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***JACC* PATIENT PATHWAYS**

Staphylococcus Aureus Infective Endocarditis

JACC Patient Pathways

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ABSTRACT

A 19-year-old female patient presented with *Staphylococcus aureus* infective endocarditis, with suspected subdural brain hemorrhage, disseminated intravascular coagulopathy, and septic renal as well as spleen infarcts. The patient had extensive vegetations on the mitral and tricuspid valves and underwent urgent mitral and tricuspid repair. This paper discusses the clinical case and current evidence regarding the management and treatment of *Staphylococcus aureus* endocarditis. (J Am Coll Cardiol 2022;79:88–99) © 2022 by the American College of Cardiology Foundation.

JACC Patient Pathways is a new initiative from the *JACC* family to reflect the multidisciplinary collaboration that contributes to optimal patient care and decision-making. The Pathways will highlight the evidence-based discussions that are necessary to solve a clinical problem through an actual patient's journey.

As clinicians are faced with challenging clinical cases, it is important to understand how current knowledge based on clinical guidelines and the published data can inform decisions. *JACC* Patient Pathways is a multiparametric approach to this patient journey that provides an interactive illustration, a paper that integrates the clinical case with current evidence, and a video discussion between expert clinicians.

This paper, which the authors are requesting to be copublished with *JACC* and *JACC: Case Reports*, begins with the clinical case and continues with mini reviews on the basic considerations of the case. The scope of the paper is not to provide an extensive review of the topic, but rather to act as guidance for clinicians who may encounter similar cases.

CASE PRESENTATION

A 19-year-old female patient presented to the emergency department with 5 days of vomiting, fever, intermittent abdominal pain, myalgia, and weakness. She arrived in the United Kingdom from Brazil 6 weeks ago during the coronavirus disease-2019 (COVID-19) pandemic. On presentation, the patient was in extremis: she was hypoxic, acidotic, and hypotensive with a blood pressure of 86/49 mm Hg, a heart rate of 140-150 beats/min, and a respiratory rate of 22 breaths/min. Electrocardiography (ECG)

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TAKE-HOME MESSAGES

- **Echocardiography** should be administered expeditiously as the optimal modality for the initial work-up of suspected IE and in the management of most patients with IE. TEE improves sensitivity and TTE improves specificity in detecting complications of IE, so both tests are necessary. TEE is superior for detecting small vegetations.
- **CTA** is highly sensitive for identifying complications of IE (eg, abscess or aneurysm) and complex IE (eg, PVE), in patients with suboptimal echo imaging and surgical planning in IE.
- **^{18}F-FDG PET-CT:** Although not sufficiently sensitive for diagnosing NVE, molecular imaging (mainly with ^{18}F-FDG PET-CT) is an important advance in PVE and CIED-IE as well as in detecting systemic infective foci/septic emboli that often lead to changes in patient management. Use of ^{18}F-FDG PET-CT influences outcomes and is recommended in European IE guidelines but not in the AHA statement.
- **WBC scintigraphy** is a specific whole-body test to locate infection in prosthetic valve and CIED IE but, currently, there is no clear recommendation in guidelines. It is quite useful in early PVE (where PET-CT, when done <3 months postsurgery, may pick up nonspecific sterile inflammation) and can best identify metastatic foci of infection.
- **Surgery:** Repair is the surgical method of choice when applicable. Main targets of surgery are the complete removal of infective tissue and reconstruction of affected tissue. In complex IE cases, bioprosthetic valves may be superior to metallic in terms of anticoagulation and have less bleeding risk.
- **Antibiotic prophylaxis:** There is harmony in the French, AHA, and ESC guidelines to limit prophylaxis to patients with the highest risk of a poor outcome with IE, including prosthetic heart valves, valve repair that includes annuloplasty rings or clips, left ventricular assist devices, complex congenital heart defect either repaired or unrepaired, and orthotopic transplanted hearts with valvulopathy. The United Kingdom's NICE took the approach of recommending ABx prophylaxis for no group on a routine basis.

demonstrated sinus tachycardia (**Figure 1**). She was subsequently referred for extracorporeal membrane oxygenation (ECMO). Her chest x-ray (**Figure 2**) demonstrated opacified lungs. It was determined that she required a full-body computed tomography (CT) scan on her way to the intensive care unit. The patient was septic and had acute renal injury. She also tested negative for COVID-19, HIV, and hepatitis. Blood cultures proved to be positive for *Staphylococcus aureus* (**Figure 3**).

We obtained collateral history from her partner, who stated that the patient had reported occasional palpitations and joint pain.

Full-body CT scan (**Figure 4**) demonstrated the following:

1. Suspected subdural hemorrhage: There was a small area of linear hyperdensity on the right of the superior sagittal sinus at the vertex, suggesting subdural hemorrhage. There was no evidence of pulmonary embolism.
2. The patient had dense consolidations throughout both lungs bilaterally with only a small area of aerated lung on the right. The airways were completely collapsed approximately 9 mm distal to the endotracheal tube.
3. There were bilateral renal and splenic infarcts.
4. There were bilateral periportal edema and moderate volume ascites.

After being transferred to the intensive care unit, she was started on noradrenaline for blood pressure stabilization. Repeated bloodwork demonstrated that the patient had a mild form of disseminated intravascular coagulation (**Figure 5**).

Shortly after undergoing CT scanning, she received a transthoracic echocardiogram (TTE) (Videos 1, 2, 3, 4, 5, and 6), which demonstrated extensive vegetations on the mitral valve and right ventricular wall and good biventricular systolic functioning. She was therefore diagnosed with *Staphylococcus aureus* endocarditis of the mitral valve and right heart chambers.

After a multidisciplinary meeting with the surgeons, critical care clinicians, hematology, infectious disease, and cardiology, it was determined that the patient required urgent surgery within 24 hours of admission. She underwent mitral and tricuspid valve repair (**Figure 6**) and experienced mild residual mitral regurgitation immediately postoperatively (Videos 7, 8, 9, 10, 11, and 12). The ECGs were performed during the same day, with TTE taking place in the morning followed by the intraoperative transesophageal echocardiogram (TEE) in the afternoon.

ABBREVIATIONS AND ACRONYMS

ABx = antibiotic

CIED = cardiac implantable electronic device

CT = computed tomography

ECG = electrocardiogram

ECMO = extracorporeal membrane oxygenation

IE = infective endocarditis

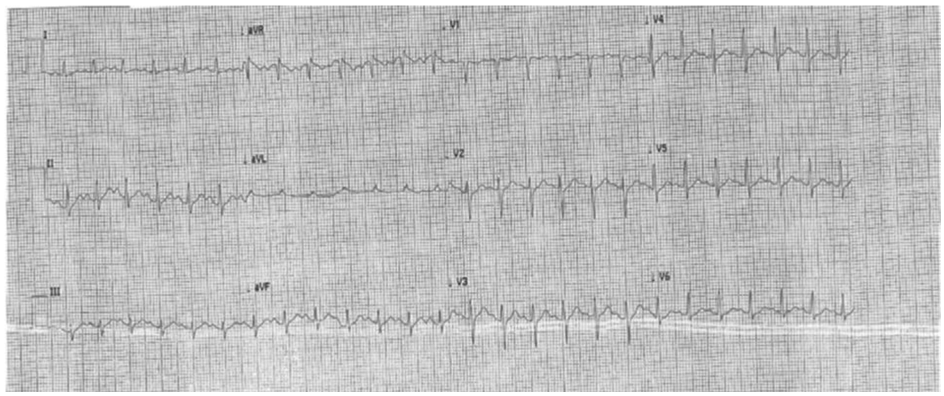
MRSA = methicillin-resistant Staphylococcus aureus

PVE = prosthetic valve infective endocarditis

TEE = transesophageal echocardiogram

TTE = transthoracic echocardiogram

FIGURE 1 Electrocardiogram on Initial Presentation of the Patient



Sinus tachycardia with no evidence of ischemic changes, or prolongation of QT or PR intervals. Furthermore, there are no pathognomonic changes compatible with arrhythmia or any cardiomyopathy. On presentation, the patient was in extremis: she was hypoxic, acidotic, and hypotensive with a blood pressure of 86/49 mm Hg, a heart rate of 140-150 beats/min, and a respiratory rate of 22 breaths/min.

During the patient's postoperative course (**Figure 7**), she was weaned successfully from ECMO. The patient also had an incidental finding of lupus, within the weeks leading to her recovery. She was discharged successfully 6 weeks after her admission (**Figure 8**).

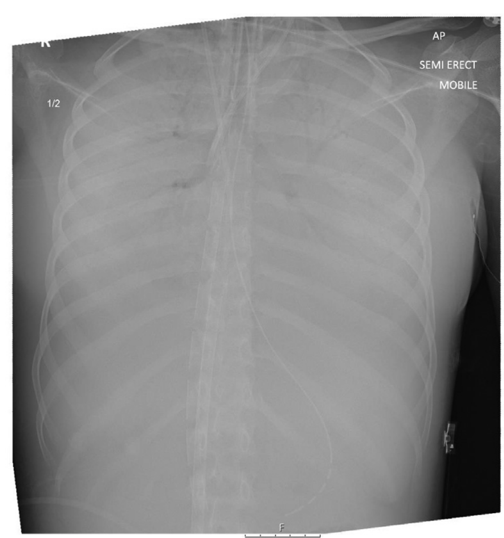
REVIEW

***STAPHYLOCOCCUS AUREUS* BACTEREMIA AND ENDOCARDITIS.** *Staphylococcus aureus* endocarditis is debilitating and requires prompt diagnosis and management for enhanced positive outcomes. Methicillin-resistant *Staphylococcus aureus* valvular endocarditis is associated with greater morbidity and mortality rates (1,2) than methicillin-sensitive *Staphylococcus aureus*. The antibiotic regimens used for the management of *Staphylococcus* bacteremia are frequently limited by toxicities and/or differing efficacies, which makes the choice of antibiotic regimen difficult. There are new parameters suggested (3) to help overcome such limitations, such as the early identification of complications, rapid pathogen identification, as well as the development of new antibiotic agents.

Modified Duke criteria (4,5) are fundamental in determining a diagnosis of IE. However, there is still active discussion on managing complications and when it is appropriate to operate on a patient with IE. (For more information regarding the Modified Duke criteria, please see the next section, "Imaging for infective endocarditis.")

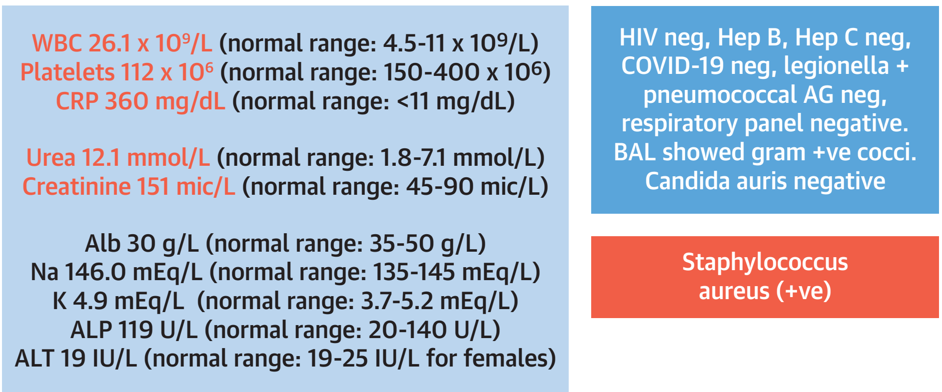
Patients with *Staphylococcus* bacteremia and endocarditis should be classified as low and high risk. They should be considered at high risk for IE (6,7) if they have a history of any of the following: embolic

FIGURE 2 Chest Radiogram on Initial Presentation of the Patient



There is complete lung opacification, and it is very difficult to characterize the cardiac silhouette; therefore, it is impossible to measure the cardiothoracic ratio. Following this chest radiogram, we were prompted to proceed to a full-body computed tomography.

FIGURE 3 Blood Test Results on Admission of the Patient



The patient was septic and had acute renal decompensation; white blood cell (WBC) count was raised and C-reactive protein (CRP) and platelets were lower than normal values. Blood cultures were positive for *Staphylococcus aureus* while the patient was coronavirus disease-2019 (COVID-19) negative. +ve = positive; AG = antigen; Alb = albumin; ALP = alkaline phosphatase; ALT = alanine transaminase; BAL = bronchoalveolar lavage; Hep = hepatitis; K = potassium; Na = sodium; neg = negative.

events, pacemaker, prosthetic valve, previous IE, or intravenous drug use. In these high-risk patients, TEE may be more appropriate than TTE in ruling out IE, and early management may be lifesaving when compared with prolonged antibiotic management (8).

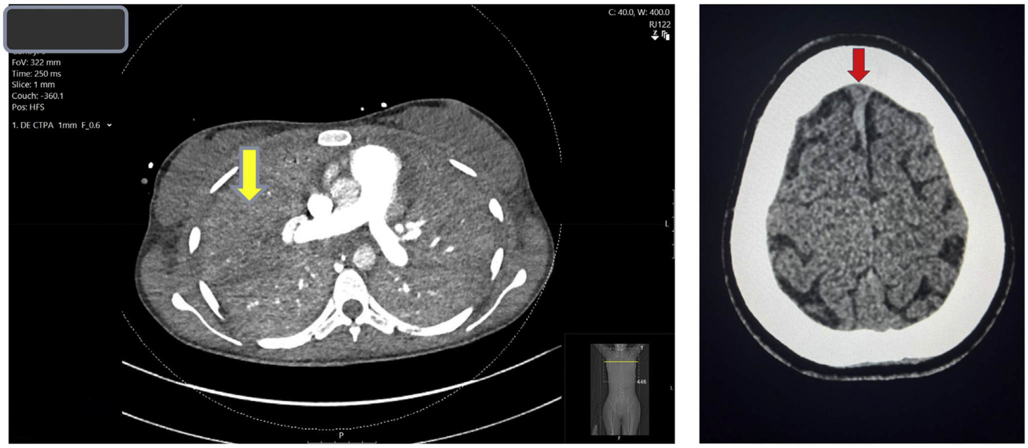
IMAGING FOR IE. Imaging is central to making a diagnosis of IE and is an essential component of the Duke criteria (9). Thoughtfully applied gated, multidetector computed tomography angiography (CTA) and nuclear medicine techniques enhance patient care (10,11). Further, recent guidelines call for a more extensive role in the use of multimodality imaging. Such imaging answers multiple questions in characterizing and managing IE, including the following:

- Is there active IE, and if so, in what specific structures?
- Is IE complicated, where the patient has developed tissue destruction, emboli, metastatic infective foci, and hemodynamic effects?
- Can we predict the development of complications, monitor efficacy of therapy, and determine the need for surgical intervention?
- ECG remains the best first-line imaging test. All patients with suspected IE need expeditious TTE (urgently in hemodynamically unstable patients), because delay in diagnosis adversely affects outcomes. Valvular vegetations are the most common markers of IE. Vegetations are most often pedunculated mobile masses, generally 1-20 mm (larger in long-duration IE in untreated patients) with density-like native tissue, but with some heterogeneity and usually on the in-flow side of the valve. They characteristically move asynchronously to the valve structures, but they can occasionally be sessile and nonmobile.
- Vegetations need to be differentiated from degenerative changes in previously diseased valves, Lambl's excrescences, Libman-Sacks endocarditis, or fibroelastomas. This can be challenging, but is achievable based on comparison with prior echocardiographic studies, presence of tissue destruction, eccentric regurgitation, and change over serial studies. Other pathology revealed by TTE may include the degree of valve and left ventricular (LV) dysfunction and complications, such as abscess, aneurysm, fistulae, or leaflet perforation.

Data regarding how well echocardiography performs in IE are dated and may not represent current-day practice and changing IE etiologies (11,12). In general, TEE has higher diagnostic accuracy mainly caused by better sensitivity (approximately 60% for TTE vs >90% for TEE) and slightly better specificity than TTE (13-15). This difference is magnified with small vegetations (<5 mm), prosthetic valve infective endocarditis (PVE), or cardiac implantable electronic device (CIED)-IE. This is also the case with invasive complications like abscess where TEE (sensitivity >85% and specificity >95%) outperforms TTE (50%) by a wide margin. Echocardiogram appears less optimal in patients with IE following transcatheter aortic valve replacement (6).

Debate continues over using TTE alone, starting with TTE followed by TEE, or going directly to TEE.

FIGURE 4 Computed Tomography of Full Body, Taken Place Immediately After the Chest Radiogram



This figure shows no evidence of pulmonary embolism, but does show lung collapse and dense consolidations **(yellow arrow)**. Furthermore, brain scan demonstrated a suspected subdural hemorrhage; a small linear area of high density in the right parafalcine region **(red arrow)**. Nonspecific differentials include a small subdural hematoma or a small thrombus within a tributary of/within the superior sagittal sinus.

This is based on fear of overuse and lack of robust data on cost-effectiveness, with weak evidence both for and against these strategies. TTE alone may be cost-effective in a low pretest probability population, especially with a structurally normal heart, good echocardiography windows, and large vegetations (>5-10 mm). TTE may be sufficient in uncomplicated right-sided IE (16) and pediatric patients.

Going straight to TEE is reasonable in high-risk situations like the following:

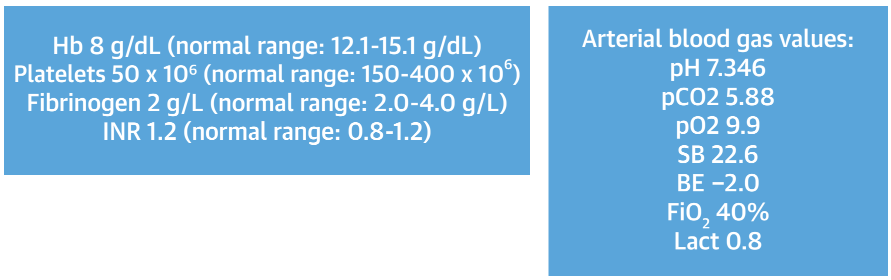
- *Staphylococcal* bacteremia (especially without a known source);
- Continued high suspicion of IE with inconclusive echocardiography;
- Complicated IE, such as severe or new valve dysfunction, suspected abscess, fungal IE, or unresponsive sepsis;
- PVE;
- CIED-IE.

However, both TTE and TEE are often needed in a majority of cases, either initially or during the course of IE. Echocardiography can miss up to one-quarter of PVE and CIED-IE complications. This is especially the case in lead infections where intracardiac echocardiography may be superior. These conditions may therefore need multimodality imaging (10).

Three-dimensional echocardiogram precisely localizes infective foci as well as complications and evaluates the mechanism of leaks, which can be helpful when considering surgery. On the other hand, its low frame rate, lower resolution, and dependency on good images makes it advantageous only in select cases. Repeat echocardiogram studies might be needed to define response to therapy, monitor vegetation size, track clinically silent complications (generally in the first 2 weeks of therapy), and adjust the duration of antibiotic treatment.

- Multimodality imaging in IE: Multiple new techniques are finding utility, especially in PVE and CIED-IE, for diagnosis, identifying complications, predicting prognosis, and following patients (17,18). These include CTA, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography and computed tomography (PET-CT), and leukocyte scintigraphy.
- However, their use is based on early data that often is obtained from expert centers. Robust studies are needed to establish diagnostic accuracy, cost-effectiveness, and effect on treatment strategies and outcomes.
- CTA is complementary to echocardiography and can reliably rule-out IE caused by its high sensitivity. It is most useful in difficult-to-diagnose IE and complicated PVE. It provides excellent morphological detail, accurately identifies tissue invasive complications and systemic IE-related pathology, and evaluates coronaries in preparation for surgery. Although not as effective as TEE in detecting small vegetations or leaflet perforation, CTA's overall sensitivity (>95%) and specificity (>85%) for diagnosing native-valve endocarditis (NVE) is comparable to TEE. CTA is also more

FIGURE 5 **Development of Disseminated Intravascular Coagulopathy Approximately 10 Hours After Presentation**



Later in the clinical course, the patient developed disseminated intravascular coagulopathy with a high value of fibrinogen, low platelets and hemoglobin (Hb), as well as a rising international normalized ratio (INR). BE = basic excess; FiO_2 = fraction of inspired oxygen; Lact = lactate; pCO2 = partial pressure of carbon dioxide; pO2 = partial pressure of oxygen; SB = bicarbonate concentration.

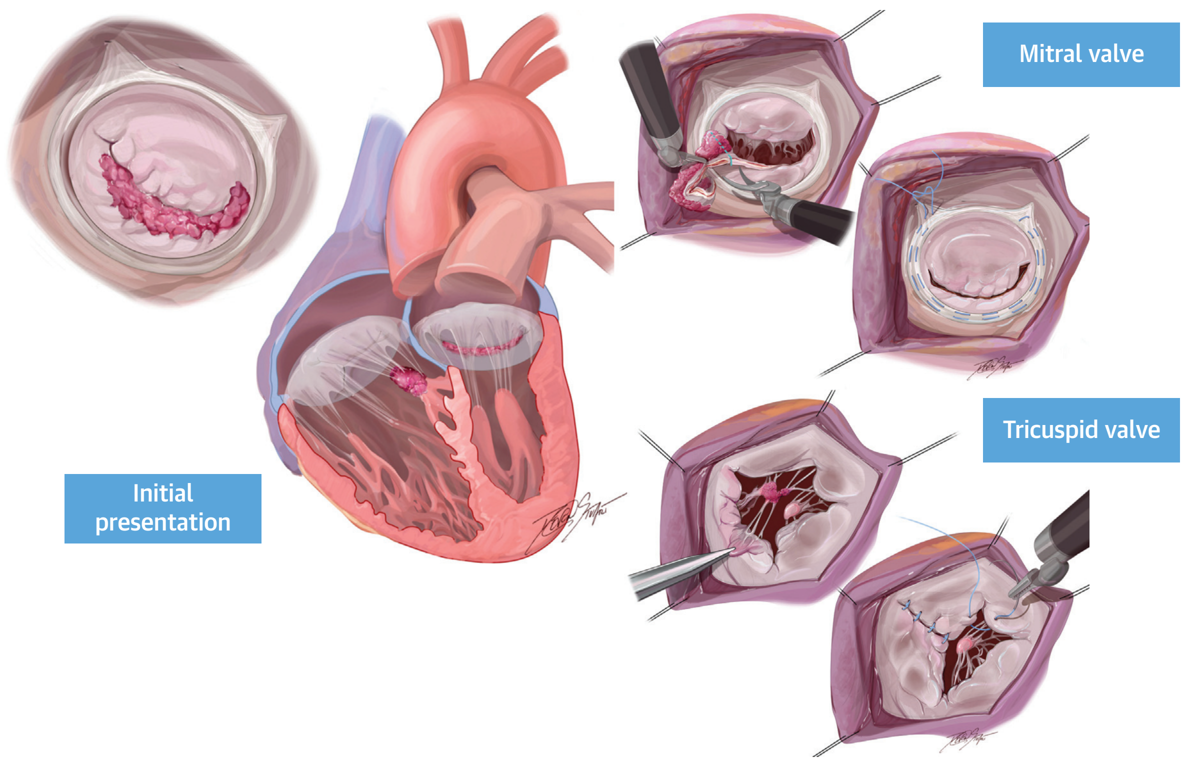
advantageous in patients with prosthesis complications like abscess and complex fistulae in defining location, extent, and complexity. CTA findings can change management in over one-quarter of patients with IE. CTA requires cooperation from the patient and expert imagers, and it has a small cost regarding radiation.

- Although molecular imaging (primarily with ^{18}F-FDG PET-CT) is not sensitive enough (19) for diagnosing NVE (10), it is an important advance in PVE, CIED-IE, and the detection of systemic infective foci/septic emboli that often leads to changes in patient management. Use of ^{18}F-FDG PET-CT influences outcomes (20,21) and is recommended in European IE guidelines. However, it is not included in the American Heart Association (AHA) statement. PVE IE sensitivity and specificity are in the 75%-80% range, and it markedly improves the accuracy of the Duke criteria. High-quality images are obtainable in two-thirds of patients with reasonable intraobserver reproducibility. New signs like diffuse splenic uptake (22) and use of gated studies (23) might improve accuracy. Expertise in reading these scans, especially in the presence of noninfective postvalve-implant inflammation, careful prescan preparation, and timing of the study can affect test performance. Combining CTA with ^{18}F-FDG PET-CT significantly improves diagnostic yield and is best conducted early in the course of the disease.
- Radiolabeled leukocyte scintigraphy (using 99mTc-HMPAO, 111In-oxine, or 67Ga) is a highly specific whole-body test to locate infection in PVE and CIED-IE. However, there are currently no clear guideline recommendations. It is quite useful in early PVE (where PET-CT, when done <3 months postsurgery, may pick up nonspecific sterile inflammation) and can best identify metastatic foci of infection (17). It also effectively predicts complications and mortality in CIED (24). However, tracer preparation is complex and time-consuming and does require the use of blood products. The better availability and lower cost of ^{18}F-FDG PET-CT is likely to make leukocyte scintigraphy less needed. It is important to note that PET-CT (10-12 mSv) and radiolabeled white blood cell (WBC) single photon emission computed tomography/computed tomography (7-8 mSv) produce significant radiation. Repeating a TTE/TEE (in 3-7 days) or even a CTA (<5 mSv with modern scanners) might be better in many stable patients with suspected NVE without a conclusive diagnosis (25).

HEMODYNAMIC STABILIZATION VS RAPID SURGICAL INTERVENTION IN IE. Because IE is a potentially life-threatening infection, patients with complications should be transferred to a tertiary center that offers both cardiology and cardiothoracic surgical expertise. The main indications for early surgery are heart failure, uncontrolled infection, and prevention of embolization or neurological complications, with prioritization as follows: emergent (within 24 hours), urgent (within a few days), and elective (after 12 weeks of antibiotic therapy).

Current international guidelines (4,5,15) recommend heart team discussion and early surgery during initial hospitalization and before completion of the antibiotic course in patients with *Staphylococcus aureus* IE, particularly those who present with valve dysfunction, resulting in heart failure (26). Our patient presented in cardiogenic shock with hemodynamic stability restored following ECMO retrieval. She also had renal and splenic septic emboli and mitral valve vegetations exceeding 10 mm in

FIGURE 6 Surgical Illustration on the Technique Followed by the Surgeon



The operative findings were infection at the leading edge of the posterior leaflet throughout its length. There were also some vegetations on the ventricular surface of the posterior leaflet. The anterior leaflet appeared unaffected, possibly with some mild prolapse. Given the integrity of the anterior leaflet, the decision was made to attempt a Prolene annuloplasty from trigone to trigone. An annuloplasty was performed in 2 layers with 2/0 Prolene tied over a 20-mm Hegar dilator. On exploration of the right atrium, there was some annular dilatation of the tricuspid valve, but this had not been regurgitant on prebypass transesophageal echocardiography. Curiously, there was a large vegetation on the tip of the papillary muscle supplying the commissure between the anterior and the septal leaflets. This was removed, causing prolapse of the adjacent portions of the leaflets. The prolapse was corrected by suturing the leaflets together and by another suture to a cleft in the anterior leaflet.

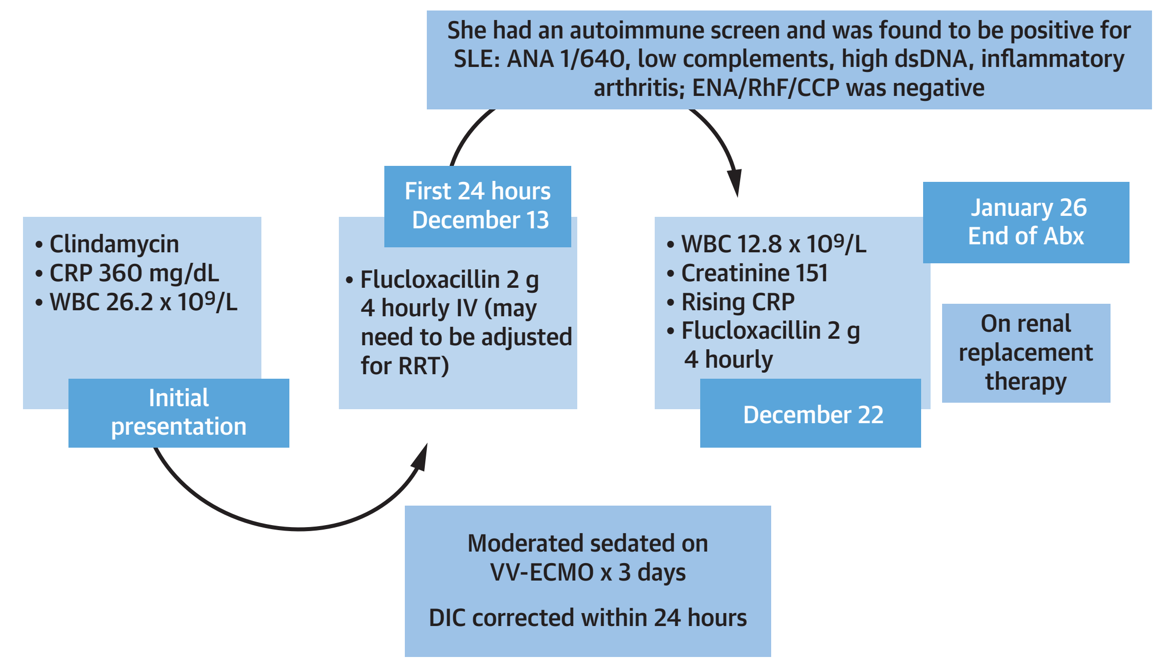
diameter, providing further guideline support for early surgery.

The presence of subdural hemorrhages and disseminated intravascular coagulation (DIC) increased the risk of periprocedural bleeding complications (27). In a recent study of 116 patients with IE-related DIC, although overall mortality and rates of recurrent IE were significantly higher in DIC patients, early surgery was associated with better outcomes (28).

SURGICAL INTERVENTION AND OUTCOMES

According to the European Society of Cardiology (ESC) EORP (EURObservational Research Programme) registry (26), 1,596 (51.2%) patients had surgery while hospitalized. However, following ESC guidelines, a theoretical indication for cardiac surgery was present in 2,160 (69.3%) patients. Surgery was performed in 53.7% of patients with NVE. Using the ESC classification, surgery was performed on an emergency basis in 6.7% of operated patients, urgently in 24.8%, after the first week in 32%, and as an elective procedure in 36.5%. Cardiac surgery was less frequently performed for possible IE (64.7%) than in definite IE (75.3%) ($P < 0.0001$). Indications for surgery were hemodynamic in 46.3% of cases, embolic in 32.1%, and infectious in 64.2%. Among factors associated with more frequent cardiac surgery by multivariable analysis, the most powerful were congestive heart failure (OR: 2.27; 95% CI: 1.57-3.28; $P < 0.0001$), vegetation length >15 mm (OR: 2.33; 95% CI: 1.75-3.10; $P < 0.0001$), cerebral complication (OR: 1.69; 95% CI: 1.13-2.53; $P = 0.0105$), abscess (OR: 4.18; 95% CI: 2.59-6.76; $P < 0.0001$), and management in an European country (OR: 1.45; 95% CI: 1.15-1.82; $P = 0.0016$). Conversely, using the Charlson comorbidity index as a surrogate of comorbidity, high Charlson index (OR: 0.94; 95%

FIGURE 7 **Postoperative Course of the Patient and Selection of Antibiotics**



The patient was moderated sedated on venovenous extracorporeal membrane oxygenation (VV-ECMO) for another 3 days, and disseminated intravascular coagulation (DIC) was corrected within 24 hours after the operation. The patient remained on renal replacement therapy (RRT) until the end of antibiotics, when her renal function optimized. ABx = antibiotics; ANA = antinuclear antibodies; CCP = cyclic citrullinated peptide; dsDNA = double-stranded DNA; ENA = extractable nuclear antigen; IV = intravenous; RhF = rheumatoid factor; SLE = systemic lupus erythematosus, other abbreviations as in Figure 3.

CI: 0.91-0.97; $P = 0.0005$) and female sex (OR: 0.73; 95% CI: 0.59-0.90; $P = 0.0028$) were associated with lower surgery rates.

A recent paper by Kilic et al (27) investigated the rate of valve repair in a single-center study. A total of 831 patients (mean age 55 years; 34.4% women) underwent surgery for IE, with methicillin-sensitive *Staphylococcus aureus* being the second most common infection (17.7%). The most common procedures included isolated aortic valve repair/replacement (18.8%), aortic root replacement (15.9%), mitral valve repair/replacement (26.7%), aortic and mitral valve replacement (8.4%), and tricuspid valve repair/replacement (7.6%). Mean follow-up was 3.4 ± 2.4 years.

In clinical practice, patients with IE have an extremely broad spectrum of presentations and levels of severity. Therefore, although published studies are informative in a general sense, they are often difficult to interpret and may be of limited value for individual patients, particularly at extremes of severity of illness. The objectives of early surgery are to remove infected tissue, foreign material, and hardware; clear and debride paravalvular infection and cavities; restore cardiac integrity and valve function; and remove threatening sources of embolism (14). The timing of surgery needs tailoring to individual circumstances. In addition, in practice, it is important to weigh the balance between the potential harms of further clinical deterioration caused by delay against the likelihood of surgical optimization by additional medical means.

In our case, the patient was a young adult in extremis, on ECMO for respiratory failure, infected with *Staphylococcus aureus*, and in cardiac and renal failure. She also had evidence of septic emboli and mitral and tricuspid regurgitation with associated vegetations, which were increasing in size. The clinical course was one of deterioration despite appropriate antibiotic therapy and maximal multiorgan support, and there appeared to be nothing to gain from delaying surgery.

The operative findings were infection at the leading edge of the posterior leaflet throughout its length. There were also some vegetations on the ventricular surface of the posterior leaflet. The anterior leaflet appeared unaffected, possibly with some mild prolapse. There did appear to be some annular dilatation.

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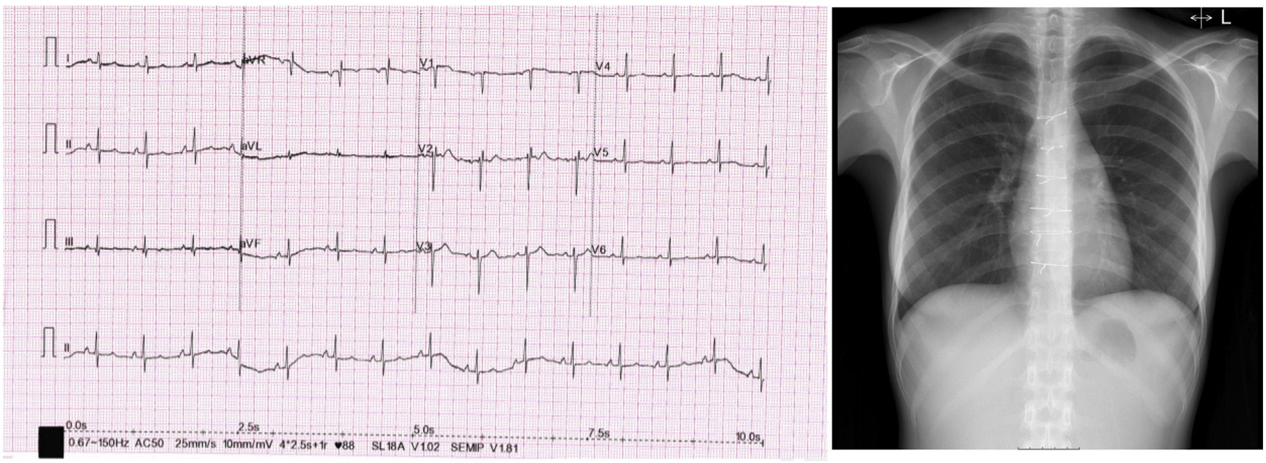
FIGURE 8 **Follow-Up 6 Weeks Postdischarge**



Electrocardiogram demonstrates sinus rhythm with normal postoperative changes, and chest radiogram has normalized; now we can identify the cardiac silhouette as well as a clear cardiothoracic ratio.

All infected material was removed, leaving a thin rim of posterior leaflet with some mural chordae attached.

Given the integrity of the anterior leaflet, the decision was made to attempt a Prolene annuloplasty from trigone to trigone to see whether the valve could be made competent before implanting a mechanical prosthesis in a young woman who may wish to start a family. An annuloplasty was performed in 2 layers with 2/0 Prolene tied over a 20-mm Hegar dilator. On testing, the valve appeared competent, although there was some midleaflet prolapse. However, this result was considered acceptable because it minimized the implantation of foreign material in an infected site and would not require postoperative anticoagulation.

On exploration of the right atrium, there was some annular dilatation of the tricuspid valve, but this had not been regurgitant on prebypass TEE. Curiously, there was a large vegetation on the tip of the papillary muscle supplying the commissure between the anterior and the septal leaflets. This was removed, causing prolapse of the adjacent portions of the leaflets. The prolapse was corrected by suturing the leaflets together and by another suture to a cleft in the anterior leaflet. Following the procedure, the valve appeared to have a reasonable degree of coaptation, but the repair was clearly imperfect. However, given the circumstances, this result was also considered acceptable. Therefore, both valves were repaired, leaving only monofilament Prolene suture material in the infected field. **Figure 6** provides a surgical illustration.

Although various surgical techniques have been described in the literature, a clear long-term advantage of any 1 technique has yet to be proven, and individualized surgical judgment is required. Regardless of approach, the additional surgical challenges inherent with endocarditis ensure that the long-term results are inferior to elective valve surgery: 10-year survival ranges from 40% to 60% (29,30).

SURGERY IN INFECTIVE ENDOCARDITIS. The most important principle of surgical management is the complete removal of infective tissue and reconstruction of the affected tissues. Valve repair is preferable when the anatomy allows. Mitral valve repair is more frequently achievable when compared with aortic valve repair, which is seldomly successful. Yet, aortic valve replacement with mechanical or bioprosthetic valve is the management of choice (5,31).

Intraoperative assessment and surgical skills are of paramount importance in achieving a durable repair. In complex cases with locally uncontrolled infection, total excision of infected and devitalized tissue should be followed by valve replacement. Both ESC and the American Association for Thoracic Surgery guidelines do not favor mechanical or bioprosthetic valves, as they have similar operative mortality (32). However, when there is a risk for postoperative bleeding or transformation of brain lesions into hemorrhagic lesions, bioprosthetic valves are preferable to avoid anticoagulation (31).

New techniques have been described, such as Ozaki aortic valve repair and transaortic mitral valve repair using autologous pericardium (33). In tricuspid valve endocarditis, per both ESC and American Association for Thoracic Surgery guidelines, the best possible repair and preservation of the patient's own valve is the first choice. If the patient has increased pulmonary pressure and resistance, excising the valve and leaving severe regurgitation are not advisable. When replacement is required, most surgeons have a preference for bioprosthetic valves (31).

PACING LEAD POSITIONING IN IE. In IE, there is a preference in positioning epicardial leads, which are less likely to become infected than transvenous leads. Therefore, it is logical to consider placing permanent epicardial leads at the end of the operation. For patients at increased risk of becoming reinfected, such as those on dialysis, those using injection drugs, or those with ongoing bacteremia at the time of pacemaker removal, a temporary system or epicardial lead is more attractive to limit the impact of the infection (5,31).

ANTIBIOTIC PROPHYLAXIS. The use of antimicrobials for prophylaxis against IE is a practice steeped in tradition but supported by little to no evidence. Although antibiotic (ABx) prophylaxis has been shown to prevent bacteremia, a causal link between transient bacteremia and IE has never been established. There are no trials of antimicrobial use demonstrating a reduction in the risk of IE.

In fact, the low incidence of IE following procedures such as dental work even in moderate- to high-risk patients challenges our ability to generate this evidence. In light of this lack of data and because there is risk in the use of antimicrobials, beginning with France in 2002, there has been an international move to restrict the use of prophylactic ABx. There is harmony in the French, AHA, and ESC guidelines to limit prophylaxis to those with the highest risk of a poor outcome with IE, including prosthetic heart valves, valve repair that includes annuloplasty rings or clips, left ventricular assist devices, complex congenital heart defect either repaired or unrepaired, and orthotopic transplanted hearts with valvulopathy. The United Kingdom's National Institute for Health and Care Excellence (NICE) took the approach of recommending ABx prophylaxis for no group on a routine basis. Since then, all major international guidelines have followed suit or even eliminated prophylaxis entirely. This change to limit the use of antibiotics has raised concern that the incidence of IE would increase as a result.

The overall incidence of IE is rising for a number of reasons, including aging populations, increased exposure to health care, an increase in implanted prosthetic devices, and illicit drug use. At the same time, the bacteriology of IE has transitioned, such that *Staphylococcus aureus* has become the dominant organism accounting for two-thirds of all cases. A systematic review of 7 studies of the incidence of IE before and after the guideline revision was led by Khan et al (34). Of these 7 studies, 1 revealed an increase in the incidence of IE after the guideline change; 2 showed no change in an already upward trend in the incidence of IE; and 4 showed a downward trend in incidence. Khan et al (34) concluded that the quality of the studies was not sufficient to provide a reliable answer to the question. Quan et al (35) investigated the incidence of IE after dental procedures before and after the NICE guideline change. They found a rising incidence of IE that preceded the guideline change. There was no inflection point after the guideline change, and although the incidence continued to rise, the relative proportion of cases related to *Staphylococcus* fell.

Our data are poor, but currently there is no strong evidence that the guideline changes have resulted in an increase in the incidence of IE related to procedures such as dental visits. The overarching take-home message is that when original behavior is based on speculation, we can only speculate on the impact of a change in behavior.

Pregnancy and endocarditis. The incidence of endocarditis during pregnancy has been based on case reports, focused mostly in women with congenital heart disease (overall incidence, 0.1%) or prosthetic heart valves (overall incidence, 0.3%-1.2%) (5). Furthermore, reported maternal endocarditis-related mortality is very high (11%-33%) (36-38). Infection susceptibility in pregnant women is not different from that of the general population (39).

Current guidelines do not recommend antibiotic prophylaxis for either vaginal or Caesarean delivery, even in groups at high risk of endocarditis (4). Women who have IE during pregnancy should be managed by a multidisciplinary care team in a center of excellence.

CONCLUSIONS

In the first case under the new initiative *JACC* Patient Pathways, we described a challenging case of *Staphylococcus aureus* IE and current evidence. Our goal with this mini review is to help clinicians understand current practice guidelines as well as gaps in evidence.

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APPENDIX For supplemental videos, please see the online version of this paper.