

PEER-REVIEW REPORT

Name of journal: World Journal of Orthopedics

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Title: Performance of Alpha-defensin Lateral Flow test after synovial fluid centrifugation for diagnosis of periprosthetic knee infection

Reviewer's code: 01587889

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Lecturer, Surgeon

Reviewer's Country/Territory: United States

Author's Country/Territory: Brazil

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Periprosthetic joint infection (PJI) following total joint arthroplasty is a serious complication that causes severe morbidity and adds a major financial burden to the healthcare system. Although there is plenty of research on the alpha-defensin (AD) test, a meta-analysis consisting of only prospective studies investigating AD's diagnostic efficacy has not been performed. Additionally, some important subgroups (such as total hip arthroplasty (THA) and Total knee arthroplasty (TKA)) have not been separately analyzed, particularly regarding two commonly used versions of the AD test, the laboratory-based (ELISA) and lateral-flow (LF). Abdo et al. is an original research article aimed to conduct a prospective, cross-section diagnostic study to assess the performance of the alpha defensin and evaluate whether a prior synovial fluid centrifugation could lead the lateral flow performance to achieve comparable results to enzyme-linked immunosorbent assay (ELISA) during Periprosthetic joint infection (PJI) diagnosis after TKA. The primary outcome was to evaluate the sensitivity, specificity, and accuracy of the lateral flow test post fluid centrifugation. Secondly, assessed the performance of the alpha-defensin ELISA in the same population of study, and compared the results between both modalities. They found that HNP1-3 lateral flow test showed high sensitivity, specificity, and accuracy after a prior synovial fluid centrifugation, achieving comparable results to ELISA. Considering the lower complexity of the lateral flow and its equivalent performance obtained in this condition, investigators concluded that a prior centrifugation might be added as a valuable step to enhance the PJI diagnosis. Recommendations: 1. The title should clearly state "human alpha-defensins (HNP1-3)". This is important to avoid confusion to readers that has nothing to do with "Alpha-defensin 5 or 6" which are Paneth cell specific and contributes to innate defense of the gastrointestinal mucosal surface. HNP1-3 triggers macrophage release of



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TNF-alpha and IFN-gamma, which act in an autocrine loop to enhance expression of CD32 and CD64 and thereby enhance phagocytosis. 2. It is mentioned that there are two commercially available methods for the determination of synovial alpha-defensin i.e., (1) the quantitative laboratory-based ELISA, that requires a centrifuged synovial fluid to assess the concentration of alpha-defensin and (2) the qualitative lateral flow test. Carefully please check the specificity of the antibody used for the ELISA whether is specific to all HNP1-3 combined or is specific to a particular defensin. This is important due to the similarity in the peptide amino acid sequence, they only differ in ONE amino acid in the head and often do cross react. 3. Synovasure Diagnostics test support diagnosis of several conditions related to joint pain. Are you quantifying pool of HNP1-3? Is it possible to narrow down and use antibody specific for HNP1, HNP2, HNP3 and HNP4? This will bring this interesting study to a more focused work.