PET-IE UK: Positron Emission Tomography in Infective Endocarditis across the United Kingdom

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Collaborating group: National Infection Trainee Collaborative for Audit and Research (NITCAR)

Full title: Positron Emission Tomography/Computed Tomography utilization in Infective Endocarditis: A Retrospective Service Evaluation in United Kingdom Hospitals

Protocol Summary:

Title: Positron Emission Tomography in Infective Endocarditis (PET-IE UK)

Full title: Positron Emission Tomography/Computed Tomography utilization in Infective Endocarditis: A Retrospective Service Evaluation in United Kingdom Hospitals

Setting: UK hospitals with established Infective Endocarditis (IE) multidisciplinary teams (MDTs) and access to PET/CT imaging

Study design: Multicenter retrospective service evaluation

Study population: Adult patients (≥18 years) who underwent PET/CT as part of the diagnostic or management work-up for suspected or confirmed IE or cardiovascular implanted electronic device (CIED) related infection.

Objectives:

Primary: To assess the current utilization and the impact of 18-FDG PET/CT on patients' management, as measured by changes in infective endocarditis therapeutic plans.

Secondary:
To evaluate the impact of 18-FDG PET/CT on the Duke-Li criteria for IE diagnosis
To evaluate whether the detection of extracardiac complications by FDG PET/CT

Timeframe: Retrospective data collection from August 2023 to present day

Collaborators: Trainee and consultant representatives from Microbiology, Infectious Diseases, Cardiology, Cardiothoracic Surgery, Radiology, and Nuclear Medicine

Number of Sites: As many UK sites as possible will be involved in this project.

1. Background:

Infective endocarditis (IE) and cardiovascular implanted electronic device (CIED) related infection pose significant challenges in clinical management, often requiring a multidisciplinary approach for accurate diagnosis and effective treatment. These conditions are associated with high morbidity and mortality rates, emphasizing the importance of timely and precise diagnostic interventions to optimize patient outcomes. Duke criteria to diagnose native valve endocarditis (NVE) have variable sensitivity and specificity. Especially in the setting of prosthetic valve endocarditis (PVE) and CIED related infection the diagnostic performance is better. The latest ESC guidelines for IE included the use of Positron Emission Tomography/Computed Tomography (PET-CT) as an additional diagnostic criterion, particularly for PVE and CIED related infection, and several studies showed enhanced sensitivity for the modified Duke criteria (1, 2).

There are two main indications for performing PET CT in patients with infective endocarditis suspicion, 1. detecting intracardiac infections and 2. detecting clinically silent disseminated infections e.g distant foci and local uncontrolled infection complications. PET CT performance depends on the presence of native valves, prosthetic valves or implanted cardiac devices. Native valve endocarditis diagnostic sensitivity is poor, a negative PET CT would not exclude native valve endocarditis. Prosthetic valve endocarditis sensitivity and specificity of PET CT is high. PET CT utilization in implanted cardiac devices should be carefully considered since the sensitivity is low for lead infections but high for pocket site infections (3).

The utilization of PET/CT in the evaluation of IE and CIED related infection infections represents a significant advancement in diagnostic imaging. By providing information on disease extent, localization of infection, and treatment response assessment, PET/CT has the potential to improve clinical decision-making and patient outcomes (3).

However, despite its potential benefits, the appropriate use and impact of PET/CT in the management of IE and CIED related infections remain areas of ongoing investigation and refinement.

2. Objectives of the study:

Primary Objective:

To measure the proportion of cases where PET/CT findings altered the diagnostic and therapeutic plan (e.g. changes in IE classification, antimicrobial duration, surgical or extraction decisions, cessation of treatment).

Secondary Objectives

1. To assess the contribution of PET/CT findings to the endocarditis classification.
2. To determine the frequency and clinical significance of extracardiac or metastatic infectious foci detected by PET/CT.
3. To evaluate compliance with 2023 ESC guideline recommendations for PET/CT use in IE and CIED related infection.

3. Study questions:

1. What proportion of PET/CT requests were guideline-compliant (per ESC 2023 recommendations)?
2. What were the clinical indications for PET/CT in IE or CIED related infection cases?
3. In how many cases did PET/CT identify new diagnostic information compared with conventional imaging?
4. In what proportion of cases did PET/CT findings result in diagnostic reclassification of IE/CIED related infection?
5. What proportion of PET/CT scans identified distant metastatic or secondary foci of infection?
6. How often did PET/CT findings influence management decisions, including antimicrobial changes, surgical referral, or device extraction?

4. Study design and setting:

This is a multicentre, retrospective service (August 2023 – present day) evaluation coordinated through NITCAR.

Participating UK hospitals will retrospectively identify consecutive eligible patients from sources such as electronic health records and MDT logs.

5. Target population and eligibility

Inclusion Criteria:

- Adults (≥18 years).
- Diagnosed with or investigated for infective endocarditis or CIED related infection and had PET/CT as part of the work up.

Exclusion Criteria:

- PET/CT performed for non-infective indications.
- Incomplete medical records or missing essential data to allow completion of the primary objective.

6. Data Sources:

- Electronic medical records (EMRs) of patients meeting the inclusion criteria.
- PET/CT reports and images.
- MDT discussion minutes or summaries.
- Microbiology laboratory data.
- Echocardiography (TTE/TOE) reports.
- ESC 2023 Guidelines as reference standards for audit compliance.

7. Data Collection and Variables

A standardized case report form (CRF) will be used across sites to collect anonymized data, including (Appendix 1):

Patient demographics and comorbidities

- Age, sex
- Underlying cardiac conditions (valvular disease, prosthesis, congenital disease).

Clinical and microbiological characteristics

- Type of IE (NVE, PVE, CIED related).
- Organisms identified in blood culture.
- Previous episodes of IE.

Imaging and diagnostic data

- Echocardiography findings (TTE/TOE).
- Date and results of PET/CT imaging.
- PET/CT indication, and interpretation (confirmed/excluded IE, distant foci, treatment response).

Clinical impact

- Management changes following PET/CT (antimicrobial duration, surgical decision, device removal, treatment cessation).
    - Number of cases where PET/CT findings contributed to diagnostic yield, influenced management (stopped treatment, modify duration for IE, removal or keeping device (if applicable)), and detected distant metastatic foci.
    - Monitoring of treatment response influenced by PET/CT findings.
- Diagnostic reclassification based on PET/CT results.

Qualitative summary of PET/CT impact:

Free-text responses will be recorded describing the clinical impact of PET/CT. These summaries will be used to provide contextual interpretation of the quantitative findings and to illustrate how PET/CT contributes to clinical decision-making in real-world practice.

Audit standards:

Appropriate indications

1. Diagnosis of IE and cardiac complications: PET/CT is recommended for patients with possible PVE (or persistent suspicion) in cases of inconclusive echocardiography to support the diagnosis.
2. Suspected CIED-related IE: Standard: In possible CIED related infection (lead or pocket) where diagnosis is uncertain, PET/CT may be considered to confirm the diagnosis
3. To search for extracardiac foci in IE: In confirmed/suspected IE (NVE or PVE), PET/CT is recommended to detect peripheral lesions or add minor diagnostic criteria.
4. Monitoring response to antimicrobial treatment: PET/CT can be used in patients with established IE and indication for surgery, but who cannot be operated on due to unacceptable high risk and remain with long-term suppressive antibiotic treatment.

8. Statistical analysis:

Descriptive statistics will be used to summarize patient demographics, clinical data, and PET/CT findings.

Compliance rates with ESC 2023 guidelines will be calculated.

Continuous variables (e.g., age, time intervals) will be analysed using mean, standard deviation (SD), median, and interquartile range (IQR).

The impact of PET/CT on diagnostic yield, treatment decisions, and patient outcomes will be analysed using appropriate statistical tests between NVE, PVE, and CIED related infection (e.g., chi-square test for categorical variables, t-test for continuous variables).

Sample size:

This is a descriptive, multicentre retrospective audit. The primary outcome is the proportion of cases in which PET/CT contributes to a management change. Sample size is therefore based on precision rather than hypothesis testing. Assuming a conservative proportion of 50%, a sample of 200 cases provides an estimated 95% confidence interval of approximately ±7% around the management-change proportion. We will aim to collect a minimum of 200 eligible cases across participating UK centres during the study period. Recruitment will remain open until the target sample size is achieved or until the end of the data collection window, whichever occurs first.

Centre contribution:

Each participating centre will be asked to contribute up to 15 consecutive eligible cases within the study period, where feasible, to limit workload and promote uniform participation.

9. Governance and Data Protection

- Each site will register locally as an audit or service evaluation as required by local procedures.
- Only de-identified data will be uploaded to the central database.
- Each local team will maintain its own secure linkage file.
- Data will be collected using TBC.
- No patient-identifiable information will be shared centrally.
- NHS mail will be used to transfer data.

10. Authorship and Acknowledgement Policy

All infectious diseases and clinical microbiology departments in the UK will be invited to participate in this study.

Participating centres contributing data will be recognised through collaborative authorship. Centres submitting at least 15 eligible cases with ≥90% completion of required data fields may nominate up to two local investigators to be listed as PubMed-citable collaborators. All investigators contributing data will be given the opportunity to review and comment on the manuscript prior to submission. Individuals contributing in a supervisory or advisory capacity without direct involvement in data collection or analysis will be acknowledged in resulting publications.

This publication policy represents the intended authorship structure and may be modified if required to comply with specific journal requirements.

11. Ethical Considerations

This project is a multicentre service evaluation of existing clinical practice and does not involve patient intervention or identifiable data collection. It therefore qualifies as service evaluation/audit under the Health Research Authority (HRA) decision tool. The completed HRA decision tool output will be appended to this protocol.

12. Dissemination

Results will be submitted for presentation at national and international meetings and for publication in a peer-reviewed journal.

13. Finance

No direct funding is required. Each site will use existing resources and local infrastructure.

Shell tables

Table 1: General characteristics of the patients

Characteristics, n (%)	**N (%)**
Biological sex, as recorded in patient notes	
Age, years, median (25-75%)	
Endocarditis risk factors	
Previous endocarditis	
Valvular heart disease present	
Prosthetic valve present	
MVR	
AVR	
MVR + AVR	
TAVI	
CIED	
PPM	
ICD	
CRTD	
Congenital heart disease present	
Other	

Table 2: Characteristics of the endocarditis work up

Endocarditis work up characteristics, n (%)	**N=**
Microorganism identified in blood cultures	
To be listed	
Indication for the PET/CT request	
Investigating possible device related endocarditis	
Investigating for CIED related infection	
Native valve endocarditis investigation	
Monitoring response	
Investigating endocarditis and distant infectious foci	
Other diagnostics not available	
Echocardiographic findings*	
Inconclusive	
Negative	
Root abscess	
Vegetation and root abscess	
Vegetation	
Not done	
Other	

Tabe 3: Added diagnostic and management value of PET/CT

Added value to diagnosis with PET/CT, n (%)	**N=**
Excluded endocarditis	
Diagnosed or confirmed endocarditis	
Improvement in follow up infection shown	
No added value	
Patient management changes made with PET/CT by MDT	
Management change	
Surgical or device extraction decision made	

References:

1. Prendergast, B. D. "Diagnostic criteria and problems in infective endocarditis." Heart 90.6 (2004): 611-613.
2. Marsan, Nina Ajmone, et al. "2023 ESC Guidelines for the management of endocarditis." European Heart Journal 44 (2023): 3948-4042.
3. Ten Hove, D., et al. "18F-FDG PET/CT in infective endocarditis: indications and approaches for standardization." Current cardiology reports 23.9 (2021): 130.

Appendix 1: PET-IE UK Case Report Form (CRF)

Section A: Patient and Baseline Characteristics

Variable	Format	Notes
Patient number	Site-specific ID	Non-identifiable
Age	Numeric (years)	At admission
Biological sex, as recorded in patient notes	M / F / Other / Unknown	
Cardiac risk factors	Free text or checkbox	
Previous infective endocarditis	Y / N / Unknown	
Valvular heart disease	Y / N	
Prosthetic valve present	Y / N	
Type of prosthetic valve	AVR / MVR / AVR+MVR / TAVI / Other	If applicable
Cardiac device present	Y / N	
Type of cardiac device	PPM / ICD / CRT-D	If applicable
Congenital heart disease	Y / N	
Previous valvular surgery	Y / N	
Other	Please indicate	

Section B: Endocarditis Evaluation

Variable	Format	Notes
Date of IE suspicion or diagnosis	Date	
Echocardiography findings	Free text	Free text to paste the ECHO findings
PET/CT indication		Free text to explain the indication
PET/CT findings	Free text	Free text to paste the report
MDT/clinical plan text	Free text	Free text to paste the MDT/clinical plan after PET done (if available)

Section C: Diagnostic/Management Impact of PET/CT

Variable	Format	Notes
Diagnostic change	Multi-select checkbox	Confirmed NVE
		Confirmed CIED IE
		Confirmed PVE
		Excluded NVE
		Excluded CIED IE
		Excluded PVE
		No diagnostic impact
Management change	Free text	Describe management change briefly
Certainty scale for management change	Multi-select checkbox	Find examples below
A. Definite PET-driven change: e.g. Explicitly documented: “Changed because of PET/CT” or “PET ruled out/confirmed → plan altered”.		
B. Probable PET contribution: e.g. PET result documented and a change occurred soon after, but not explicitly linked		
C. Possible PET contribution: PET result available; change may have occurred but due to multiple factors		
D. Unlikely / no PET contribution: e.g. Management unchanged, or change clearly due to something else		
E. Not assessable: e.g. Missing documentation		
Distant foci identified with PET CT	Multi-select checkbox	Yes / No
Treatment response shown (follow-up PET)		Yes / No / Not applicable
Surgical or device extraction decision made		Yes / No / Not applicable
Briefly describe the main clinical impact of PET/CT in this case:	Free text	Free text

Section D

Centre based questions

Participating centre	Free text	List of sites
How many cases of infective endocarditis (IE) are managed annually at your centre?	Dropdown	0–5 / 6–20 / 21-30 / 31–50 / 51–100 / >100
Does your centre have a regular Infective Endocarditis (IE) multidisciplinary team (MDT) meeting?	Dropdown	Yes – regular formal MDT / Yes – ad hoc or informal / No
How are decisions made to request PET/CT in suspected IE? *(select all that apply)*	Multi-select	IE MDT discussion / Cardiology decision / Microbiology or Infectious Diseases advice / Radiology or Nuclear Medicine recommendation / Local protocol or pathway / Case-by-case clinician decision / Other
Which guideline or pathway is most commonly followed when considering PET/CT in IE?	Dropdown	ESC 2023 guidelines / Local protocol / Combination of ESC + local protocol / No formal guideline / Not sure
Is PET/CT imaging available on-site at your centre?	Dropdown	Yes – on-site / No – referred to another centre