F-18 FDG/PET in Infection and Inflammation

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Abstract

One of the lessons learnt from F-18 FDG imaging of cancer is that it is possible to have non-specific uptake of F-18 FDG in patients with inflammatory conditions. It may be possible to use F-18 FDG PET-CT to identify and localize occult sites of infection and early work has suggested that this may play a clinically important role. As more patients are scanned new indications emerge. Like Gallium-67 before it F-18 FDG was identified as false positive uptake (for cancer) occurring in acute infection and active inflammation as both dividing lymphocytes and activated macrophages are glucose avid. Initial studies and reports have suggested that F-18 FDG PET could be useful, if used in the right setting, in the management of fever of unknown origin, osteomyelitis and tuberculosis.

Key words: F-18 FDG PET, Infection, Inflammation

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Introduction

One of the lessons learnt from F-18 FDG imaging of cancer is that it is possible to have non-specific uptake of F-18 FDG in patients with inflammatory conditions. It may be possible to use F-18 FDG PET-CT to identify and localize occult sites of infection and early work has suggested that this become a clinically important role. There is some good evidence that F-18 FDG PET may have role in TB but neither optimal imaging time and the significance of the SUV in Tb has been established yet. Therefore much more evidence is needed before F-18 FDG PET can be offered as standard of care in the infected patient. FDG PET has probably become one of the fastest growing tests in nuclear medicine. In the last decade hundreds of PET scanners have been sold. However, 95% of the scans performed are for cancer, a lesser proportion for cardiology and a small number for neurology. As more patients are scanned new indications emerge. Like Gallium-67 before it F-18 FDG was identified as false positive uptake (for cancer) occurring in acute infection and active inflammation as both dividing lymphocytes and activated macrophages are glucose avid.

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However it is true in nuclear medicine that what rapidly appears as one man's false positive becomes another man's indication, Therefore over the past few years aided by the advances in PET-CT there has been a serious suggestion that F-18 FDG PET can be used to identify both infection and inflammation (1). Could F-18 FDG PET be used to actively search for occult infection and inflammation.

Fever of Unknown Origin (FUO)

The original Petersdorf criteria for pyrexia of unknown origin (2) are rarely applicable today. The idea that a patient can languish in a ward with an undiagnosed fever is just not sustainable in the modern health economics. The advent of the antibiotic era has resulted in those patients with fever presenting a significant diagnostic quandary.

Most studies show that even with an extensive search for a cause of fever the situation will only be resolved with a diagnosis in about 50% of patients (3). Non-infective causes include sarcoid, amyloid, connective tissue disease and tumors in all of these cases very specific tests such as labeled leucocytes may not be useful but F-18 FDG may be able to identify other diseases (4-6) though the pattern may help diagnosis it can only be confirmed by biopsy.

In head to head comparisons in patients with a PUO studies suggest that F-18 FDG PET compares well with labeled leucocytes and in some situations such as the spine and TB be superior (7,8). It was noted that in 40% of patients studied with pyrexia but normal CT and MRI, F-18 FDG PET found a clinically useful answer. A negative F-18 FDG PET excluded any significant disease and patients with such a study tended to resolve spontaneously.

Osteomyelitis

One area where there has been specific studies using F-18 FDG PET-CT has been in osteomyelitis. There are distinct advantages over single photon imaging in that the resolution is higher and with PET-CT localization is improved. However the issues of non-specificity remain an issue for example would uptake around a possible infected knee replacement in a patient with rheumatoid arthritis suggest an infected prosthesis or an active synovitis? Clearly the treatment of these two conditions would be very different.

There have been a few small series of patients imaged with suspected joint and bone infection but these have produced rather disparate results with one paper looking at possibly infected total knee replacement showed a similar sensitivity for labeled leucocytes and F-18 FDG (9) but with a high specificity for F-18 FDG. A second paper looking at F-18 FDG PET and labeled leucocytes found a similar sensitivity for both agents though the PET imaging was a little better in the spine where labeled leucocytes is often insensitive (10). However it is doubtful that the additional cost can really be

justified in this patient group. Also most studies exclude diabetics the main patient group with suspected osteomyelitis in the developed world.

Tuberculosis

The original issue of F-18 FDG PET and TB was the fact that when imaging for cancer mycobacterial infections would appear very glucose avid. This could lead to confusion in diagnosis. In addition some of the conditions leading for TB could be associated with cancers and if patients with cancer are given immunosuppressive drugs such as chemotherapy it would be possible for dormant TB to be re-activated. One Australian group has suggested using F-18 FDG to "screen" patients at high risk of TB to exclude any occult disease before giving any anti-cancer medication (11). More recent work from Japan has suggested that F-18 FDG can identify both pulmonary and extra-pulmonary TB caused by both TB and other mycobacterial infections, though they noted neither site of disease or causative organism had an effect on the SUV (12).

This indication shows great promise as world wide the burden of TB is as great as cancer but F-18 PET imaging has to show it can provide unique information about the diagnosis or disease monitoring of Tb that can not be shown by other methods is a cost effective way.

Inflammation

There is less evidence for the use of F-18 FDG in inflammatory conditions though it would be logical to use such techniques in monitoring systemic inflammatory conditions A study from the Netherlands showed that only 29% of joints in patients with rheumatoid arthritis had F-18 FDG uptake not much higher than the 6% of joints with uptake of F-18 FDG but no evidence of rheumatoid arthritis (13). Though there have been case reports of F-18 FDG uptake in a variety of inflammatory lesions there are few prospective trials and no consensus on how such imaging would be applied clinically.

There has however been greater success in identifying vasculitis especially in the great vessels with reports of uptake in disease such as Takayasu's disease (14, 15)

The case of F-18 PET imaging in infection and inflammation is yet to be made there are some early suggestions that it may provide the most new information in PUO and TB but even in these scenarios the role and advantages of PET imaging remains unclear.

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