Letter to the Editor regarding Falstie-Jensen et al

Wouthuyzen-Bakker, Marjan; Signore, Alberto; Gheysens, Olivier; Jutte, Paul C.; Glaudemans, Andor W. J. M.

Published in:
Journal of Shoulder and Elbow Surgery

DOI:
10.1016/j.jse.2019.03.025

Publication date:
2019

J Shoulder Elbow Surg (2019) 28, e250–e251

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

Letter to the Editor regarding Falstie-Jensen et al: "Labeled white blood cell/bone marrow single-photon emission computed tomography with computed tomography fails in diagnosing chronic periprosthetic shoulder joint infection"

To the Editor:

We have read with interest the article "Labeled white blood cell/bone marrow single-photon emission computed tomography with computed tomography fails in diagnosing chronic periprosthetic shoulder joint infection" by Falstie-Jensen et al,[3] recently published in the *Journal of Shoulder and Elbow Surgery*. The authors address an important clinical challenge in diagnosing low-grade prosthetic joint infections (PJIs) of the shoulder. Low-grade infections, in particular caused by *Cutibacterium acnes*—a common causative microorganism of shoulder PJIs—induce a marginal inflammatory response and are, therefore, difficult to diagnose.[7] In line with this, the authors demonstrate an overall sensitivity of merely 19% to diagnose chronic PJI of the shoulder using 111-indium (^{111}In)-oxine labeled white blood cell (WBC)/bone marrow (BM) Single Photon Emission Computed Tomography (SPECT) combined with low dose computed tomography (SPECT/CT). However, in our opinion, some important aspects concerning the applied imaging modality should be clarified and some statements by the authors should be refined.

First, the authors state that "no exact diagnostic approach has yet been established despite extensive research in biomarkers, radionuclide imaging, and the use of consensus infectious criteria…." We would like to point out that the Infection and Inflammation Committee of the European Association of Nuclear Medicine (EANM), together with the European Society of Radiology (ESR), the European Bone and Joint Infection Society (EBJIS), and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) recently published an evidence-based consensus document for the diagnosis of PJI including the indication for and time frame within a WBC scintigraphy should be performed.[9] In addition, the authors also state that "SPECT/CT is the current technique of choice in diagnosing infections of the skeletal system." This is not in line with the existing guidelines, in which diagnosis of infection should be based on the planar images of at least 2 time points and SPECT/CT should only be applied to determine the exact location of the infection.[9]

Second, in this study, ^{111}In was used to label WBCs. However, as described in the European Nuclear Medicine Guide from the EANM, 99m-technetium (^{99m}Tc) is preferred over ^{111}In to label WBCs because of more optimal physical characteristics, availability, costs, and lower radiation burden.[2] Moreover, an EANM procedural guideline was published, describing the correct use of image acquisition and data interpretation for WBC scintigraphy.[8] According to the known biodistribution of labeled WBCs in blood, bone marrow, reactive inflammation and infection, at least 2 sets of planar images should be acquired of the region of interest.[5] For ^{99m}Tc-labeled WBCs, delayed images (between 2 and 4 hours postinjection [p.i.]) and late images (between 20 and 24 hours p.i.) are mandatory. In addition, the duration of the delayed and late images should be corrected for the isotope half-life. For ^{111}In-labeled WBCs, at least 2 imaging time points are required as well, usually 3-4 hours and 20-24 hours p.i., which was not applied in the current study. Based on these time points, the diagnosis of infection should be made by comparing the delayed and late planar images. In case of infection, tracer accumulation is observed in both the delayed and late images, with an increase in size or uptake over time. In equivocal cases, a semiquantitative analysis or performing a BM scintigraphy might be considered,[8] thereby avoiding in most patients the need for a second nuclear imaging method (the BM scan).

Based on the available data, it is likely that the low diagnostic sensitivity observed by Falstie-Jensen et al is due to the fact that the above-mentioned evidence-based acquisition protocols and interpretation criteria were not applied. Several studies have demonstrated the potential of ^{99m}Tc-labeled WBC scintigraphy for infections of the musculoskeletal system. To illustrate, large retrospective studies demonstrated a diagnostic accuracy of 98% in patients with suspected hip and knee PJI.[1,4] In addition, in 192 consecutive WBC scintigraphies performed in patients with suspected peripheral fracture-related infections, a high diagnostic accuracy of

DOI of original article: https://doi.org/10.1016/j.jse.2018.10.024

https://doi.org/10.1016/j.jse.2019.03.025

92% was found.[6] All of these studies were performed according to correct acquisition protocols and interpretation criteria. Indeed, no formal study using WBC scintigraphy on failed shoulder arthroplasties has yet been published, and the high diagnostic accuracy in these former studies on hip and knee PJI may not apply for low-grade shoulder PJIs. However, it has been recently demonstrated that the leucocyte count in synovial fluid in chronic shoulder PJIs is, unexpectedly, much higher compared with chronic hip and knee PJIs.[10] For this reason, when using the correct protocols, the diagnostic accuracy in shoulder PJIs might be even higher compared with hips and knees.

In conclusion, we disagree with the final conclusion and title of Falstie-Jensen et al that WBC/BM scintigraphy fails in diagnosing chronic PJI of the shoulder. We would like to encourage the authors to further evaluate nuclear imaging modalities in patients with suspected chronic shoulder PJIs, applying the above-mentioned guidelines. Only when nuclear medicine techniques are correctly applied, a firm conclusion about their added value can be made, which may lead to improved evidence-based guidelines and diagnostic flow charts.

Marjan Wouthuyzen-Bakker, MD, PhD
Department of Medical Microbiology and Infection Prevention
University Medical Center Groningen
University of Groningen
Groningen, the Netherlands

Alberto Signore, MD, PhD
Nuclear Medicine Unit
Department of Medical-Surgical Sciences and of Translational Medicine
"Sapienza" University of Rome
Rome, Italy
Department of Nuclear Medicine and Molecular Imaging
University Medical Center Groningen
University of Groningen
Groningen, the Netherlands

Olivier Gheysens, MD, PhD
Nuclear Medicine and Molecular Imaging
University Hospital Leuven
Leuven, Belgium

Paul C. Jutte, MD, PhD
Department of Orthopaedic Surgery
University of Groningen
University Medical Center Groningen
Groningen, the Netherlands

Andor W.J.M. Glaudemans, MD, PhD
Department of Nuclear Medicine and Molecular Imaging
University Medical Center Groningen
University of Groningen
Groningen, the Netherlands
E-mail: a.w.j.m.glaudemans@umcg.nl

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References

1. Erba PA, Glaudemans AWJM, Veltman NC, Sollini M, Pacilio M, Galli F, et al. Image acquisition and interpretation criteria for ^{99m} Tc-HMPAO labelled white blood cell scintigraphy: results of a multicenter trial. Eur J Nucl Med Mol Imaging 2014;41:615-23. https://doi.org/10.1007/s00259-013-2631-4
2. European Nuclear Medicine Guide. EANM and UEMS/EBNM. www.nucmed-guide.app; 2019, accessed May 14, 2019.
3. Falstie-Jensen T, Daugaard H, Søballe K, Ovesen J, Arveschoug AK, Lange J, ROSA study group. Labeled white blood cell/bone marrow single-photon emission computed tomography with computed tomography fails in diagnosing chronic periprosthetic shoulder joint infection [Epub ahead of print]. J Shoulder Elbow Surg 2019. https://doi.org/10.1016/j.jse.2018.10.024
4. Glaudemans AWJM, de Vries EFJ, Vermeulen LEM, Slart RHJA, Dierckx RAJO, Signore A. A large retrospective single-centre study to define the best imaging acquisition protocols and interpretation criteria for white blood cell scintigraphy with ^{99m}Tc-HMPAO-labelled leucocytes in musculoskeletal infections. Eur J Nucl Med Mol Imaging 2013;40:1760-9. https://doi.org/10.1007/s00259-013-2481-0
5. Glaudemans AWJM, Galli F, Pacilio M, Signore A. Leukocyte and bacteria imaging in prosthetic joint infections. Eur Cell Mater 2013;25:61-77. https://doi.org/10.22203/eCM.v025a05
6. Govaert GAM, Bosch P, Ijpma FFA, Glauche J, Jutte PC, Lemans JVC, et al. High diagnostic accuracy of white blood cell scintigraphy for fracture related infections: results of a large retrospective single-center study. Injury 2018;49:1085-90. https://doi.org/10.1016/j.injury.2018.03.018
7. Nodzo SR, Boyle KK, Bhimani S, Duquin TR, Miller AO, Westrich GH. *Propionibacterium acnes* host inflammatory response during periprosthetic infection is joint specific. HSS J 2017;13:159-64. https://doi.org/10.1007/s11420-016-9528-2
8. Signore A, Jamar F, Israel O, Buscombe J, Martin-Comin J, Lazzeri E. Clinical indications, image acquisition and data interpretation for white blood cells and anti-granulocyte monoclonal antibody scintigraphy: an EANM procedural guideline. Eur J Nucl Med Mol Imaging 2018;45:1816-31. https://doi.org/10.1007/s00259-018-4052-x
9. Signore A, Sconfienza LM, Borens O, Glaudemans AWJM, Casar-Pullicino V, Trampuz A, et al. Consensus document for the diagnosis of prosthethic joint infections: a joint paper by the EANM, EBJIS and ESR (with ESCMID endorsement). Eur J Nucl Med Mol Imaging 2019;46:971-88. https://doi.org/10.1007/s00259-019-4263-9
10. Strahm C, Zdravkovic V, Egidy C, Jost B. Accuracy of synovial leucocyte and polymorphonuclear cell count in patients with shoulder prosthetic joint infection. J Bone Jt Infect 2018;3:245-8. https://doi.org/10.7150/jbji.29289