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QUESTION 3: What is the role of nuclear medicine imaging modalities (three-phase bone scintigraphy, bone marrow scintigraphy, white blood cell (WBC) scintigraphy [with ^{99m}Tc or 111In], anti-granulocyte monoclonal antibody scintigraphy and fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) scan in diagnosing periprosthetic joint infection (PJI)?

RECOMMENDATION: Nuclear imaging may be used for the diagnosis of hip and knee PJI in a select group of patients. The test may be ordered in patients in whom PJI is suspected but when other tests are inconclusive, such as patients with dry aspiration of the joint.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 85%, Disagree: 10%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

The utility of nuclear medicine imaging modalities for diagnosis of PJI has been studied extensively and continues to be debated [1,2]. Two recently published systematic reviews and meta-analysis have evaluated this topic, providing guidance about the utility of nuclear imaging modalities for diagnosis of PJI. Verberne et al. evaluated 31 studies published related to the use of nuclear medicine imaging techniques for the diagnosis of PJI in the hip and found highest accuracy for WBC scintigraphy and highest specificity for combined WBC and bone marrow scintigraphy. FDG-PET and bone scintigraphy were not supported as first imaging technique. FDG-PET showed appropriate accuracy, but its higher costs and limited availability were limitations and bone scintigraphy showed lowest specificity [3]. In a follow-up study, Verberne et al. analyzed 23 publications focused on total knee infections [4]. The authors concluded that antigranulocyte scintigraphy and combined WBC scintigraphy and bone marrow scintigraphy presented the highest specificity values (95% and 93% respectively). In this review (for the knee) bone scintigraphy and FDG-PET/CT were not supported as preferred imaging modality. Bone scintigraphy was not preferred because of low specificity, and FDG-PET/CT was not preferred because of costs and its limited effectiveness in confirming infection for diagnosis of hip and knee PJI.

It is important to realize some facts regarding the nuclear medicine imaging modalities. The three phase bone scan carries a low specificity and low diagnostic accuracy in patients with suspected PJI, particularly in patients with uncemented components and during the early years of arthroplasty [1]. However, the study has a high sensitivity, and normal findings (e.g., no increased perfusion or blood-pool, no periprosthetic uptake in the late phase) can be considered as strong evidence against the presence of infection [5–9]. When having a positive three-phase bone scan in patients with suspected PJI, another imaging modality is necessary. White blood cell scintigraphy is the first nuclear imaging modality of choice in these cases because of the high diagnostic accuracy (> 90%). When correctly labelled, performed and interpreted, FDG-PET/CT has also been used to diagnose PJI. FDG is taken up both in reactive inflammation due to metallic implants such as prosthetic joints and in infection. The differentiation between both is often difficult, leading to lower specificity rates for FDG-PET/CT. Reinartz et al. [10] reviewed the literature on the diagnostic performance of FDG-PET and WBC count scintigraphy in periprosthetic joint infections. They reported higher sensitivity but lower specificity for FDG-PET compared to WBC scintigraphy. In addition, the accuracy for FDG-PET was slightly higher in hip cases than in knee cases. Similarly, a recent review article by Gemmel et al. reported a pooled sensitivity and specificity of 84% for PJI using FDG-PET, which was more accurate for hip than for knee prosthesis [11]. The European Association of Nuclear Medicine/The Society of Nuclear Medicine and Molecular Imaging (EANM/SNMMI) guidelines, based on both review of existing literature data and expert opinion, for the use of FDG in inflammation and infection reported an overall sensitivity of 95% and specificity of 98% for knee and hip periprosthetic infections with FDG-PET [12]. Moreover, the range for both sensitivity (28 to 91%) and specificity (34 to 97%) of the individual studies is quite large, which can be partly explained by the different study design and the lack of standardization in the interpretation criteria (visual interpretation using pattern recognition). Large prospective studies comparing the diagnostic performance of WBC scintigraphy and FDG-PET for PJI are required.

The American College of Radiology published their appropriateness criteria for imaging after total knee replacement [13]. After an extensive literature review by a panel of experts, they recommend that the use of three-phase bone scintigraphy and white blood cell scintigraphy (labelled with In-111 and with SPECT/CT if necessary for exact location) may be appropriate in the particular setting of pain after total knee arthroplasty when joint aspiration culture(s) are negative or inconclusive and the clinician still has strong suspicion of PJI.

Recently, in a well-designed study, Kwee et al. analyzed the added value of FDGPET /CT to conventional tests performed for the diagnosis of PJI, such as radiography, serum markers and synovial fluid-based tests [14]. They demonstrated that when erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were not elevated and/or serum tests were normal, FDG-PET/CT did not add any diagnostic value. Based on the available data, it is difficult to support the routine use of FDG-PET/CT for the workup of patients suspected of having PJI.

The American Academy of Orthopaedic Surgeons (AAOS) guidelines also state that the nuclear medicine imaging modalities are certainly an option for diagnosis of PJI in a selected group of patients suspected of PJI in whom diagnosis of PJI could not be reached or refuted, such as patient with failed attempts to retrieve synovial fluid. [15].

In summary, there is a role for nuclear imaging modalities in select group of patients with suspected PJI. However, they should not be used as a first diagnostic test. In patients with a low probability of PJI and not within the first years after surgery, three-phase bone scintigraphy can be a good option. When negative, it excludes an infection. However, a positive result requires additional workup using other nuclear imaging modalities. White blood cell scintigraphy is then first choice because of its high diagnostic accuracy when correctly performed and interpreted. Antigranulocyte monoclonal antibody scintigraphy can be a second choice option for those centers that cannot perform labelling of the leukocytes. At this moment, routine use of FDG-PET/CT in patients with (suspected) PJI is not supported.

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