Infective Endocarditis in the Emergency Department: A Systematic Review of the Challenges and Advancements in Early Diagnosis

Kezia Elizabeth Philip
University of Texas at Dallas

Abstract

Background: Infective endocarditis (IE) remains an elusive diagnosis for emergency physicians due to its presentation with very non-specific symptoms. Prompt diagnosis of infective endocarditis is critical to earlier intervention and treatment outcomes. This review provides a detailed insight into the challenges of diagnosing infective endocarditis and uses an evidence-based approach to determine the most effective diagnostic strategies that will allow prompt diagnosis.

Methods and findings: A comprehensive literature search was conducted using PubMed, MEDLINE, Cochrane, and Google Scholar. The search terms included 'Infective endocarditis', 'emergency department', 'diagnosis', and 'challenges'. The inclusion criteria were any articles that discussed the challenges and advancements in the early diagnosis of infective endocarditis. The risks of bias and methodological quality of the studies were assessed. The data from these articles were then collected, documented, and used to construct an evidentiary table. The search identified over 17,800 results. Out of those, 100 articles were selected based on the relevance of the title. 45 articles that fulfilled the inclusion criteria were then critically reviewed. 29 of the screened publications were case reports, 8 were reviews, 5 were cohort studies, and there was one publication each of a case control study, experimental study, and case series.

Conclusion: Prompt use of advanced imaging techniques and new diagnostic tools can add significantly to the diagnostic momentum. Key presentations and risk factors for infective endocarditis should be considered in clinical decision making to maximize outcomes for patients.

Introduction

Infective endocarditis (IE) is a bacterial infection of the endocardium and/or the heart valves that is associated with significant morbidity and mortality. It remains an elusive diagnosis for emergency physicians due to its presentation with very non-specific symptoms such as fever, chills, fatigue, and shortness of breath (Harky et al., 2020). These symptoms may be subtle or completely absent in some patients, and the foundational tests commonly used to establish a diagnosis, such as lab cultures and definitive echocardiographic findings, may not be considered during a patient's time in the emergency department (ED). Prolonged hospitalization is usually necessary in order to collect the necessary clinical data to fulfill the Duke criteria, a set of major and minor clinical and pathological criteria that are used to diagnose a patient with infective endocarditis (Hubers et al., 2020). Further exacerbating the challenge of diagnosis, patients may also lack well-known risk factors such as intravenous drug use, hemodialysis, immunosuppression, previous history of infective endocarditis or congenital heart disease, and prosthetic heart valves. Thus, inclusion of the diagnosis of infective endocarditis in the differential diagnosis becomes more difficult, especially during such times as influenza seasons and the ongoing novel coronavirus disease (COVID-19) pandemic in which a multitude of patients present with flu-like symptoms (Long & Koyfman, 2018). Delays in diagnosis and treatment can result in complications, such as sepsis, valvular damage, systemic embolism, and heart failure (Hackett & Stuart, 2020).

There is an abundance of literature that outlines the epidemiology, pathophysiology, and challenges of infective endocarditis. However, diagnostic and treatment advances have failed to have an impact on the outcomes of the disease due to a delay in the initial detection of the disease. Indeed, infective endocarditis is a rare disease, but its impact is significant. It affects up to 10 per 100,000 per year in the population at large, and epidemiological studies suggest that the incidence is rapidly rising (Cahill et al., 2017). On average, there are 40,000 to 50,000 new cases each year in the United States, and hospital charges may exceed $120,000 per patient (Cahill et al., 2017). Although there have been advances in earlier diagnosis and surgical intervention, the mortality rate due to infective endocarditis has not improved in nearly 20 years (Hackett & Stuart, 2020). In a meta analysis of global incidences involving 22,382 patients, mortality rates within a month of hospitalization was 20% whereas long-term post-discharge mortality rates were nearly 30% (Hackett & Stuart, 2020). Hence, early consideration, recognition, and treatment of infective endocarditis are crucial for improved outcomes. Emerging advances in imaging modalities and treatment options are playing an increasing role in the diagnosis and management of infective endocarditis. Multidisciplinary care is vital to the management of infective endocarditis, often requiring the expertise of infectious diseases specialists, cardiologists, radiologists, cardiothoracic surgeons, and

neurologists (Hubers et al., 2020). Thus, prompt diagnosis of infective endocarditis is critical to earlier intervention and treatment outcomes. This review provides a detailed insight into the challenges that emergency medicine clinicians face in diagnosing infective endocarditis. Additionally, this review also uses an evidence-based approach to determine the most effective diagnostic strategies that will allow prompt diagnosis and institution of effective antimicrobial therapy to reduce the risk of complications and improve outcomes of treatment.

Methods

A comprehensive literature search was conducted using PubMed, MEDLINE, Cochrane, and Google Scholar from inception to 26th December, 2021. The search terms included 'infective endocarditis', 'emergency department', 'diagnosis', and 'challenges'. These terms were searched in all fields of the publications. Research articles that did not have the challenges and diagnosis of infective endocarditis as the primary focus were excluded. The searches were limited by year of publication as any articles that predated 2000 were also excluded in order to ensure that only the latest challenges and developments are evaluated. The inclusion criteria were any articles that discussed the challenges and advancements in the early diagnosis of infective endocarditis. The titles and abstracts of the articles were screened by an independent reviewer to determine inclusion. Articles included experimental studies, observational studies, case controlled studies, reviews, randomized controlled trials, clinical trials, and meta-analyses. The references of the identified articles were then searched for other potentially relevant articles that could be included. The systematic review was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline.

The retrieved articles were then further assessed by an independent reviewer based on the previously mentioned eligibility criteria. A variety of quality assessment tools, such as AMSTAR 2 checklist and Joanna Briggs Institute critical appraisal checklist for case reports, were used to assess the risk of bias and to critically appraise the methodological quality of the studies. This allowed for an objective review of the literature in a consistent manner. The data from these articles were collected in a Microsoft Excel spreadsheet. Finally, an evidentiary table was constructed, (Table 1) which included the article title, authors, year of publication, study design type, sample size, challenges identified, and developments in diagnostic measures.

Results

The initial search produced over 18,500 results. Duplicates were removed and out of the remaining results, 100 articles were selected based on the relevance of the title. The relevance of the title was determined based on

the presence of at least one search term in the title. Only 69 publications had full text or abstracts that were relevant. 45 articles that fulfilled the inclusion criteria (Figure 1) were then critically reviewed using AMSTAR 2 and Joanna Briggs Institute Critical Appraisal Tools (S1). The challenges of infective endocarditis diagnoses and the recent developments that can aid early diagnosis of the disease in the ED were identified and are presented in Table 1. 29 of the screened publications were case reports, 8 were reviews, 5 were cohort studies, and there was one publication each of a case control study, experimental study, and case series. The case reports presented unusual and rare clinical cases of patients who displayed atypical symptoms but were eventually diagnosed with infective endocarditis. The common challenge identified in almost all of the publications was the heterogeneous nature of the disease in terms of clinical manifestations, etiology, and course. The developments in diagnostic strategies in the recent years included emerging advancements in imaging technology, an increasing record of potential causative microorganisms, and the modification of certain existing diagnostic measures, such as the Duke criteria.

Although the Duke criteria has been a long established standard for diagnosing IE, patients that do not meet the criteria but with a high suspicion of IE presenting symptoms such as fever and acute heart failure have been found to be later diagnosed with IE (Hackett & Stuart, 2020; Pierce et al., 2012; Topan et al., 2015). Risk factors such as a history of intravenous drug use, cardiac valvular disease, and prosthetic valves can potentially result in IE (Hubers et al., 2020; Long & Koyfamn, 2018; Seif et al., 2013). Imaging techniques such as point of care ultrasound, transthoracic echocardiogram, transesophageal echocardiogram, and 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (F-FDG-PET/CT) can be used to visualize potential valvular lesions, abscesses, or vegetations, in addition to impaired cardiac contractility, which are all indicative of IE (Ulloa et al., 2020; Micks & Sue, 2020; Molnar et al., 2016; de Camargo et al., 2020; Mgbojikwe et al., 2019). However, these imaging modalities can have varying sensitivities that limit their use to only certain applications (Molnar et al., 2016; Musci et al., 2018; Mgbojikwe et al., 2019). Recent advancements in diagnostic strategies have identified a modified PCR assay, an IE predictive instrument, and IE scoring tool that can all be used to identify or predict the occurrence of IE. (Palraj et al., 2015; Rothman et al., 2002; Chung-Esaki et al., 2014). The onset of IE is often accompanied by other unusual symptoms such as splenic abscess, embolization, pulmonary lesions, neurological complications, surgical abdomen, and bacteremia, among many others (Eid, 2021; Carmelli et al., 2018; Martindale & Hayden, 2012; Chase et al., 2012; Donovan et al., 2014). In addition to the microorganism, *Staphylococcus aureus*, that is commonly associated with IE, other causative bacteria such as *Pseudomonas aeruginosa*, *Staphylococcus warneri, Streptococcus gallolyticus, Enterococcus*

faecalis, *Staphylococcus lugdunensis*, and *Stenotrophomonas maltophilia* have also been identified to cause IE (Hagiya et al., 2016; Diaconu et al., 2019; Shapira et al., 2021; Tamura et al., 2017; Douedi et al., 2020; Kogler et al., 2019).

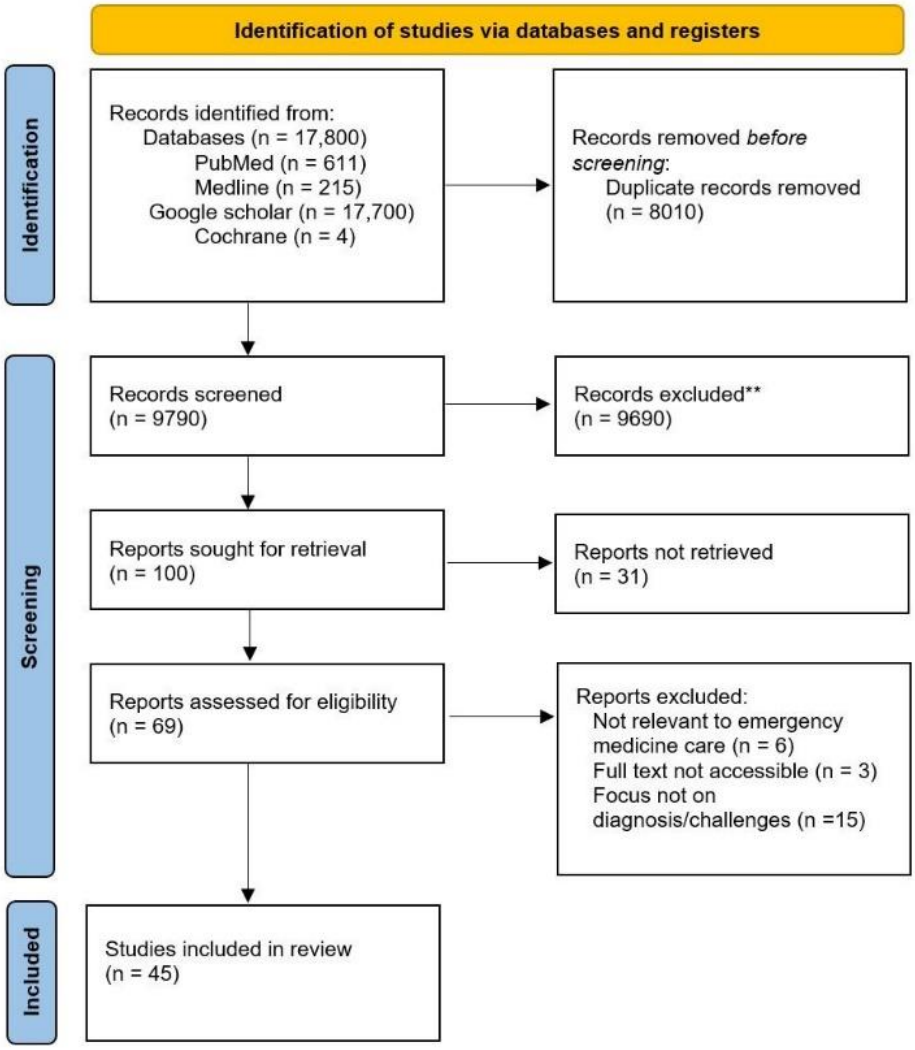

FIGURE 1. PRISMA flow diagram

Discussion

Infective endocarditis is difficult to diagnose due to its protean nature, as it varies according to the initial clinical manifestations, the causative microorganism, the underlying cardiac disease, underlying patient characteristics, and the presence or absence of potentially fatal complications. Currently, the universally accepted diagnostic approach is using the modified Duke criteria, which is a series of guidelines that is

intended to help physicians establish a diagnosis based on certain predetermined major and minor criteria. Positive blood culture results and evidence of endocardial abnormality through echocardiography are the two major Duke criteria (Topan et al., 2015). Minor criteria are fever, prior cardiac condition, vascular and immunological clinical manifestations, as well as microbiologic and echocardiogram evidence that do not fulfill the major criteria (Topan et al., 2015). A clinical diagnosis of "definite IE" is determined based on either the simultaneous presence of two major criteria, the presence of only one major and 3 minor criteria, or in the presence of five minor criteria (Topan et al., 2015). On the other hand, a diagnosis of "possible IE" includes all cases that are not meeting the criteria for "definite IE" but are not "rejected IE" (Tousoulis, 2020). Despite the widespread use of the Duke criteria for the diagnosis of IE, there are still considerable limitations and a substantial proportion of patients (around 33%) who fall into the "possible IE" category (Hubers et al., 2020).

However, emergency clinicians should still consider IE in cases that involve a rapid onset of multisystem symptoms and a range of differential diagnoses, especially if the patient presents with commonly associated risk factors. For example, IE should be suspected in patients who present with fever without a source and in young patients with a sudden onset of acute heart failure, stroke, or multifocal pneumonia (Hackett & Stuart, 2020; Pierce et al., 2012). Additionally, patients with a history of intravenous drug use, a known risk factor of IE, presenting nonspecific flu-like symptoms should trigger the consideration of IE (Long & Koyfman, 2018). A careful observation of the patient's living environment should alert EMT and paramedics to potential IE if there are indications of intravenous drug use. This could expedite the diagnosis and treatment of IE as soon as the patient is transported to the emergency department, which is especially critical in cases of a high index of suspicion of IE and in patients of higher risk. Furthermore, the presence of prosthetic valves and an ongoing use of antibacterial therapy also reduce the sensitivity of the Duke criteria (Hackett & Stuart, 2020). Recent studies have suggested the adoption of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (F-FDG-PET/CT) as an additional diagnostic tool to improve the accuracy of the modified Duke Criteria among patients with suspected prosthetic valve endocarditis and cardiac device infections (de Camargo et al., 2020). However, these studies fail to elucidate the impact of its use in patients with suspected native valve endocarditis. A recent case report recorded the first case of prosthetic tricuspid valve endocarditis caused by a rare but causative microorganism called *Streptococcus gallolyticus* (Shapira et al., 2021). This case is another example that highlights the importance of maintaining a high index of suspicion for the diagnosis of IE despite atypical clinical manifestations. Thus, newly identified imaging technologies, causative pathogens, and uncharacteristic symptoms can all significantly accelerate

the diagnosis of infective endocarditis in the emergency department.

Obtaining timely blood culture tests and the utilization of imaging modalities are essential to producing a major impact by expediting proper care and preventing the development of complications through delayed diagnoses (Ulloa et al., 2020; Micks & Sue, 2020; Luca et al., 2021; Fischer & Baduashvili, 2019). In a case report of a patient with no prior history of cardiac valvular disease and who did not meet the criteria for the diagnosis of IE using the traditional Duke criteria, bedside emergency ultrasound was used to identify tricuspid valve vegetation (Seif et al., 2013). With an increasing list of applications, including detecting valvular lesions, pericardial effusions, and the assessment of cardiac function, bedside emergency ultrasound allows for earlier aggressive intervention and treatment of IE (Seif et al., 2013; Micks & Sue, 2020; Fischer & Baduashvili, 2019; Cohen et al., 2020; Gallagher et al., 2020). Emergency physicians are increasingly performing echocardiography exams as part of their clinical evaluations, which is crucial to detecting the disease at an early stage (Ulloa et al., 2020; Cheng et al., 2012; Molnar et al., 2016).

Transthoracic echocardiogram (TTE) is the most commonly performed imaging technique used by clinicians when there is a high suspicion of IE (Hubers et al., 2019). TTE is a non-invasive and safe imaging technique that is used to visualize the morphology and function of cardiac and valvular structures (Ulloa et al., 2020). Due to its convenience and non-invasiveness, it is the initial imaging modality that clinicians use for the evaluation of IE in the emergency department. However, transesophageal echocardiogram (TEE) has been found to be more sensitive and specific than TTE, and it is also recommended in cases where TTE results are negative (Hackett & Stuart, 2020; Mgbojikwe et al., 2019). The sensitivity of TTE is only 71% for detecting vegetations on native valves and 50% for prosthetic valves, whereas TEE has up to 96% and 92%, respectively (Ulloa et al., 2020; Molnar et al., 2016; Mgbojikwe et al., 2019). There is also a direct correlation between the size of the vegetation and the sensitivity of TTE. 25% of vegetations <5 mm and 70% of those between 6-10 mm were identified by TTE (Molnar et al., 2016). The poorer imaging quality of TTE can be attributed to the impedance caused by the lung and probing distance in the chest. A case study by Molnar A et al. reported that the presence of periannular abscess and ventricular septal defect was only revealed by TEE, which repeated TTE tests failed to detect (Molnar et al., 2016). Similarly, TEE allowed the visualization of central venous catheter vegetations that TTE did not detect in another case report (Musci et al., 2018). Both of these cases strongly reinforce the importance of using TEE for accurate recognition of complications, which is an essential part of preoperative diagnosis.

Point of Care Ultrasound (POCUS) can also be used as an adjunct to medical history, physical examination, and other investigations (Micks & Sue, 2020). POCUS involves the practice of using ultrasound by trained medical professionals to diagnose problems at the location where the

patient is being treated, including in an ambulance, a hospital, or in a remote/rural setting. For example, POCUS can be used by paramedics or EMT to scan a patient while in transit to the emergency room. Similarly, POCUS can be used to assess patients in the trauma bay after being transported to the emergency department. POCUS can assess left and right ventricular function and also provide information on the mechanism and haemodynamic severity of valvular lesions (Micks & Sue, 2020). POCUS has been used to expedite diagnosis and management of IE in multiple case reports involving patients presenting with non-specific rheumatologic symptoms and glomerulonephritis, evaluating wall motion abnormalities to identify indications of myocardial ischemia, and detecting aortic vegetation and heart failure in the absence of risk factors (Micks & Sue, 2020; Fischer & Baduashvili, 2019; Cheng et al., 2012; Cohen et al., 2020; Gallagher et al., 2020). This imaging modality has been shown to be an invaluable tool in the ED as it can aid in the diagnosis of IE in patients presenting with nonspecific symptoms but who cannot be excluded from the diagnostic criteria (Fischer & Baduashvili, 2019). It is particularly useful for diagnosing IE in remote and rural settings where TEE and TTE are of limited availability (Micks & Sue, 2020). Thus, it enables clinicians to treat patients quicker, more accurately and in a non-invasive manner at the point of care, whether that is in a routine clinical environment, remote location, or in an ambulance.

Alternative imaging modalities are being increasingly adopted in clinical settings for the effective diagnosis and treatment of IE. For example, multi-slice computed tomography (MSCT), magnetic resonance imaging (MRI), 4-dimensional computed tomography (4D CT), and F-FDG-PET/CT have all been found to expedite diagnosis due to their higher sensitivity and ability to detect abnormalities (Luca et al., 2021; de Camargo et al., 2020; Tousoulis, 2020). Although F-FDG-PET/CT has been found to increase the performance of the Duke criteria in patients with prosthetic valve endocarditis, it has significantly lower sensitivity in patients with native valve endocarditis, according to meta-analyses studies (de Camargo et al., 2020). Additionally, 3D echocardiography has enabled a better spatial resolution and visualization of cardiac structures, allowing the identification of any valvular vegetations, abscesses, or nodules (Musci et al., 2018). Certain radiographic findings may also provide clues to an underlying etiology. A case report identified a Hampton’s Hump in a patient who was later diagnosed with IE (Earle et al., 2021). Though nonspecific, the radiographic finding of Hampton’s Hump may help emergency providers identify potential embolic or occlusive pathology earlier in the patient's clinical course and prompt further investigation (Earle et al., 2021). More recent innovative approaches include a modification of a PCR involving broad-range eubacterial primers selected from the 16S rRNA gene (Rothman et al., 2002). This assay provides a promising diagnostic for rapid identification of bacteremia, particularly valuable in acute care settings (Rothman et al., 2002). However, there are

certain limitations to this study. The assay does not allow for speciation of bacterial organisms and there is insufficient data to conclude whether the titer profiles are adequate for consistently identifying bacteremia. Alternatively, a decision tool that was designed to identify patients at very low risk for endocarditis using available clinical data was tested to rule out endocarditis in febrile IDUs (Prediction Rule for Endocarditis in Injection Drug Users [PRE-IDU]) (Chung-Esaki et al., 2014). The instrument predicted IE with high sensitivity and ruled out IE with high negative predictive value (Chung-Esaki et al., 2014). Thus, the PRE-IDU instrument and the associated logistic regression model may help guide hospital admission and diagnostic testing in evaluation of febrile IDUs in the ED (Chung-Esaki et al., 2014). Similarly, a scoring tool was developed to predict the risk of endocarditis in patients with *Staphylococcus aureus* bacteremia (SAB) in order to guide the use of echocardiography (Palraj et al., 2015). The study found that a 2-stage screening strategy can be applied on the day of SAB diagnosis (day1) and when results of day 3 blood cultures are available (day 5) to help guide the optimal use of the transesophageal echocardiogram (Palraj et al., 2015). However, the results of this study may not be completely applicable to patients with history of intravenous drug use as they comprised a very small sub-set of the cohort. Although these new approaches require further investigations and trials to further establish validity and reliability, they could significantly improve the pace of diagnosis in the emergency department if implemented.

Clinical presentations and microbiological information are also crucial to determining a diagnosis of infective endocarditis. IE typically presents with variable symptoms emphasizing constitutional complaints, or complaints that focus on primary cardiac effects or secondary embolic phenomena (Chung et al., 2014). However, a high index of suspicion is required, especially in patients with additional findings such as splenic abscess, embolic phenomenon, focal neurologic deficit, mycotic aneurysm, decompensated heart failure, new murmurs, or pleural effusions (Carmelli et al., 2018; Martindale & Hayden, 2012; Donovan et al., 2014). Although rare, skin manifestations of infective endocarditis may be the initial presenting symptoms and often represent an increased infection burden and severity. (Degheim et al., 2020) Due to the myriad clinical presentations of IE, there are a range of initial differential diagnoses that it is mistaken for. Case reports detailing unusual manifestations of the disease broaden the increasing list of conditions that emergency physicians should pay close attention to while diagnosing IE. Aneurysmal disease of visceral arteries coupled with signs of infection, inflammation and cardiac murmur should raise suspicion of IE (Pinder et al., 2018). Patients with permanent pacemakers displaying fever and complications of pulmonary lesion should be assessed for endocarditis related to pacemaker lead infection (Pchejetski et al., 2017; Rezar et al., 2021). Additionally, case reports have also shown that one-and-a half syndrome, surgical abdomen, septic arthritis, and persistent bacteremia are all potential

indications of IE (Tsai et al., 2013; Eid, 2021; Abideen et al., 2020; Chase et al., 2012). In around 20-40% of cases, neurological complications that occur as a result of embolization from endocardial vegetation are one of the early manifestations of IE (Martindale & Hayden, 2012; Male et al., 2008). In a cohort study of 251 patients with suspected IE, elevated levels of the quantitative marker B-type natriuretic peptide (BNP) were concluded to provide incremental value for early and accurate risk prediction of in-hospital mortality (Siciliano et al., 2014). However, this study was considerably limited due to the exclusion of patients who did not receive a diagnosis of IE based on the Duke criteria and those who did not have their BNP levels obtained upon admission. Uncommon risk factors such as poor dentition, multiple sites of infection, and abnormal culture results with atypical organisms should also be considered (Long & Koyfman, 2018). *Staphylococcus aureus* is the primary bacteria associated with IE, but increasing case reports of other infective pathogens causing IE suggest that physicians should be mindful of other causative microorganisms in their clinical evaluations (Palraj et al., 2015; Lafon et al., 2019; Chase et al., 2012). This review identified 6 other pathogens that can cause infective endocarditis: *Pseudomonas aeruginosa*, *Staphylococcus warneri, Streptococcus gallolyticus, Enterococcus faecalis*, *Staphylococcus lugdunensis*, and *Stenotrophomonas maltophilia* (Hagiya et al., 2016; Diaconu et al., 2019; Shapira et al., 2021; Tamura et al., 2017; Douedi et al., 2020; Kogler et al., 2019). In the absence of conspicuous symptoms that are representative of IE, emergency physicians should consider these multisystem manifestations and atypical pathogenic infections while making a diagnosis of infective endocarditis.

This review highlights the challenges that clinicians face in diagnosing infective endocarditis in the emergency department and also provides a substantial new insight into the latest advances in diagnostic strategies that will enable prompt diagnosis of the disease. Infective endocarditis is an elusive disease that continues to cause significant mortality worldwide due to its multifaceted manifestations and rapidly progressing nature. Prompt diagnosis and immediate institution of effective antimicrobial therapy is crucial to earlier intervention and improved treatment outcomes. This review critically analyzes the most recent advances in diagnostic tools, imaging modalities, and clinical presentations to inform emergency medicine clinicians of the latest developments in the diagnosis and management of infective endocarditis, with particularly important implications for clinical care. One of the main strengths of this review is that clearly defined inclusion and exclusion criteria were used, along with a range of quality assessment tools, to ensure objectivity and consistency while screening for potentially relevant studies. However, this review may have been limited by the exclusion of potentially relevant articles that were not included in the search results due to differences in search functions between the databases. Another limitation is the lack of quantitative analysis that could elucidate the

statistical significance of the data. Without direct statistical comparison between alternative diagnostic tools, such as the PRE-IDU instrument, modified PCR, and scoring tool that were previously mentioned in this review, it is difficult to establish their comparative effectiveness in a clinical setting. Additionally, there is a risk of researcher bias due to the screening of studies being conducted by a single reviewer, but this can be avoided by including multiple reviewers in the screening process.

The review relies heavily on unusual clinical findings from case reports to construct an expansive list of atypical symptoms, courses of illnesses, and complications of interventions that emergency physicians can utilize to detect similar or identical cases. One of the main drawbacks of this method is the inability to generalize the findings and establish a cause-effect relationship. Case reports are not generated from representative population samples and causality cannot be inferred merely based on rare observations. Thus, it is not possible to establish generalizability and causal inference based on case reports. However, these studies provide invaluable information in terms of clinical novelties and complexities that would otherwise be undetected. Clinicians can incorporate this knowledge into their clinical practice, enabling them to heed the myriad manifestations that IE can present as. Literature reviews were also significantly considered in this review, primarily due to their comprehensive summation of a vast range of recently published literature. Although there is a potential risk of bias and duplication of original data as a result of using literature reviews, this review ensured that these articles were critically assessed for quality of evidence before drawing conclusions based on the available data. These articles also served as a means to identify further studies that were potentially relevant to our review. Several papers provided unified opinions and they have been collectively summarized and analyzed where applicable within this review.

Conclusion

Infective endocarditis (IE) can be difficult to diagnose in the emergency department because its signs and symptoms can resemble many different clinical conditions. Key presentations and risk factors for infective endocarditis should be considered in clinical decision making to maximize outcomes for patients. A patient with a history of intravenous drug use, cardiac disease, or prosthetic valve presenting in the ED with sudden fever, or atypical symptoms such as embolization, bacteremia, or neurological complications, should immediately prompt physicians to consider IE as a diagnosis. Prompt use of advanced imaging techniques and new diagnostic tools can add significantly to the diagnostic momentum. In the event of a high index of suspicion of IE, emergency physicians should use TEE or POCUS to visualize and assess potential valvular vegetations, abscesses, or lesions. A variety of different

opportunistic pathogens have now been found to cause IE, and its detection in blood cultures must alert emergency physicians to a possible occurrence of infective endocarditis. In addition to *Staphylococcus aureus,* titer profiles that indicate the presence of *Pseudomonas aeruginosa*, *Staphylococcus warneri, Streptococcus gallolyticus, Enterococcus faecalis, Staphylococcus lugdunensis,* or *Stenotrophomonas maltophilia* should cause the consideration of IE. Patients who are in need of prompt antibiotic therapy and potentially emergent surgical intervention must be diagnosed as early as possible to prevent complications. Therefore, prompt diagnosis of infective endocarditis is critical to earlier intervention and improved treatment outcomes.

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