A SYSTEMATIC REVIEW AND META-ANALYSIS

Is D-dimer a reliable biomarker compared to ESR and CRP in the diagnosis of periprosthetic joint infection?

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Aims
The diagnosis of periprosthetic joint infection (PJI) has always been challenging. Recently, D-dimer has become a promising biomarker in diagnosing PJI. However, there is controversy regarding its diagnostic value. We aim to investigate the diagnostic value of D-dimer in comparison to ESR and CRP.

Methods
PubMed, Embase, and the Cochrane Library were searched in February 2020 to identify articles reporting on the diagnostic value of D-dimer on PJI. Pooled analysis was conducted to investigate the diagnostic value of D-dimer, CRP, and ESR.

Results
Six studies with 1,255 cases were included (374 PJI cases and 881 non-PJI cases). Overall D-dimer showed sensitivity of 0.80 (95% confidence interval (CI) 0.69 to 0.87) and specificity of 0.76 (95% CI 0.63 to 0.86). Sub-group analysis by excluding patients with thrombosis and hyper-coagulation disorders showed sensitivity of 0.82 (95% CI 0.70 to 0.90) and specificity of 0.80 (95% CI 0.70 to 0.88). Serum D-dimer showed sensitivity of 0.85 (95% CI 0.76 to 0.92), specificity of 0.83 (95% CI 0.74 to 0.90). Plasma D-dimer showed sensitivity of 0.67 (95% CI 0.60 to 0.73), specificity of 0.58 (95% CI 0.45 to 0.72). CRP showed sensitivity of 0.78 (95% CI 0.72 to 0.83), specificity of 0.81 (95% CI 0.72 to 0.87). ESR showed sensitivity of 0.68 (95% CI 0.63 to 0.73), specificity of 0.83 (95% CI 0.78 to 0.87).

Conclusion
In patients without thrombosis or a hyper-coagulation disorder, D-dimer has a higher diagnostic value compared to CRP and ESR. In patients with the aforementioned conditions, D-dimer has higher sensitivity but lower specificity compared to ESR and CRP. We do not recommend the use of serum D-dimer in patients with thrombosis and hyper-coagulation disorders for diagnosing PJI. Serum D-dimer may perform better than plasma D-dimer. Further studies are needed to compare serum D-dimer and plasma D-dimer in arthroplasty patients.

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Article focus
- Investigate how D-dimer, CRP, and ESR perform in patients without thrombosis and hyper-coagulation disorder.

Key messages
- D-dimer has higher sensitivity and lower specificity when compared with that of CRP and ESR.
Introduction

The need for arthroplasty surgeries continues to grow rapidly worldwide.1 Periprosthetic joint infection (PJI) is a devastating complication following arthroplasty surgeries. The reported prevalence of PJI varies greatly in different literatures: 1% to 4% after total knee arthroplasty (TKA) and 1% to 2% after total hip arthroplasty (THA), causing great social and economic burden in the healthcare system.2,3

The diagnosis of PJI has always been challenging and there is no 'gold standard' so far. Different techniques and biomarkers have been explored to improve diagnostic accuracy.4-6 The Musculoskeletal Infection Society (MSIS) criteria integrate laboratory and clinical findings and showed high reliability in clinical practice. In 2018, Parvizi et al7 updated the MSIS criteria by adding D-dimer as a minor criteria. Two points are scored if a patient has an elevated CRP or D-dimer, suggesting equal diagnostic value between CRP and D-dimer. Since 2018, several studies have looked into the diagnostic value of D-dimer:5 Huang et al8 suggested D-dimer is not suitable for distinguishing between PJI and aseptic loosening; Li et al9 and Xiong et al10 reported limited diagnostic value of D-dimer; and Shahi et al11 reported that D-dimer outperformed ESR and CRP in the diagnosis of PJI. Because PJI is a low-incidence complication following arthroplasty, there is still controversy over the diagnostic value of D-dimer. We aimed to gather existing evidence from published literature and conduct a meta-analysis based on large samples for the first time. The aim of this meta-analysis and systematic review is to: 1) investigate the diagnostic value of D-dimer as a biomarker in diagnosing PJI; 2) compare the diagnostic value of D-dimer, ESR, and CRP; and 3) explore potential causes influencing the diagnostic value of D-dimer.

Methods

Search strategy. PubMed, Embase, and the Cochrane Library were comprehensively searched in February 2020. Related search terms included: D-dimer, fibrin fragment D, joint, periprosthetic, arthroplasty, and infection. The search terms used in PubMed are as follows: \(	ext{(("fibrin fragment D"[supplementary Concept] OR "fibrin fragment D"[All Fields] OR "d dimer"[All Fields]) OR "fibrin fragment D"[supplementary Concept]) AND (("joints"[MeSH Terms] OR "joints"[All Fields] OR "joint"[All Fields]) AND ("infection"[MeSH Terms] OR "infection"[All Fields]))})\). All articles published before 2 February 2020 were screened. Additional studies were identified from references of retrieved articles.

Inclusion and exclusion criteria. Clinical trials were included if they: 1) included patients with previous history of arthroplasty surgery of the hip and knee; 2) applied clear and well-recognized diagnostic criteria for PJI; 3) investigated the diagnostic value of D-dimer in diagnosing PJI; 4) reported sensitivity, specificity, and other
IS D-DIMER A RELIABLE BIOMARKER IN THE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION?

Fig. 2

Quality assessment of all included studies using Quality Assessment of Diagnostic Accuracy Studies Version 2 (QUAdAs-2).

Table I. Study characteristics. All studies focused on both hip and knee arthroplasty.

| Author name | Country | Pub year | PJi, n | Non-PJi, n | Diagnostic criteria |
|-------------|---------|----------|--------|------------|---------------------|
| Huang J     | China   | 2019     | 31     | 70         | MSIS                |
| Li R        | China   | 2019     | 76     | 363        | ICM                 |
| Qin L       | China   | 2020     | 55     | 67         | MSIS                |
| Shahi       | USA     | 2017     | 23     | 86         | MSIS                |
| Xiong L     | China   | 2019     | 26     | 54         | MSIS                |
| Xu H        | China   | 2019     | 129    | 189        | MSIS                |

ICM, International Consensus Meeting; MSIS, Musculoskeletal Infection Society; PJi, periprosthetic joint infection; Pub, publication.

Results

Study characteristics. Basic characteristics of included studies are listed in Table I. Clear exclusion criteria were applied in five studies8–11,13 to rule out other confounding factors such as thrombosis and hyper-coagulation disorder, which may influence the interpretation of index results. The cut-off value of D-dimer ranged from 0.76 mg/l to 1.25 mg/l. All studies were published within the last three years. Blood sample was acquired after admission and prior to surgeries. Four studies tested serum D-dimer8,10,11,13 and two studies tested plasma D-dimer.9,14 Measuring techniques were not specified (Table I). Quality of included studies was assessed using QUADAS-2 and is shown in Figure 2.

Diagnostic value of D-dimer. Six studies were all included in our analysis, with 374 PJi cases and 881 non-PJi cases. Pooled sensitivity for D-dimer was 0.80 (95% CI 0.69 to 0.87) and pooled specificity was 0.76 (95% CI 0.63 to 0.86) (Figure 3). The area under the ROC curve (AUC) was 0.85 (95% CI 0.81 to 0.88) (Figure 4). The DOR for D-dimer was 12.06 (95% CI 3.96 to 36.74). Different exclusion criteria were applied in five studies8–11,13 which all excluded patients with thrombosis and hyper-coagulation disorders. A sub-group analysis was conducted including these five studies, the results are as follows: sensitivity 0.82 (95% CI 0.70 to 0.90), specificity 0.80 (95% CI 0.70 to 0.88), AUC 0.88 (95% CI 0.85 to 0.90), DOR 17.76 (95% CI 4.54 to 69.51). Pooled analysis for CRP and ESR were also conducted. Results from this analysis were recorded in Table II.

Sensitivity analysis. I² analysis showed substantial heterogeneity in sensitivity (I² = 87.68, 95% CI 79.26 to 96.09)
Fig. 3
Forest plot of the accuracy of d-dimer in the diagnosis of prosthetic joint infection. All p-values were calculated using bivariate effect model with logit transition. CI, confidence interval.

and specificity ($I^2 = 95.69$, 95% CI 95.53 to 97.86). The correlation (mixed model) was 0.83 and the proportion of heterogeneity likely due to threshold effect was 0.69, suggesting that threshold effect could be one of the causes for heterogeneity. Bivariate box plot (Figure 5) was then drawn to identify source of heterogeneity, which showed that five studies were within the 95% CI; using Stata 16 we were able to identify the one study11 outside the 95% CI zone. Sensitivity analysis was conducted by excluding the source of heterogeneity identified, which yielded the following results: sensitivity 0.80 (95% CI 0.66 to 0.89), specificity 0.73 (95% CI 0.66 to 0.80), and AUC 0.81 (95% CI 0.77 to 0.84). The result was consistent with previous analysis except for a small climb in specificity.

To further address a potential source of heterogeneity, multivariate meta-regression was performed to combine results from multiple studies with attention to between-study variation. Covariates including country, comorbidity, and serum/plasma test were analyzed (Table II). The results showed that serum or plasma testing method is a major cause of heterogeneity ($p = 0.01$). Sub-group analysis of serum and plasma D-dimer was conducted and results are listed in Table II. There are not enough studies to generate a summary ROC and DOR for plasma D-dimer.

**Publication bias.** Publication bias was assessed with Deek’s Funnel Plot Asymmetry Test (Figure 6). The p-value was 0.19; no significant publication bias was found.

**Discussion**
D-dimer is a fibrin degradation product produced in the coagulation process. Some studies have shown a correlation between coagulation and inflammation: coagulation-related biomarkers have a proinflammatory effect and persistent inflammatory response contributes to a hyper-coagulable state.15–17 Therefore, coagulation biomarkers including D-dimer may be elevated in infectious disease. Studies have reported D-dimer as diagnostic marker in infectious and inflammatory diseases including rheumatoid arthritis, bacteremia, endocarditis, pneumonia caused by *Mycoplasma pneumoniae*, and spontaneous bacterial peritonitis.18–22

Our analysis included six studies and 1,255 cases; pooled analysis of D-dimer showed sensitivity of 80% and specificity of 76%. Summary ROC curve suggested
IS D-DIMER A RELIABLE BIOMARKER IN THE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION?

Summary receiver operating characteristic (SROC) area under the curve (AUC) for the diagnostic value of D-dimer in prosthetic joint infection. SENS, sensitivity; SPEC, specificity.

Table II. Diagnostic value of D-dimer, CRP, and ESR. Values are displayed as estimates and 95% confidence intervals.

| Overall diagnostic accuracy of D-dimer, CRP, and ESR | Sensitivity       | Specificity       | SROC AUC           | DOR               |
|-----------------------------------------------------|------------------|------------------|-------------------|------------------|
| D-dimer                                             | 0.80 (0.69 to 0.87) | 0.76 (0.63 to 0.86) | 0.85 (0.81 to 0.88) | 12.06 (3.96 to 36.74) |
| CRP                                                 | 0.78 (0.72 to 0.83) | 0.81 (0.72 to 0.87) | 0.84 (0.81 to 0.87) | 15.17 (11.14 to 20.66) |
| ESR                                                 | 0.68 (0.63 to 0.73) | 0.83 (0.78 to 0.87) | 0.72 (0.68 to 0.76) | 10.03 (6.67 to 15.10) |

| In patients without thrombosis and hypercoagulation disorder | Sensitivity       | Specificity       | SROC AUC           | DOR               |
|---------------------------------------------------------------|------------------|------------------|-------------------|------------------|
| D-dimer                                                       | 0.82 (0.70 to 0.90) | 0.80 (0.70 to 0.88) | 0.88 (0.85 to 0.90) | 17.76 (4.54 to 69.51) |
| CRP                                                           | 0.77 (0.69 to 0.84) | 0.79 (0.68 to 0.87) | 0.84 (0.80 to 0.87) | 13.38 (9.29 to 19.27) |
| ESR                                                           | 0.68 (0.62 to 0.74) | 0.83 (0.77 to 0.88) | 0.71 (0.67 to 0.75) | 10.38 (5.99 to 17.99) |

| Diagnostic performance of D-dimer | Sensitivity       | Specificity       | SROC AUC           | DOR               |
|-----------------------------------|------------------|------------------|-------------------|------------------|
| Serum                             | 0.85 (0.76 to 0.92) | 0.83 (0.74 to 0.90) | 0.91 (0.88 to 0.93) | 28.25 (9.60 to 83.15) |
| Plasma                            | 0.67 (0.60 to 0.73) | 0.58 (0.45 to 0.72) | N/A               | N/A              |

AUC, area under the curve; DOR, diagnostic odds ratio; N/A, not available; SROC, summary receiver operating characteristic.

All studies were within the 95% prediction contour. The AUC was 0.85. Within the range of 0.5 to 1, the diagnostic value increases as AUC increases. The DOR was 12.06, exhibiting high diagnostic value. DOR reflects the connection between index result and the disease. In the case of DOR > 1, the diagnostic value increases as DOR increases. A Fagan nomogram (Figure 7) shows us the likelihood of a patient having PJI when the index test result is positive or negative through likelihood ratio and post-test probabilities. Given the pre-test probabilities of
50%, the post-test probabilities of a positive result was 77%, and the probabilities of a negative result was 21%. The positive likelihood ratio of 3 suggests that a patient with PJi is three-times more likely to have a positive test result than patients who do not have PJi.

When comparing D-dimer to CRP and ESR, D-dimer showed the highest sensitivity (similar to CRP), and the lowest specificity. The more false positives in D-dimer might be subjected to comorbidity of included patients. Five studies excluded patients with thrombosis and hyper-coagulable disorders, and subgroup analysis including these five studies yielded increased sensitivity (82%), specificity (80%), and the highest AUC and DOR compared to ESR and CRP. The result from our analysis did not perform as well as Shahi et al.,11 which may be due to patient population: Shahi et al11 and Parvizi et al7 included patients in the USA, and reported positively about the diagnostic value of D-dimer, while other studies8–10,13,14,23 in our analysis included an Asian population and the results were less optimal. We also found that serum D-dimer outperformed plasma D-dimer in sensitivity and specificity. Paniccia et al24 found that serum D-dimer is higher than plasma D-dimer in both pregnant and non-pregnant women. Our analysis showed that serum D-dimer outperforms plasma D-dimer in diagnostic value. Further studies are needed to compare serum and plasma D-dimer in arthroplasty patients.

The diagnosis of chronic PJi and PJi caused by low-virulence pathogens is more challenging. Positive culture is always difficult to acquire; it has been reported that the responsible pathogens are not identified in up to 50% of sepsis patients.25 Other auxiliary tests become critical when the major criteria are not met. CRP and ESR are the two most common biomarkers used in diagnosing PJi, but their limited diagnostic value have been reported in both chronic PJi and low-virulence-pathogen-related PJi.26,27 Qin et al13 found higher sensitivity (92.73%) of D-dimer compared to ESR and CRP in patients who had PJi-related symptoms for more than six weeks. Shahi et al11 reported five cases with elevated D-dimer, two of
which had a positive culture from samples taken during revision surgery; ESR and CRP were normal in these two patients. Lee et al. investigated the natural progression of D-dimer, CRP, and ESR; they found that D-dimer showed a more rapid rise and fall in early postoperative two weeks, which can be effective in early detection of PJ.

The diagnostic threshold for D-dimer varied among studies. Measured in mg/l, the threshold was 0.85 for Huang et al., 1.25 for Li, 1.17 for Qin, 0.85 for Shahi, 0.76 for Xiong, and 1.02 for Xu. An appropriate threshold was 0.85 for PJ. Studies measured in mg/l, the threshold was 0.85 for PJ. A more rapid rise and fall in early postoperative studies. Measured in mg/l, the threshold was 0.85 for PJ. The diagnostic threshold for D-dimer varied among studies. Measured in mg/l, the threshold was 0.85 for PJ. Which had a positive culture from samples taken during revision surgery; ESR and CRP were normal in these two patients. Lee et al. investigated the natural progression of D-dimer, CRP, and ESR; they found that D-dimer showed a more rapid rise and fall in early postoperative two weeks, which can be effective in early detection of PJ. The diagnostic threshold for D-dimer varied among studies. Measured in mg/l, the threshold was 0.85 for PJ. A more rapid rise and fall in early postoperative studies. Measured in mg/l, the threshold was 0.85 for PJ.

The limitations of our study are as follows: firstly, the test result of D-dimer was interpreted as positive or negative with different thresholds, and the level of D-dimer may change according to the severity of infection. Secondly, serum/plasma testing methods and comorbidity may cause heterogeneity. However, subgroup analysis conducted to investigate the diagnostic value of D-dimer in serum samples, plasma samples, and in patients without thrombosis and hyper-coagulation disorder. Thirdly, most of our included studies were retrospective due to the nature of our research. Finally, patients from Asia and the USA were all included in our analysis, which could be a source of bias.

The strengths of our study are as follows: firstly, PJ is a low-incidence complication following arthroplasty surgeries, and the sample sizes in studies investigating D-dimer in PJ diagnosis are relatively small. Our analysis gathered available data and provided results based on a relatively large sample size. Secondly, we further investigated any potential factors that might influence the diagnostic accuracy. We found that D-dimer has higher diagnostic value in patients without thrombosis and hyper-coagulation disorders, and also that serum D-dimer may perform better than plasma D-dimer.

In summary, in patients without thrombosis or a hyper-coagulation disorder, D-dimer has a higher diagnostic value compared to CRP and ESR. In patients with the aforementioned conditions, D-dimer has higher sensitivity but lower specificity compared to ESR and CRP. We do not recommend the use of serum D-dimer in patients with thrombosis and hyper-coagulation disorders for diagnosing PJ. Serum D-dimer may perform better than plasma D-dimer. Further studies are needed to compare serum D-dimer and plasma D-dimer in arthroplasty patients.

References
1. Maradit Kremers H, Larson DR, Crowson CS, et al. Prevalence of total hip and knee replacement in the United States. J Bone Joint Surg Am. 2015;97-A(17):1386–1397.
2. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty. 2012;27(8 Suppl):S1–S65.
3. Ahmed SS, Haddad FS. Periprosthetic joint infection. Bone Joint Res. 2019;8(11):570–572.
4. Chen M-F, Chang C-H, Chiang-Ni C, et al. Rapid analysis of bacterial composition in prosthetic joint infection by 16S rRNA metagenomic sequencing. Bone Joint Res. 2019;8(9):367–377.
5. Saleh A, George J, Facour M, Klika AK, Higuera CA. Serum biomarkers in periprosthetic joint infections. Bone Joint Res. 2018;7(1):85–93.
6. Chen M-F, Chang C-H, Yang L-Y, et al. Synovial fluid interleukin-16, interleukin-18, and CRELD2 as novel biomarkers of prosthetic joint infections. Bone Joint Res. 2019;8(4):179–188.
7. Parvizi J, Tan TL, Goswami K, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33(6):1305–1314.
8. Huang J, Zhang Y, Wang Z, et al. The serum level of D-dimer is not suitable for distinguishing between prosthetic joint infection and aseptic loosening. J Orthop Surg Res. 2019;14(1):407.
9. Li R, Shao H-Y, Hao L-B, et al. Plasma fibrinogen exhibits better performance than plasma D-dimer in the diagnosis of periprosthetic joint infection: a multicenter retrospective study. J Bone Joint Surg Am. 2019;101-A(7):613–619.
10. Xiong L, Li S, Dai M. Comparison of D-dimer with CRP and ESR for diagnosis of periprosthetic joint infection. J Orthop Surg Res. 2019;14(1):240.
11. Shahi A, Kheir MM, Tarabichi M, Hosseinzadeh HR, Tan TL, Parvizi J. Serum D-dimer test is promising for the diagnosis of periprosthetic joint infection and timing of reimplantation. J Bone Joint Surg Am. 2017;99-A(17):1419–1427.
12. Wade R, Corbett M, Eastwood A. Quality assessment of comparative diagnostic accuracy studies: our experience using a modified version of the QUADAS-2 tool. Res Synth Methods. 2013;4(3):280–286.
13. Qin L, Li F, Gong X, Wang J, Huang W, Hu N. Combined measurement of D-dimer and C-reactive protein levels: highly accurate for diagnosing chronic periprosthetic joint infection. J Arthroplasty. 2020;35(1):229–234.
14. Xu H, Xie J, Huang Q, Lei Y, Zhang S, Fei F. Plasma fibrin degradation product and D-dimer are of limited value for diagnosing periprosthetic joint infection. J Arthroplasty. 2019;34(10):2454–2460.
15. Cicala C, Cirino G. Linkage between inflammation and coagulation: an update on the molecular basis of the crosstalk. Life Sci. 1998;62(20):1817–1824.
16. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. Circulation. 2001;103(3):1718–1720.
17. Chung S, Kim J-E, Park S, Han K-S, Kim HK. Neutrophil and monocyte activation markers have prognostic impact in disseminated intravascular coagulation: in vitro effect of thrombin on monocyte CD163 shedding. Thromb Res. 2011;127(5):450–456.
18. Mikouta T, Sagula M, Jabouisaka J, et al. Significance of heparin-binding protein and D-dimers in the early diagnosis of spontaneous bacterial peritonitis. Mediat Inflamm. 2018;2018:1–6.
19. Turak C, Canpolat U, Ozcan F, et al. D-dimer level predicts in-hospital mortality in patients with infective endocarditis: a prospective single-centre study. Thromb Res. 2014;134(3):587–592.
20. Schwamweiss M, Steiner MM, Schörgenhofer C, et al. D-dimer and histamine in early stage bacteremia: a prospective controlled cohort study. Eur J Intern Med. 2015;26(10):782–786.
21. Mielé N, Turc G. Stroke associated with recent Mycoplasma pneumoniae infection: a systematic review of clinical features and presumed pathophysiological mechanisms. Front Neurol. 2018;9:1109.
22. Tan L, Wang Q, Zeng T, et al. Clinical significance of detecting HLA-DR, 14-3-3 protein and D-dimer in the diagnosis of rheumatoid arthritis. Biomark Med. 2018;12(7):697–705.
23. Fu J, Ni M, Chai W, Li X, Hao L, Chen J. Synovial fluid viscosity test is promising for the diagnosis of periprosthetic joint infection. J Arthroplasty. 2019;34(6):1192–1200.
24. Pasinella R, Prisco D, Bandinelli B, et al. Plasma and serum levels of D-dimer and their correlations with other hemostatic parameters in pregnancy. Thromb Res. 2002;105(3):257–262.
25. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348(16):1548–1554.
26. Akgün D, Müller M, Perka C, Winkler T. The serum levels of C-reactive protein alone cannot be used for the diagnosis of prosthetic joint infections, especially in those caused by organisms of low virulence. Bone Joint J. 2018;100-B(11):1482–1486.
27. Pérez-Prieto D, Portillo ME, Puig-Verdier L, et al. C-reactive protein may misdiagnose prosthetic joint infections, particularly chronic and low-grade infections. Int Orthop. 2017;41(7):1315–1319.

28. Lee YS, Lee YK, Han SB, Nam CH, Parvizi J, Koo KH. Natural progress of D-dimer following total joint arthroplasty: a baseline for the diagnosis of the early postoperative infection. J Orthop Surg Res. 2018;13(1):36.

Author contributions:
- X Chen: Acquired the data, Conducted the statistical analysis, Wrote the manuscript.
- H Li: Crosschecked the data, Handled the reviewer correspondence.
- S Zhu: Conducted the statistical analysis, Extracted the data, Assessed the quality of the included studies.
- Y Wang: Co-wrote the manuscript, Extracted the data.
- W Qian: Designed the study, Oversaw the study’s quality control.

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