Does positron emission tomography/computed tomography aid the diagnosis of prosthetic valve infective endocarditis?

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Abstract

A best evidence topic was constructed according to a structured protocol. The question addressed was whether 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) aids the diagnosis of prosthetic valve endocarditis (PVE)? A total of 107 publications were found using the reported search, of which 6 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. The reported outcome of all studies was a final diagnosis of confirmed endocarditis on follow-up. All the six studies were non-randomized, single-centre, observational studies and thus represented level 3 evidence. The diagnostic capability of PET/CT for PVE was compared with that of the modified Duke Criteria and echocardiography, and reported in terms of sensitivity, specificity and positive and negative predictive values. All studies demonstrated an increased sensitivity for the diagnosis of PVE when PET/CT was combined with the modified Duke Criteria on admission. A higher SUVmax on PET was found to be significantly associated with a confirmed diagnosis of endocarditis and an additional diagnostic benefit of PET/CT angiography over conventional PET/non-enhanced CT is reported due to improved anatomical resolution. However, PET/CT was found to be unreliable in the early postoperative period due to its inability to distinguish between infection and residual postoperative inflammatory changes. PET/CT was also found to be poor at diagnosing cases of native valve endocarditis. We conclude that PET/CT aids in the diagnosis of PVE when combined with the modified Duke Criteria on admission by increasing the diagnostic sensitivity. The diagnostic ability of PET/CT can be potentiated by the use of PET/CTA; however, its use may be unreliable in the early postoperative period or in native valve endocarditis.

Keywords: Positron emission tomography/computed tomography • Valve surgery • Infective endocarditis

INTRODUCTION

A best evidence topic was constructed according to a structured protocol as fully described in ICVTS [1].

THREE-PART QUESTION

In [patients with previous prosthetic valve implantation] does [the use of PET/CT] aid [the diagnosis of infective endocarditis]?

CLINICAL SCENARIO

A 54-year old gentleman is admitted with low-grade fever and general malaise at 6 months following aortic valve replacement for infective endocarditis. On admission, he is noted to have an ejection systolic murmur in keeping with his tissue aortic valve and no obvious sources of infection. His inflammatory markers are raised, and blood cultures on admission grew Staphylococcus aureus. Transoesophageal echocardiography demonstrates moderate aortic regurgitation and no obvious vegetations. You suspect the patient may have prosthetic valve endocarditis (PVE) and have heard that positron emission tomography/computed tomography (PET/CT) scanning has been reported as aiding diagnosis in this setting. You are not aware of the current evidence supporting its use and decide to review the literature.

SEARCH STRATEGY

A literature search of Medline was performed using the Pubmed interface with the terms (positron [All Fields] AND emission [All Fields] AND tomography [All Fields]) AND (endocarditis [All Fields]).

SEARCH OUTCOME

A total of 107 publications were found using the reported search. Of these, six represented the best available evidence to answer the clinical question. These are summarized in Table 1.
Table 1: Best evidence papers

<table>
<thead>
<tr>
<th>Author, date, journal and country</th>
<th>Study type</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Saby et al. (2013), J Am Coll Cardiol, France [2]</td>
<td>Prospective observational study (level III evidence)</td>
<td>72 patients with PVE</td>
<td>Diagnosis of PVE on 3-month follow-up (classified as definite, possible or rejected)</td>
<td>Diagnostic ability for PVE&lt;br&gt;PET/CT alone: sensitivity 73%; specificity 80%; PPV 85%; NPV 67%&lt;br&gt;Diagnostic ability of Duke Criteria (DC) vs that of Duke Criteria + PET&lt;br&gt;Sensitivity of DC: 70% (95% CI 83–99%)&lt;br&gt;Sensitivity of DC + PET: 97% (95% CI 52–83%)&lt;br&gt;*P = 0.0008&lt;br&gt;Specificity of DC: 50% (95% CI 30–70%)&lt;br&gt;Specificity of DC + PET: 40% (95% CI 22–61%)&lt;br&gt;*P = 0.5&lt;br&gt;SUVmax increased in cases of ‘definite PVE’ in comparison with ‘possible PVE’ or ‘rejected PVE’&lt;br&gt;*P &lt; 0.05</td>
<td>The addition of PET/CT as a major criterion in the Duke Criteria increased its sensitivity without a significant reduction in specificity. With the addition of PET/CT to echocardiography, no patients with ‘definite PVE’ were misdiagnosed.</td>
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<td>Bartoletti et al. (2013), BMC Res Notes, Italy [3]</td>
<td>Case series (level III evidence)</td>
<td>6 patients with suspected aortic PVE—TEE negative</td>
<td>PVE confirmed or not confirmed</td>
<td>PET/CT indicated PVE in all 6 cases. Four cases operated—PVE confirmed on histology on resected tissue. All 6 showed regression on PET following their surgery</td>
<td>Very small numbers but consistent results. Showed a reduction in SUVmax following antibiotic therapy on serial PET/CT.</td>
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<td>Ricciardi et al. (2014), Int J Infect Dis, Italy [4]</td>
<td>Retrospective observational study (level III evidence)</td>
<td>22 patients with IE and PET/CT + TTE/TEE results</td>
<td>IE confirmed/not confirmed</td>
<td>Overall comparison of diagnostic ability for PVE</td>
<td>In the whole population of PVE and NVE, echocardiography had a higher sensitivity than PET/CT. For PVE, PET/CT was the most sensitive modality and increased ability to rule out IE.</td>
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<td>Group 1: 15 patients with suspected PVE and PET/CT + TTE/TEE results</td>
<td>Group 2: 7 patients with native valve endocarditis (NVE)</td>
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<td>Comparison for Group 1 (PVE)</td>
<td>DC: sensitivity 77%; specificity 100%; PPV 100%; NPV 40%&lt;br&gt;Echocardiography: sensitivity 69%; specificity 100%; PPV 100%; NPV 33%&lt;br&gt;PET/CT: sensitivity 85%; specificity 100%; PPV 100%; NPV 50%</td>
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<td>Comparison for Group 2 (NVE)</td>
<td>DC: sensitivity 57%; specificity*; PPV 100%; NPV*&lt;br&gt;Echocardiography: sensitivity 100%; specificity*; PPV 100%; NPV*</td>
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*Indicates significant difference.

Continued
### Table 1 (Continued)

<table>
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<tr>
<th>Author, date, journal and country Study type (level of evidence)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Rouzet et al. (2014), <em>J Nucl Med</em>, France [5]</td>
<td>39 patients with suspected PVE undergoing both PET/CT and SPECT imaging</td>
<td>Definite, possible or excluded PVE</td>
<td>PET/CT: sensitivity*, specificity*, PPV*, NPV*</td>
<td>PET/CT was found to have higher sensitivity than SPECT but reduced specificity. Specificity was improved by excluding all patients who were within 2 months of valve implantation to avoid false-positives from postoperative inflammation.</td>
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<td>Pizzi et al. (2015), <em>Circulation</em>, Spain [6]</td>
<td>Overall 92 patients with suspected PVE and CDE</td>
<td>Group 1: 64 patients with suspected PVE Group 2: 28 patients with suspected CDE Group 3: 76 patients with suspected PVE and CDE who underwent CTA</td>
<td>Group 1 (PVE): comparison of diagnostic ability for PVE Duke Criteria: sensitivity 51%; specificity 92%; PPV 91%; NPV 55%. PET/CT: sensitivity 87%; specificity 92%; PPV 95%; NPV 82%. DC + PET/CT: sensitivity 90%; specificity 88%; PPV 92%; NPV 85%.</td>
<td>PET/CTA had improved sensitivity for the diagnosis of IE in both PVE and CDE. PET/CTA was found to have additional benefit over conventional PET/NECT. A positive correlation was shown between median SUVmax and confirmed diagnosis of PVE.</td>
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* PET/CT: sensitivity: sensitivity; specificity: specificity; PPV: PPV; NPV: NPV.
RESULTS

All studies compared the diagnostic ability of PET/CT scan with a 'final diagnosis' gold standard. The exact method of determining this gold standard varied between studies but in all cases was based on a combination of the modified Duke’s Criteria, imaging and microbiological findings over the follow-up period (ranging from hospital discharge to 3 months). Where further information such as intraoperative findings and histology were available, these were included in the final diagnostic criteria.

Saby et al. [2] were the first to conduct a study of the diagnostic impact of PET/CT in the setting of PVE. In their prospective observational study of 72 patients with suspected PVE on admission, the addition of a positive PET/CT scan as a major criterion in the modified Duke Criteria (DC) significantly increased its sensitivity from 70 to 97% (P < 0.008) without a significant reduction in specificity. This increase was attributed to a significant reduction in cases classified as 'possible PVE' from 40 to 23 (P < 0.0001). However, it should be noted that part of this reclassification resulted in 10 of 22 patients originally correctly classified as 'possible PVE' being incorrectly reclassified as 'definite PVE'. The clinical implications of this are not known. The SUV_{max} on PET/CT in cases of 'definite PVE' was also significantly increased in comparison with cases of possible or rejected PVE (P < 0.05).

Bartoletti et al. [3] reported a small case series of 6 patients with suspected aortic PVE and negative echocardiographic findings. Final diagnoses were based on histology in 4 cases and by clinical response to treatment in the remaining 2 cases. PET/CT successfully diagnosed PVE in all 6 cases and showed a consistent reduction in SUV_{max} on repeat scanning following antibiotic therapy.

Ricciardi et al. [4] conducted a retrospective study of 22 patients with suspected endocarditis (15 PVE and 7 native valve endocarditis). PET/CT had a greater sensitivity for detecting confirmed PVE at 85% compared with 77% for transthoracic echocardiography/transoesophageal echocardiography and 77% for DC on admission. However, in 7 patients with native valve endocarditis, PET/CT failed to detect infection in all cases (P < 0.001). As such, the authors advise against the use of PET/CT in this setting.

Rouzet et al. [5] compared PET/CT and single-photon emission computed tomography (SPECT) in the diagnosis of 92 cases of suspected PVE with inconclusive echocardiographic results. PET/CT was found to be a more useful initial test due to its greater sensitivity for PVE (93% vs 64%) although SPECT had a greater specificity (100 vs 71%). This reduced specificity was in part due to 6 cases of false-positive PET/CT results, all of which were within 2 months of...
valve implantation. The authors conclude that postoperative $^{18}$F-fluorodeoxyglucose uptake in inflammatory tissues can mimic infection and result in false-positives in this time period. When patients within 2 months of prosthetic valve implantation were excluded from the analysis, the sensitivity and specificity of PET/CT for detecting PVE were 92 and 100%, respectively.

Pizzi et al. [6] analysed the relative performance of PET/CT and PET/CT angiography (PET/CTA) in the diagnosis of patients with suspected PVE and cardiac device-related endocarditis. They report that adding PET/CT to modified DC on admission significantly increased diagnostic sensitivity for patients with PVE from 51 to 90% ($P$-value not quoted). PET/CTA was found to confer an additional advantage of PET/non-enhanced CT (PET/NECT) by reducing the number of possible cases on PET/NECT from 20 to 8% ($P < 0.001$). PET/CTA offers additional diagnostic ability due to its use of ECG-gated, contrast-enhanced anatomical images. In a similar result to that demonstrated by Saby et al., $SU_{max}$ was significantly higher in cases of definite PVE (median $SU_{max}$ of 7.36 for definite PVE; 2.37 for possible PVE and 0.5 for rejected PVE).

Fagman et al. [7] performed a prospective study that included a control group of patients with prosthetic valves undergoing PET scan for malignancy. They showed that $SU_{max}$ and SUV ratio were both significantly lower in this cohort than in a cohort of 8 patients with a final diagnosis of definite PVE. They also showed good diagnostic ability of PET/CT for PVE, but this result was not contextualized by comparison with any other methods such as the modified DC or echocardiography.

**CLINICAL BOTTOM LINE**

Current evidence suggests that PET/CT aids the diagnosis of PVE when combined with the modified DC on admission by increasing the diagnostic sensitivity. The diagnostic ability of PET/CT can be potentiated by the use of PET/CTA. However, PET/CT is unreliable in the early postoperative period or in native valve endocarditis.

**Conflict of interest:** none declared.

**REFERENCES**


