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INFECTION

Centrifugation may eliminate false-positive leucocyte esterase strip test results caused by inflammatory arthritis in the diagnosis of knee infection

A PILOT STUDY

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Aims

The purpose of this study was to validate our hypothesis that centrifugation may eliminate false-positive leucocyte esterase (LE) strip test results caused by autoimmune diseases in the diagnosis of knee infection.

Methods

Between January 2016 and May 2019, 83 cases, including 33 cases of septic arthritis and 50 cases of aseptic arthritis, were enrolled in this study. To further validate our hypothesis, another 34 cases of inflammatory arthritis from the Department of Rheumatology of our institution were also included. After aspiration, one drop of synovial fluid was applied to LE strips before and after centrifugation. The results were recorded after approximately three minutes according to the different colour grades on the colour chart. The differences of LE results between each cohort were analyzed.

Results

Before centrifugation, 46% (23/50) of the LE strip tests in the aseptic arthritis group were false-positives. Most of the false-positive results were due to inflammatory arthritis; after centrifugation, 78.3% (18/23) of the tests yielded negative results. Similar results were observed in cases from the Department of Rheumatology. The sensitivity of the centrifuged LE strip test was 0.818 (0.639 to 0.924), which is still an acceptable level compared with the uncentrifuged results, which yielded a sensitivity of 0.909 (0.745 to 0.976). However, the specificity was increased from 0.540 (0.395 to 0.679) to 0.900 (0.774 to 0.963) after centrifugation.

Conclusion

Although inflammatory arthritis can yield a false-positive LE strip test result in the diagnosis of knee infection, centrifugation may eliminate these false-positive results.

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Keywords: Leucocyte esterase, Infection, Inflammatory arthritis

Article focus

- A thorny problem facing surgeons in the diagnosis of septic arthritis is the interference of autoimmune diseases causing inflammatory arthritis.
- The results of the leucocyte esterase (LE) strip test may both positive for these diseases.
- The present study focuses on whether centrifugation would eliminate these false-positive LE results caused by inflammatory arthritis.

Key messages

- The present study illustrates that although inflammatory arthritis can yield

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a false-positive LE strip test result in the diagnosis of knee infection, centrifugation may eliminate this false-positive result.

Strengths and limitations

- This is the first study to discuss the phenomenon that centrifugation may eliminate false-positive leucocyte esterase strip test results caused by inflammatory arthritis in the diagnosis of knee infection.
- Cases from the Department of Rheumatology of our institution were included as corroborative evidence.
- A limitation is that the sample size was not large.

Introduction

The presentation of a patient with a painful and/or swollen native knee, especially with an elevated ESR or CRP, is not uncommon in orthopaedic outpatient clinics, and septic arthritis may be one of the major concerns in the broad differential diagnosis of this condition. However, in addition to septic arthritis, the symptoms may also be caused by inflammatory arthritis such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS).[1] Timely and accurate differentiation of septic arthritis from inflammatory arthritis is critical because these two diseases require very different treatments. Targeted antibiotics or joint debridement are necessary for the treatment of septic arthritis, whereas steroids and/or immunosuppressive drugs, which could aggravate septic cases, may be required for inflammatory arthritis. However, the diagnosis of septic arthritis can be challenging, even for doctors skilled in the management of musculoskeletal disease.[2]

Synovial fluid culture can be key in the diagnosis of septic arthritis. However, these cultures are positive in only 67% of non-gonococcal arthritis cases,[3] and if the specimens are obtained after the initiation of antibiotic treatment a positive culture may be more difficult to obtain. Moreover, obtaining the results of culture usually requires multiple days or even weeks. Other indicators, such as the white blood cell (WBC) count, ESR, and serum CRP may not distinguish septic arthritis from other forms of acute arthritis.[4] In addition, synovial fluid markers, including the synovial WBC count and polymorphonuclear percentage (PMN%), can also be imprecise.[5,6] Thus, using these markers may not be ideal for solving this problem.

The use of the leucocyte esterase (LE) strip test in the diagnosis of prosthetic joint infection (PJI) has been well studied since it was first reported in 2011.[7–10] Additional studies demonstrated that this simple and fast method could perform well in detecting native joint infections.[11, 12] However, there is a concern that inflammatory arthritis may yield false-positive results, although this concern has not been well researched. Thus, cases with such conditions were excluded in a previous study that evaluated the false-positive rates of the LE strip test in the diagnosis of native joint infection.[12] In our previous clinical experience, we found that inflammatory arthritis indeed causes false-positive LE strip test results in the diagnosis of joint infection. However, an interesting phenomenon was observed accidently. We found that several false-positive LE results in cases with inflammatory arthritis became negative after centrifugation. Thus, we hypothesized that centrifugation could eliminate autoimmune disease-induced false-positive LE strip test results in the diagnosis of joint infection, and that the LE strip test can be used as a simple method to distinguish inflammatory arthritis from septic arthritis.

The purpose of this study was to validate our hypothesis by analyzing the results of LE strip tests with or without centrifugation in septic, aseptic, and inflammatory arthritis cohorts.

Methods

Our institution's research ethics board approved this study, and all patients who participated in this study provided written informed consent. Between January 2016 and May 2019, we performed diagnostic aspirations on 108 consecutive native knees with any suspicion of infection. Cases meeting the following criteria were excluded: no valid synovial fluid samples (11 cases); unreadable LE strip test results without centrifugation due to colour disturbance caused by blood contamination (five cases); and loss of follow-up or any other reasons leading to insufficient information for confirming or ruling out infection (nine cases). Finally, 83 cases were included in the study.

After aspiration, one drop of synovial fluid was immediately applied to LE strip test pads (10PA AUTION Sticks; Arkray, Kyoto, Japan). The LE strip test results were read based on the change in the strip pad colour after approximately three minutes (Figure 1). When the LE strip test was complete, the synovial fluid was centrifuged (6,600 rpm, 180 seconds, as recommended by Aggarwal et al).[13] After centrifugation, we collected the supernatant and applied one drop to a new LE strip test pad, and the results were recorded. Different colour grades were used according to a colour chart (Figure 1). We divided the results into three grades. Grade 3 was positive (dark purple, labeled as "500" on the colour chart), Grade 2 was intermediate (light purple, labeled as "250" on the colour chart), and Grade 1 was negative (others). Based on a previous study,[14] we defined only Grade 3 as positive before centrifugation and both Grade 3 and Grade 2 as positive after centrifugation. The LE results of the samples before and after centrifugation were read by RL, CW, QYZ, XL, and MN (any three of these authors for each case). The observers were blinded to any diagnostic information about the patients. If there were any inconsistencies in the recorded results among the three observers, the grade with the highest agreement was considered the final result.

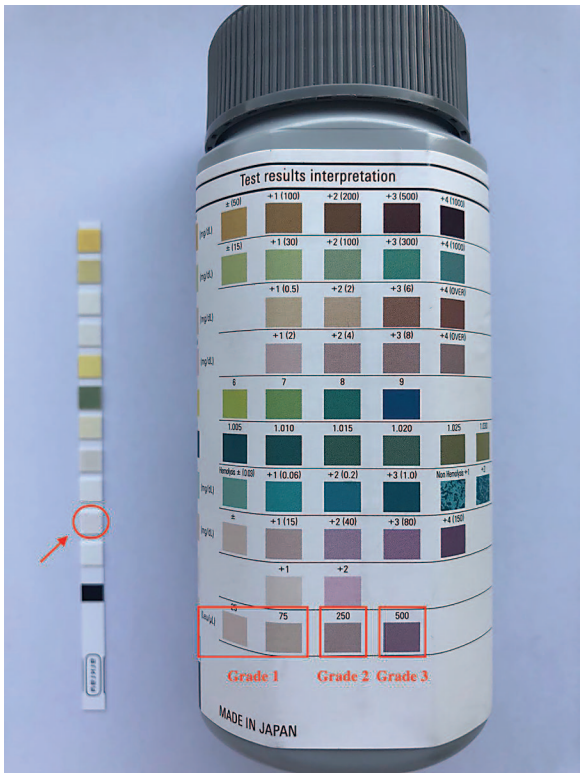

Fig. 1

Definitions of colour grades. The arrow points to the area where one drop of synovial fluid was applied. The results were read based on the change in the strip pad colour after approximately three minutes. We divided the results into three grades: Grade 3 (dark purple, "500", equal to + +) was positive, Grade 2 (light purple, "250", equal to +) was intermediate, and Grade 1 (other colours) was negative.

In addition, to further confirm our results 34 cases from the Department of Rheumatology of our institution were also enrolled in this study. All patients were diagnosed with inflammatory arthritis by their physicians and required intra-articular injection of betamethasone and/or etanercept (tumour necrosis factor (TNF) inhibitor) into their knees. The synovial fluid was collected before the injection. The LE strip test procedure was the same as that performed on the patients from the Department of Orthopedics of our institution.

We defined septic arthritis as: two positive cultures with phenotypically identical organisms; a sinus tract communicating with the joint; or a single positive culture and cure with sensitive antibiotic treatment. The confirmation of noninfectious arthritis depended on the presence of a negative culture and cure or remission of symptoms without antibiotic treatment. All patients had at least three months of follow-up. In addition, in the aseptic arthritis group from the Department of Orthopedics patients with any suspicion of inflammatory arthritis were referred to a rheumatologist for further confirmation.

Statistical analysis. The statistical analysis was performed using IBM SPSS Statistics for Mac version 21.0.0.0 (IBM, Armonk, New York, USA), and $p < 0.05$ was considered significant. We used the Mann-Whitney U test to analyze continuous variables, and a chi-squared test was used for categorical variables. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and corresponding 95% confidence intervals (CIs) of the LE strip test results were calculated using a statistics website (http://vassarstats.net/clin1.html).[15]

Results

Among the cases from the Department of Orthopedics of our institution, 33 cases had septic arthritis and 50 cases had aseptic arthritis. The characteristics of these patients are shown in Table I. In the septic arthritis group, the pathogens included six cases of *Staphylococcus aureus*, five cases of coagulase-negative staphylococci, three cases of *Aspergillus* species, three cases of *Candida* species, two cases of Gram-positive bacilli, two cases of *Nocardia* species, one case of *Brucella* species, one case of *Cutibacterium acnes*, one case of *Enterococcus faecium*, one case of non-tuberculous mycobacteria, one case of *Acinetobacter baumannii*, one case of *Escherichia coli*, three cases of multiple infection, and two cases of negative culture.

The results of the LE strip tests in these cases are shown in Table II. After centrifugation, in the septic arthritis group three cases were downgraded from Grade 3 to Grade 2, four cases were downgraded from Grade 3 to Grade 1, and one case was downgraded from Grade 2 to Grade 1. One case remained in Grade 2, one case remained in Grade 1, and all others remained in Grade 3. Based on the abovementioned methods, we used Grade 3 as the positive threshold for cases without centrifugation, and both Grade 3 and Grade 2 cases were considered positive after centrifugation. Thus, 12.1% (4/33) of

Table I. Characteristics of the cases enrolled from the Department of Orthopedics, Chinese PLA General Hospital, Beijing, China

Variable	Septic arthritis (n = 33)	Aseptic arthritis (n = 50)	p-value
Sex, n (%)			0.103*
Male	15 (45.45)	14 (28.00)	
Female	18 (54.55)	36 (72.00)	
Median age, yrs (IQR)	62 (57 to 69)	63 (55 to 69)	0.915†
Median BMI, kg/m^2 (IQR)	25.95 (21.94 to 27.10)	24.22 (22.08 to 27.12)	0.682†
Median ESR level, mm/h (IQR)	51 (29 to 79)	32 (15 to 54)	0.017†
Mean serum CRP level, mg/l (IQR)	16.00 (11.32 to 53.32)	10.55 (2.23 to 21.75)	0.035†

*Chi-squared test.
†Mann-Whitney U test.
BMI, body mass index; IQR, interquartile range.

Table II. Leucocyte esterase strip test results with and without centrifugation

Diagnosis	Before centrifugation, n				After centrifugation, n			
	Grade 3	Grade 2	Grade 1	Total	Grade 3	Grade 2	Grade 1	Total
Septic arthritis	30	2	1	33	23	4	6	33
Aseptic arthritis	23	4	23	50	1	4	45	50
Inflammatory arthritis*	29	2	3	34	0	6	28	34

*Cases were recruited from the Department of Rheumatology, Chinese PLA General Hospital, Beijing, China.

the cases of positive LE strip test results became negative. In the aseptic arthritis group, 46% (23/50) of the cases were false-positives (Grade 3) before centrifugation. However, 78.3% (18/23) of the LE false-positive cases became negative after centrifugation. The sensitivity, specificity, PPV, and NPV of the uncentrifuged LE strip test were 0.909 (0.745 to 0.976), 0.540 (0.395 to 0.679), 0.566 (0.424 to 0.699), and 0.900 (0.723 to 0.974), respectively. In contrast, a centrifuged LE strip test yielded a sensitivity, specificity, PPV, and NPV of 0.818 (0.639 to 0.924), 0.900 (0.774 to 0.963), 0.844 (0.665 to 0.941), and 0.882 (0.754 to 0.951), respectively.

In a further review of these false-positive cases (Grade 3) before centrifugation (shown in Table III), most cases had an elevated level of ESR, CRP, synovial WBC count, or synovial PMN%. After the review of the cases, 5/23 remained false-positives even after centrifugation (cases 19 to 23). For the other 18 cases with changed results (from Grade 3 to Grade 1 after centrifugation), 61.1% (11/18) of the cases were given a definite diagnosis of inflammatory disease by Prof Jiang-Lin Zhang (see Acknowledgements) and author XJJ at the Department of Rheumatology, including eight cases of RA, one case of PsA, and two cases of reactive arthritis. Notably, although the other 7/18 cases did not receive a definitive diagnosis by a rheumatologist, after at least three months of follow-up all of these cases exhibited remission with steroid therapy, physical therapy, or traditional Chinese medicine therapy without any antibiotic usage. After a review of the LE-negative cases, most were given a definitive diagnosis of osteoarthritis. These findings strongly suggest that: inflammatory arthritis could cause a false-positive LE strip test result; centrifugation may eliminate inflammatory arthritis-induced false-positive LE strip tests in the diagnosis of knee infection; and that when the result of an LE strip test changes from positive to negative after centrifugation, the diagnosis is likely inflammatory arthritis.

A similar phenomenon, that centrifugation eliminated false-negative LE results, was also observed for cases enrolled from the Department of Rheumatology. The 34 cases included 19 cases of RA, three cases of AS involving the knee, three cases of spondyloarthritis (SPA) involving the knee, three cases of gout, two cases of RA combined with AS, two cases of Behçet's disease involving the knee, one case of PsA, and one case of RA combined with PsA. The LE strip test results are shown in Table II. We determined that 85.3% (29/34) of the inflammatory arthritis cases exhibited positive results on the LE strip test before centrifugation. After centrifugation, only 17.6% (6/34) of the cases exhibited positive results. The results of approximately 79.3% (23/29) of false-positive cases changed after centrifugation, which further confirmed our conclusion.

Discussion

A thorny problem facing surgeons in the diagnosis of septic arthritis is the interference of autoimmune diseases causing inflammatory arthritis. The present study illustrates that although inflammatory arthritis could yield false-positive LE strip test results in the diagnosis of knee infection, centrifugation may eliminate most of these false-positives.

The use of the LE strip test in the diagnosis of PJI has been well studied since it was first reported in 2011.[7–9] For native joints, the LE strip test has been demonstrated to be a good method for the diagnosis of septic arthritis.[11,12] However, there is still concern that this simple yet accurate method may be inaccurate in the presence of autoimmune disease. In the present study, 46% (23/50) of the LE strip test results in the aseptic arthritis group were falsely positive before centrifugation. After reviewing these false-positive cases (Table III), most cases had inflammatory arthritis. In addition, 85.3% (29/34) of inflammatory arthritis cases from the Department of Rheumatology were positive results. These findings confirm that inflammatory arthritis could yield a false-positive result.

However, after centrifugation, 78.3% (18/23) of these false-positive cases became negative results. The sensitivity of the centrifuged LE strip test was 0.818 (0.639 to 0.924), which is still an acceptable level compared with the uncentrifuged results, which yielded a sensitivity of 0.909 (0.745 to 0.976). However, the specificity was increased from 0.540 (0.395 to 0.679) to 0.900 (0.774 to 0.963) after centrifugation. Most of these cases with changed results involved inflammatory arthritis. Although some other cases have no final definite diagnosis yet, their elevated synovial WBC count and PMN% highly suggest a noninfectious inflammatory condition of the joints (Table III). The results of approximately 79.3% (23/29) of the false-positive cases from the Department of Rheumatology changed after centrifugation, supporting the findings observed in cases from the Department of Orthopedics. Thus, simple centrifugation could eliminate the interference of intra-articular inflammatory conditions in the diagnosis of septic arthritis.

Table III. Characteristics of cases with false-positive leucocyte esterase results before centrifugation in the aseptic arthritis group

Case	Diagnosis	LE strip test		Sex	Age, yrs	BMI, kg/m²	ESR, mm/h	CRP, mg/l	Synovial WBC count*	Synovial PMN%*	Culture	Outcome
		Before centrifugation	After centrifugation									
1	Aseptic (RA)	Grade 3	Grade 1	M	54	24.22	39	14.36	11,100	0.92	Negative	Remission
2	Aseptic (RA)	Grade 3	Grade 1	M	62	24.30	63	8.44	NR	NR	Negative	Remission
3	Aseptic (RA)	Grade 3	Grade 1	M	59	21.51	45	50.10	18,000	0.50	Negative	TKA after remission
4	Aseptic (RA)	Grade 3	Grade 1	F	72	27.12	56	84.20	NR	0.75	Negative	TKA after remission
5	Aseptic (RA)	Grade 3	Grade 1	F	52	22.19	65	30.40	43,200	0.98	Negative	TKA after remission
6	Aseptic (RA)	Grade 3	Grade 1	F	63	27.34	33	18.27	NR	NR	Negative	TKA after remission
7	Aseptic (RA)	Grade 3	Grade 1	F	57	23.33	90	12.50	11,040	0.96	Negative	Remission
8	Aseptic (RA)	Grade 3	Grade 1	F	70	35.16	30	20.28	9,030	0.70	Negative	Remission
9	Aseptic (PsA)	Grade 3	Grade 1	F	57	28.31	32	9.74	46,800	0.95	Negative	Remission
10	Aseptic (reactive arthritis)	Grade 3	Grade 1	F	55	28.72	34	22.00	29,030	0.87	Negative	Remission
11	Aseptic (reactive arthritis)	Grade 3	Grade 1	F	29	23.88	51	21.00	47,700	0.98	Negative	Remission
12	Aseptic (NDD)	Grade 3	Grade 1	F	64	25.39	62	84.59	15,000	0.60	Negative	Remission
13	Aseptic (NDD)	Grade 3	Grade 1	F	60	20.83	114	92.87	6,210	0.94	Negative	Remission
14	Aseptic (NDD)	Grade 3	Grade 1	F	69	29.59	74	42.72	2,070	0.74	Negative	TKA after remission
15	Aseptic (NDD)	Grade 3	Grade 1	M	59	27.68	2	1.00	5,600	0.84	Negative	TKA after remission
16	Aseptic (NDD)	Grade 3	Grade 1	F	28	17.78	48	1.00	58,400	0.98	Negative	Remission
17	Aseptic (NDD)	Grade 3	Grade 1	F	64	22.04	88	18.32	NR	NR	Negative	Remission
18	Aseptic (NDD)	Grade 3	Grade 1	F	31	30.04	55	227.00	12,400	0.90	Negative	Remission
19	Aseptic (RA)	Grade 3	Grade 3	F	59	23.63	91	128.00	NR	NR	Negative	TKA after remission
20	Aseptic (RA)	Grade 3	Grade 2	M	78	16.90	31	27.62	900	NR	Negative	TKA after remission
21	Aseptic (NDD)	Grade 3	Grade 2	F	81	27.11	92	98.60	NR	NR	Negative	Remission
22	Aseptic (NDD)	Grade 3	Grade 2	F	64	20.03	38	41.00	14,400	0.97	Negative	Remission
23	Aseptic (NDD)	Grade 3	Grade 2	F	51	26.56	32	10.49	11,100	0.92	Negative	Remission

*Data marked "NR" were not reported by the Medical Laboratory Center, because the synovial fluid was too viscous and the white blood cell count or polymorphonuclear percentage could not be counted.
BMI, body mass index; LE, leucocyte esterase; NDD, no definite diagnosis; PMN%, polymorphonuclear percentage; PsA, psoriatic arthritis; RA, rheumatoid arthritis; TKA, total knee arthroplasty; WBC, white blood cell.

The mechanisms of this interference removal method remain unclear. Only a few studies have evaluated the impact of centrifugation on LE strip test results.[14,16] However, none of these studies could provide any information to help explain why most of the results of inflammatory arthritis cases would become negative after centrifugation, namely, why there was very little LE left in the supernatant. LE is an enzyme secreted by activated neutrophils that have been recruited to areas of infection, and is found both inside and outside of neutrophils.[16] As centrifugation is used to separate the cells (relatively heavier substances) from the fluid, it has very little influence on relatively lighter substances, such as LE. One possible explanation for this phenomenon may be that in inflammatory arthritis, although many neutrophils are recruited to the joint (as in septic arthritis), the neutrophils are not fully activated to secrete LE, or passively released LE is not caused by the lysis of leucocytes after phagocytizing bacteria, and very little or no LE is secreted outside of the cell. Alternatively, perhaps after centrifugation, the LE is eliminated along with the neutrophils from the supernatant. Thus, the LE strip test results turn negative. However, confirming these hypotheses requires further investigation by specifically designed studies.

Nevertheless, the results of this study show very promising prospective applications for the LE strip test. First, although centrifugation could not eliminate all false-positive cases, it could correct most of the false-positive results, especially those caused by inflammatory arthritis, and highly improve the diagnostic accuracy of the LE strip test. Additionally, based on our data, 61.1% (11/18) of the cases with changed results had a definitive diagnosis of inflammatory arthritis and a similar phenomenon was also observed for cases enrolled from the Department of Rheumatology. These may indicate that when the result of an LE strip test changes from positive to negative after centrifugation, doctors should be aware of the possibility of inflammatory arthritis and consider whether a specialist consultation is needed, especially for cases that do not have a definite diagnosis of infection.

There were several limitations to the present study. First, when interpreting the LE results, the readers were

blinded only to diagnostic information about patients and not to the LE results prior to centrifugation. Knowledge of the results obtained before centrifugation might, in theory, have influenced the subsequent reading. In addition, different brands of LE strips and different centrifugation conditions may influence the results. Whether changes in these parameters will affect the results requires further confirmation. Finally, since this study was a pilot study, the sample size was not large. Additional studies with a larger number of cases may be needed to further confirm our conclusions.

In conclusion, although inflammatory arthritis can yield a false-positive LE strip test result in the diagnosis of knee infection, centrifugation may eliminate these false-positive results. When the result of the LE strip test changes from positive to negative after centrifugation, inflammatory arthritis should be taken into consideration, especially for cases that do not have a definite diagnosis of infection.

References

1. **Ledingham J, Snowden N, Ide Z.** Diagnosis and early management of inflammatory arthritis. *BMJ.* 2017;358:j3248.
2. **Mathews CJ, Weston VC, Jones A, Field M, Coakley G.** Bacterial septic arthritis in adults. *Lancet.* 2010;375(9717):846-855.
3. **Weston VC, Jones AC, Bradbury N, Fawthrop F, Doherty M.** Clinical features and outcome of septic arthritis in a single UK Health District 1982-1991. *Ann Rheum Dis.* 1999;58(4):214-219.
4. **Söderquist B, Jones I, Fredlund H, Vikerfors T.** Bacterial or crystal-associated arthritis? Discriminating ability of serum inflammatory markers. *Scand J Infect Dis.* 1998;30(6):591-596.
5. **Kortekangas P, Aro HT, Tuominen J, Toivanen A.** Synovial fluid leukocytosis in bacterial arthritis vs. reactive arthritis and rheumatoid arthritis in the adult knee. *Scand J Rheumatol.* 1992;21(6):283-288.
6. **Löffler C, Sattler H, Peters L, et al.** In arthritis the Doppler based degree of hypervascularisation shows a positive correlation with synovial leukocyte count and distinguishes joints with leukocytes greater and less than 5/nL. *Joint Bone Spine.* 2016;83(5):517-523.
7. **Parvizi J, Jacovides C, Antoci V, Ghanem E.** Diagnosis of periprosthetic joint infection: the utility of a simple yet unappreciated enzyme. *J Bone Joint Surg Am.* 2011;93-A(24):2242-2248.
8. **Lee YS, Koo KH, Kim HJ, et al.** Synovial fluid biomarkers for the diagnosis of periprosthetic joint infection: a systematic review and meta-analysis. *J Bone Joint Surg Am.* 2017;99-A(24):2077-2084.
9. **Shahi A, Tan TL, Kheir MM, Tan DD, Parvizi J.** Diagnosing Periprosthetic Joint Infection: And the Winner Is? *J Arthroplasty.* 2017;32(9S):S232-S235.
10. **Zagra L, Villa F, Cappelletti L, Gallazzi E, Materazzi G, De Vecchi E.** Can leucocyte esterase replace frozen sections in the intraoperative diagnosis of prosthetic hip infection? *Bone Joint J.* 2019;101-B(4):372-377.
11. **Gautam VK, Saini R, Sharma S.** Effectiveness of leucocyte esterase as a diagnostic test for acute septic arthritis. *J Orthop Surg (Hong Kong).* 2017;25(1):2309499016685019.
12. **McNabb DC, Dennis DA, Kim RH, Miner TM, Yang CC, Jennings JM.** Determining false positive rates of leukocyte esterase reagent strip when used as a detection tool for joint infection. *J Arthroplasty.* 2017;32(1):220-222.
13. **Aggarwal VK, Tischler E, Ghanem E, Parvizi J.** Leukocyte esterase from synovial fluid aspirate: a technical note. *J Arthroplasty.* 2013;28(1):193-195.
14. **Li R, Lu Q, Zhou YG, Chai W, Lu SB, Chen JY.** Centrifugation May Change the Results of Leukocyte Esterase Strip Testing in the Diagnosis of Periprosthetic Joint Infection. *J Arthroplasty.* 2018;33(9):2981-2985.
15. **No authors listed.** From an Observed Sample: Estimates of Population Prevalence, Sensitivity, Specificity, Predictive Values, and Likelihood Ratios. 2019. http://vassarstats.net/clin1.html (date last accessed 21 August 2019).
16. **Ruangsomboon P, Chinprasertsuk S, Khejonnit V, Chareancholvanich K.** Effect of depth of centrifuged synovial fluid on leukocyte esterase test for periprosthetic joint infection. *J Orthop Res.* 2017;35(11):2545-2550.

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Author contributions

- R. Li: Collected and analyzed the data, Performed the methodology, Wrote and edited the original draft of the manuscript.
- C. Wang: Collected and analyzed the data, Performed the methodology, Wrote and edited the original draft of the manuscript.
- X-J. Ji: Collected the data, Performed the methodology, Wrote and edited the manuscript.
- Q-Y. Zheng: Collected and analyzed the data, Wrote and edited the manuscript.
- X. Li: Collected the data, Wrote and edited the manuscript.
- M. Ni: Collected the data, Wrote and edited the manuscript.
- G-Q. Zhang: Conceptualized and supervised the study, Performed the validation, Wrote and edited the manuscript.
- J-Y. Chen: Conceptualized and supervised the study, Performed the validation, Wrote and edited the manuscript.

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Conflict of interest statement

- None declared

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Ethical review statement

- This article has been approved by the Medical Ethics Committee of the Chinese PLA General Hospital.