[14] showed when PC/MPV > 31.70 and FIB > 4.01 µg/mL was set as the optimum threshold value for the PJI diagnosis, PC/MPV and plasma Fibrinogen can be used as the PJI diagnosis markers. However, no subsequent studies were done since then. So, we compared the sensitivity and specificity of serum CRP, ESR, PC/MPV and plasma Fibrinogen in diagnosis of PJI among patients from three different groups.

As shown in Table 2, the sensitivity of plasma Fibrinogen is similar with CRP and ESR, while the sensitivity of PC/MPV is lower than CRP and ESR. However, when the specificity of serum CRP, ESR, PC/MPV and plasma Fibrinogen in PJI diagnosis were compared among patients from three different groups, the differences are not statistically significant. All these data indicate that plasma Fibrinogen can be used as a new marker for PJI diagnosis, while, PC/MPV should not be used as a new marker for PJI diagnosis.

Discussion

Considering that the high rate of success of joint arthroplasty, the number of patients receiving joint arthroplasty has been increasingly year by year. However, Andrew M. et al estimated that the incidence of Hip and Knee Arthroplasty revision surgery in the United States to 2030 is projected to increase [17]. In 2017, papers published by Delanois et al and Gwam et al showed that PJI is the most common reason for
revision in total knee arthroplasty patients [18] and the fourth most common reason for revision in total hip arthroplasty patients in the United States [19]. Although one stage or two stage revision surgery combined with antibiotics treatment exert excellent clinical effect, it is still not easy to make a prompt and accurate PJI diagnosis, PJI diagnosis remains challenging.

Despite numerous efforts have been tried to increase the accuracy of PJI diagnosis, until now, there is still no consensus on the superiority of one method better than another. Compared with other methods, blood examination, which has the merit low-risk, non-invasion and rapidity, is always the first screening option for clinicians to make a PJI diagnosis. Though CRP and ESR are still widely used as first-line screening markers for PJI, they are non-specific blood inflammatory markers and could be influenced by many factors [20]. So, lots of researchers are trying to evaluate the meaning of some other blood markers in PJI diagnosis.

Despite coagulation markers such as Platelet Count and Mean Platelet Volume ratio [21], D-Dimer [22] and plasma Fibrinogen[23] have been used in inflammation and infection diseases diagnosis [10, 11], the role of these coagulation markers in PJI diagnosis is still unknow. Although the role of D-Dimer [12, 13] plasma Fibrinogen [15], Platelet Count and Mean Platelet Volume ratio [14] were evaluated in PJI diagnosis, no subsequent studies were published thereafter.

In this study, we retrospectively analyzed the sensitivity and specificity of serum CRP, ESR, Platelet Count and Mean Platelet Volume ratio (PC/MPV) and plasma Fibrinogen in PJI diagnosis. Similar with Li’s [15] study, we found that plasma Fibrinogen can be used for as a new marker for PJI diagnosis. However, different from Paziuk’s study[14], our data demonstrated that PC/MPV should not be selected as the first option for PJI diagnosis. But we think our conclusion still make sense and the reasons is that we take the MSIS criterion[1] which recommend ESR>30 mm/h,CRP>10 mg/L other than Paziuk’s ESR>46 mm/h,CRP>1.5 mg/L as the optimum threshold value for PJI diagnosis. As a result, our conclusion performs better than Paziuk’s in clinical utilization.

However, there are several limitations in our study: 1, the number of included patients in our study is only 160, much lesser than Paziuk’s (4938 patients), which indicates our conclusion is less reliable than Paziuk’s to some extent; 2, we excluded those have rheumatologic disease, which constitute almost 10% patients in our department, which also to some extent decreased the reliability of our conclusion.

**Conclusion**

Overall, in this study, different from previous studies, which focused on inflammatory markers other than coagulation-related indicators in PJI diagnosis, we found that PC/MPV should not be selected as the first option for PJI diagnosis, whereas, the plasma Fibrinogen can be used for as a new marker for PJI diagnosis.

**Abbreviations**
PJ1: periprosthetic joint infection; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; Platelet Count and Mean Platelet Volume ratio (PC/MPV)

**Declarations**

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**Availability of data and materials**

The data and materials are available from the department of Orthopedics, Henan Provincial People's Hospital. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

This retrospective study was approved by the Ethics Committee of Henan Provincial People's Hospital and performed in accordance with the Helsinki Declaration. All patients agreed to participate and provided written informed consent prior to treatment.

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All the authors declare no conflict of interest.

**Authors' contributions**

JCH, JYZ and ZYG participated in the design of the study and the acquisition and interpretation of data, performed the statistical analysis, and drafted the manuscript. XC, ZPD, WDZ and YHD participated in the acquisition and interpretation of data and helped to draft the manuscript. JJL, JZ and YJ participated in the design of the study, and helped to statistical analysis and to draft the manuscript. YJ conceived of the study, participated in its design and coordination, helped to statistical analysis and to draft the manuscript. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

This retrospective study was approved by ethics board of Henan Provincial People's Hospital. All the data used in this study were anonymised before use.

**Consent for publication**
Not applicable.

Competing interests

The authors declare that they have no competing interests.

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**Tables**

| Table 1 | Comparison of the general data among patients from three different groups |
|---------|--------------------------------------------------------------------------------|
| Group   | A | B | C | Age | 63.13±9.53 | 64.57±12.23 | 67.20±10.80 | F=1.794 | P=0.170 |
| Gender  | Male | 11 | 20 | 16 | χ²=2.590 | P=0.274 |
|         | Female | 41 | 38 | 34 |                 |               |

| Table 2 | Comparison of the sensitivity of serum CRP, ESR, PC/MPV and plasma Fibrinogen in diagnosis of PJI among patients from three different groups |
|---------|--------------------------------------------------------------------------------|
|         |                  | True positive | False negative | sensitivity |
| CRP≥10 mg/L | 42 | 16 | 0.72<sup>a</sup> |
| ESR≥30 mm/h | 44 | 14 | 0.76<sup>b</sup> |
| PC/MPV≥31.70 | 27 | 31 | 0.47<sup>c</sup> |
| Plasma Fibrinogen≥4.01 μg/mL | 44 | 14 | 0.76<sup>d</sup> |

χ²=15.979, p=0.015. p<sub>ab</sub>=0.842; p<sub>ac</sub>=0.000, p<sub>ad</sub>=0.097, p<sub>bc</sub>=0.001, p<sub>bd</sub>=1.000; p<sub>cd</sub>=0.001. There are statistically significant differences when compared sensitivity of serum CRP and PC/MPV, ESR and PC/MPV, PC/MPV and plasma Fibrinogen in diagnosis of PJI among patients from three different groups when P value less than 0.017 was considered as significant difference.
### Table 3: Comparison of the specificity of serum CRP, ESR, PC/MPV and plasma Fibrinogen in diagnosis of PJI among patients from three different groups

| Test                  | True negative | False positive | Specificity |
|-----------------------|---------------|----------------|-------------|
| CRP ≤ 10 mg/L         | 88            | 14             | 0.86        |
| ESR ≤ 30 mm/h         | 87            | 15             | 0.85        |
| PC/MPV ≤ 31.70 µ/L    | 81            | 21             | 0.79        |
| Plasma Fibrinogen ≤ 4.01 µg/mL | 87            | 15             | 0.85        |

χ² = 2.251, p = 0.522. There are no statistically significant differences when compared specificity of serum CRP, ESR, PC/MPV and plasma Fibrinogen in diagnosis of PJI among patients from three different groups.