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Artificial Intelligence in Diagnosis of Infective Endocarditis: Current Evidence and Future Directions

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Abstract :

Background: Infective endocarditis (IE) is a life-threatening infection of the cardiac endocardium affecting one or more heart valves, with in-hospital mortality of 15–30% and universally fatal if untreated. [1,2] IE may be acute, most commonly caused by Staphylococcus aureus with rapid valvular destruction, or subacute, typically caused by viridans streptococci in patients with pre-existing valvular disease, congenital heart defects, or prosthetic valves. [1] Diagnosis is guided by the 2023 Duke-ISCVID criteria, yet significant diagnostic gaps persist, particularly in prosthetic valve endocarditis (PVE). [3] Artificial intelligence (AI) and machine learning (ML) offer transformative potential to address these limitations across multiple diagnostic domains.

Methods: A narrative review of literature published between 2019 and 2025 was conducted using PubMed, Scopus, and EMBASE.

Results: ML-based models including SABIER and SYSUPMIE outperform conventional clinical scoring. [4,5] AI-enhanced echocardiography and FDG-PET/CT improve sensitivity and specificity for vegetation detection and PVE. [6,7] ML-identified biomarkers IL-15 and CCL4 predict IE mortality with 91% accuracy. [8] Large language models (LLMs) demonstrate early promise in clinical decision support. [9]

Conclusion: AI is a promising diagnostic adjunct in IE. Prospective validation and regulatory frameworks are essential before routine clinical integration.

1.INTRODUCTION

Infective endocarditis (IE) is a life-threatening infection of the cardiac endocardium that typically affects one or more heart valves and is uniformly fatal if left untreated. [1] In adults, IE most commonly arises from bacteraemia secondary to dental procedures, surgery, distant primary infections, or non-sterile injections; in children, congenital heart defects and invasive procedures are predominant risk factors. [1,2] IE may present as acute disease — caused most commonly by Staphylococcus aureus with rapid destruction of endocardial tissue — or as subacute disease developing over weeks to months, typically due to viridans streptococci in patients with pre-existing valvular damage, congenital cardiac anomalies, or prosthetic valves. [1]

Clinical features include constitutional symptoms such as fever, fatigue, chills, and malaise, alongside pathological cardiac signs including new or changed heart murmur and features of heart failure. [1]Systemic complications including septic embolic stroke and glomerulonephritis may precede or accompany the cardiac diagnosis, further complicating clinical recognition. [1,2] The global incidence of IE ranges from 3 to 10 cases per 100,000 person-years and is rising, with IE associated with 2.23 million disability-adjusted life years (DALYs) worldwide in 2017, a 17.1% increase from 2007. [10]

Diagnosis is guided by the 2023 Duke-ISCVID criteria, which integrate microbiological, echocardiographic, nuclear imaging, and clinical findings. [3] Initial management involves empirical intravenous antibiotics adjusted based on blood culture results and continued for several weeks; surgery may be required in complex cases involving valve perforation or perivalvular extension. [1,3] Despite these established management frameworks, in-hospital mortality remains 15–30%, underscoring the urgent need for earlier and more accurate diagnosis. [2,3]

Artificial intelligence (AI) encompassing machine learning (ML), deep learning (DL), natural language processing (NLP), and large language models (LLMs) has emerged as a compelling adjunct to conventional IE diagnostic pathways. [11] By analysing high-dimensional, multimodal clinical data without the constraints of prespecified variable weighting, AI offers the prospect of more objective, reproducible, and earlier IE diagnosis. [11,12] This narrative review synthesises current evidence on AI applications across the IE diagnostic spectrum and evaluates barriers to clinical translation

2. Current Diagnostic Challenges in IE

2.1 Limitations of the Duke Criteria

The modified Duke Criteria classify IE based on assigned major and minor criteria, yet their binary weighting structure does not reflect the probabilistic nature of clinical diagnosis. [3] Sensitivity for PVE is substantially reduced at 45–70% due to echocardiographic limitations posed by prosthetic material artefacts. [3,12] Significant interobserver variability in integrating vascular and immunological phenomena further limits their reliability. [12] Although the 2023 ISCVID revision introduced molecular diagnostics and intraoperative inspection as new major criteria, the core binary scoring architecture remains unchanged. [3]

2.2 Echocardiographic Limitations

Transthoracic echocardiography (TTE) detects vegetations in only 40–80% of native valve IE cases. [1,12] Transesophageal echocardiography (TEE) improves sensitivity to approximately 90% but is semi-invasive and is further limited by acoustic shadowing artefacts from prosthetic materials. [1,12] Interobserver variability in vegetation sizing — a key surgical decision threshold (>10 mm) — remains a clinically important, underaddressed problem. [12]

2.3 PET/CT Interpretation Challenges

FDG-PET/CT is now a major diagnostic criterion for PVE in the 2023 ESC Guidelines, yet its interpretation remains highly subjective. [3] Spatial resolution of 3–4 mm is insufficient for fine valvular anatomy, and cardiac and respiratory motion degrades image quality. [7] Distinguishing active infection from post- surgical inflammatory uptake is unreliable without quantitative tools, resulting in significant interinstitutional variability. [7]

2.4 Microbiological Challenges

Blood cultures are negative in 10–30% of IE cases due to prior antibiotic therapy, fastidious organisms such as Coxiella burnetii, Bartonella species, and Tropheryma whipplei, or fungal aetiology. [1,2] In culture-negative IE, loss of the microbiological major criterion substantially reduces Duke Criteria sensitivity, delaying targeted therapy. [3,12] Even in culture-positive cases, the 24–72 hour blood culture turnaround necessitates empirical treatment during a critical diagnostic interval. [1]

Table 1. Key Diagnostic Limitations in IE and Their Clinical Impact

Domain	Key Limitation	Clinical Impact
Duke Criteria	Binary weighting; low PVE sensitivity (45–70%); interobserver variability	Misclassification; diagnostic delay
TTE/TEE	TTE sensitivity 40–80%; prosthetic artefacts; operator dependency	Missed vegetations; inconsistent surgical thresholds
FDG-PET/CT	Subjective interpretation; motion artefacts; post-surgical uptake overlap	Inconsistent thresholds; false positives post-surgery
Blood Cultures	10–30% culture-negative; 24–72h turnaround; fastidious organisms missed	Empirical therapy; delayed targeted treatment

3. Applications of Artificial Intelligence in IE Diagnosis

AI has been applied to IE across six principal domains: clinical risk scoring, echocardiography, PET/CT interpretation, biomarker profiling, microbiology, and large language model-based decision support. [11,12]

3.1 ML-Augmented Clinical Risk Scoring

Lai et al. developed the SABIER score using a random forest algorithm applied to 15,741 S. aureus bacteraemia episodes, achieving an AUCROC of 0.74 and a negative predictive value (NPV) of 0.980 at the point of blood culture positivity. [4] The four most

discriminatory features were age, prior history of IE, pre-existing valvular heart disease, and community-onset bacteraemia. [4] In the prospective PRO-ENDOCARDITIS cohort, neural networks and logistic regression outperformed the modified Duke Score, suggesting ML could safely reduce unnecessary TEE referrals. [5] The MEFIER score extended ML risk stratification to Enterococcus faecalis bacteraemia, achieving AUCROC of 0.79 and NPV of 0.98. [13]

3.2 AI in Echocardiography

Sineglazov et al. developed a CNN and Visual Transformer (ViT) ensemble for vegetation segmentation from echocardiographic images, achieving a Dice score of 0.886 with integrated automated volume quantification. [14] Castillo-Dominguez et al. trained YOLO and DETR architectures across seven hospitals in 329 IE patients for TEE vegetation detection at both frame and patient level. [6] Esmaely et al. applied radiomics-based ML to 286 TEE scans and demonstrated enhanced diagnostic accuracy for mechanical prosthetic valve cases when combined with clinician reporting. [15]

3.3 AI-Enhanced PET/CT

Godefroy et al. demonstrated that a radiomics ML approach increased PVE sensitivity from 59% to 72% with specificity of 83% when integrated with ESC criteria. [7] A proof-of-concept ML model applied to Duke/ESC 2015 criteria achieved an ensemble AUC of 0.917, substantially exceeding conventional classification performance. [16] AI motion correction algorithms further improve image quality by compensating for cardiac and respiratory artefacts inherent to cardiac PET imaging. [7]

3.4 Biomarker Identification and Post-Surgical Immunological Profiling

Ris et al. demonstrated that ML identified IL-15 and CCL4 as inflammatory biomarkers predictive of IE mortality with 91% accuracy. [8] Luo et al. developed SYSUPMIE — an XGBoost model incorporating eight variables including platelet count, serum albumin, and vegetation size — achieving AUC of 0.813 in internal and 0.812 in external validation, outperforming EuroSCORE II in IE surgical patients. [17] A 2024 study developed an ML model predicting post-surgical acute kidney injury (AKI) using LASSO feature selection and SHAP-based explainability across 527 IE surgical patients. [18] These models collectively enable personalised perioperative risk stratification across the full post-operative trajectory. [17,18]

3.5 AI in Microbiology

ML has been applied to MALDI-TOF mass spectrometry data to improve organism identification for phylogenetically closely related species relevant to IE. [19] AI models have demonstrated capacity to predict antimicrobial resistance profiles from MALDI-TOF spectra, offering actionable susceptibility predictions prior to formal testing. [20] NLP has enabled automated identification of high-risk IE populations — including people who inject drugs — from unstructured EHR text, supporting proactive echocardiographic surveillance. [21]

3.6 Large Language Models and Clinical Decision Support

Rizwan et al. demonstrated that ChatGPT correctly diagnosed IE from a structured clinical vignette and generated a guideline-consistent treatment framework, though outputs were general rather than patient-specific. [9] A 2025 evaluation of seven LLMs against AHA guideline questions on IE prophylaxis found variable accuracy across clinical domains. [22] NLP applied to cardiac EHR records has enabled automated extraction of echocardiographic measurements and IE risk factors, opening the possibility of AI-assisted population-level IE surveillance. [21]

4. Limitations of Current AI Approaches

4.1 Methodological Limitations

Most AI studies in IE are single-centre, retrospective, and of limited sample size, creating risk of overfitting and poor generalisability. [11,12] Class imbalance is pervasive ,IE occurs in only 4.18% of SAB cases in derivation cohorts — biasing models towards the majority class if not appropriately corrected. [4] Most existing models predate the 2023 ISCVID Duke Criteria revision and are therefore misaligned with current diagnostic standards. [3]

4.2 Incorporation Bias and Lack of Prospective Validation

A fundamental challenge is the use of the modified Duke Criteria as ground truth for model training, creating circular dependency in which AI is trained to replicate the system it aims to improve. [12] No major AI model in IE has undergone prospective validation, and real-world performance under clinical workflow conditions remains unknown. [11,12]

4.3 Explainability and Regulatory Barriers

The opaque nature of ensemble and deep learning models limits clinician trust in high-stakes IE diagnosis. [11] Explainable AI frameworks such as SHAP and LIME offer partial solutions and should be incorporated as standard in future IE AI development. [18] No AI model reviewed has received regulatory approval for clinical IE diagnosis, and training data may reflect historical diagnostic inequities affecting performance in underrepresented populations. [11,12]

5. Future Directions

Prospective, multicentre validation of leading AI models using the 2023 ISCVID Duke Criteria as the reference standard represents the most urgent research priority. **[3,11]** Future AI systems should pursue multimodal integration, combining imaging, clinical scoring, biomarker, and microbiological data within a unified probabilistic framework. **[11,12]** Federated learning — enabling model training across decentralised institutions without transferring raw patient data — offers a privacy-preserving solution to the limited dataset sizes constraining IE AI development. **[11]** Culture-negative IE, representing 10–30% of cases where conventional diagnostic tools fail most severely, represents the highest-priority underserved subgroup for AI development. **[1,3]** Real-time endocarditis team decision-support dashboards integrating ML risk scores, echocardiographic AI, and quantitative PET/CT analysis represent a near-term translational goal with significant potential to reduce diagnostic delay. **[12]**

6. Conclusion

Infective endocarditis remains one of the most diagnostically challenging conditions in modern medicine, with the limitations of the Duke Criteria, echocardiography, FDG-PET/CT, and blood cultures collectively creating a diagnostic gap in which AI is uniquely positioned to intervene. **[1,3,12]** ML-based risk scores, deep learning echocardiographic tools, radiomics-enhanced PET/CT, and AI-driven biomarker profiling have each demonstrated clinically meaningful improvements in diagnostic accuracy and outcome prediction. **[4,5,6,7,8]** However, prospective validation, explainability, equity, and regulatory approval represent fundamental barriers that must be addressed before responsible clinical integration. **[11,12]** As multicentre datasets mature and AI frameworks advance, AI-assisted IE diagnosis holds genuine promise to reduce diagnostic delay, standardise care across institutions, and ultimately improve outcomes for patients with this severe and complex disease. **[11]**

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