Role of echocardiography in the evaluation of patients with Staphylococcus aureus bacteraemia: time to look at the heart

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This editorial refers to ‘Prevalence of infective endocarditis in patients with Staphylococcus aureus bacteraemia: the value of screening with echocardiography’ by R.V. Rasmussen et al., on page 414.

Introduction

In the industrialized countries, the prevalence of Staphylococcus aureus infections is constantly rising, due to the increasing population age and modern invasive medical techniques.1 Staphylococcus aureus bacteraemia is frequently hospital- or health-care-related, encountered in post-operative patients, and almost any organ system can be involved. Owing to systemic dissemination, metastatic abscess, osteomyelitis, septic arthritis, and endocarditis can occur.

Staphylococcus aureus is now the leading cause of infective endocarditis especially in Europe and the USA, and associated with high morbidity and mortality despite advances in antibiotic and surgical therapy options. Positive blood cultures and echocardiography are the pivotal cornerstones of diagnosis in infective endocarditis with the modified Duke criteria.2 Clinical manifestations of endocarditis are often unspecific or missing, new murmurs may occur during the course of disease, and immunologic or vascular phenomena may occur as splinter haemorrhages, Janeway lesions, or Roth spots in some patients. Intravenous drug abuse presents another cause of increase in S. aureus infections especially in larger cities and western countries, frequently leading to right-sided endocarditis.

In this issue of the European Journal of Echocardiography, a multi-centre study of 244 patients with S. aureus bacteraemia in six Danish hospitals prospectively examined the prevalence of endocarditis with echocardiography screening.3 A key finding was the strikingly high prevalence of 22% of endocarditis even in patients without clinical manifestations pointing to valvular involvement. In view of the high mortality of untreated endocarditis even in the modern era, this finding underscores the importance of performing early and repeat echocardiography in all patients with S. aureus bacteraemia, as has been recommended by the current ESC guidelines.2 However, many patients still do not undergo routine echo examination despite these recommendations. Even in the present cohort only 73% of eligible patients with S. aureus were screened with echocardiography. Therefore, the present study can help to enforce the guidelines as S. aureus infections and antibiotic resistant strains are increasingly developing.

Interestingly, despite the therapeutic advances, the rate of endocarditis has not decreased during the previous decade, and remains at about a quarter of patients with S. aureus bacteraemia (22–25%).3,4 Furthermore, Rasmussen et al.3 illuminate the significant prevalence of endocarditis of 38% in patients with prosthetic valves or cardiac rhythm devices and S. aureus bacteraemia. Other predisposing conditions were other pre-existing heart valve diseases and intravenous drug abuse, as expected.3–5 The high prevalence of S. aureus endocarditis might also be considered related to recruitment or referral bias in the population studied, or different local factors.

Imaging of infective endocarditis

Major echocardiographic criteria in the diagnosis of infective endocarditis are vegetation, abscess, and new dehiscence of a prosthetic valve1,6 (Table 1).

Vegetations are defined as oscillating or non-oscillating intracardiac masses on valves or endocardial structures or implanted intracardiac material. Typically, vegetations are attached on the low-pressure side of the valve, especially prone to embolism when large (>10–15 mm) and mobile, or located on the anterior mitral leaflet. Embolism risk is highest in the first days of antibiotic therapy. The current sensitivity of transthoracic echo (TTE) for detection of vegetations is only 75%, depending on the individual patient’s echo quality; for transesophageal echo (TEE) a sensitivity
of 90% has been reported, with a specificity of >90% for combined TTE and TEE.6

An abscess is defined by a perivalvular cavity with necrosis and purulent material not communicating with the cardiovascular lumen, and is seen as a thickened, non-homogeneous perivalvular area with echo-dense or echolucent appearance. Pseudoaneurysms present as a pulsatile echo-free space with detectable colour Doppler flow in a perivalvular cavity communicating with the cardiovascular lumen. In fistula formation, a colour Doppler communication between two neighbouring cavities through perforation can be established. Valve leaflet aneurysm leads to saccular outpouching of valvular tissue. Dehiscence of a prosthetic valve is imaged as new paravalvular regurgitation with or without rocking motion of the prostheses, and is best visualized by TEE in the mitral position.6

The study presented in this issue of the Journal3 provides compelling, current evidence that all patients with Staphylococcus aureus bacteremia should undergo TTE and TEE in order to avoid missing the potentially lethal diagnosis of infective endocarditis. A limitation of the study, however, was that not all eligible patients were included in the echocardiography screening, probably reflecting common practice as echocardiography is not always considered in these patients or immediately available. A high mortality was observed in these patients, further underscoring the necessity of performing echocardiography to exclude cardiac involvement in S. aureus infection. Although echocardiography is not 100% sensitive for the detection of endocarditis and negative echocardiograms may occur due to very small vegetations early in the disease, TTE and TEE constitute safe, non-invasive examinations that can be repeatedly performed in all patients with suspected endocarditis.1 A negative TEE early in the course of infection should generally be repeated within 7–10 days. Importantly, in S. aureus infection, the repetition of TTE and TEE is recommended even earlier, due to the virulence of the organism and the devastating effects of intracardiac infection.2

With the progressive use of intracardiac rhythm devices, such as pacemakers, cardiac resynchronization devices, or intracardiac defibrillators, the prevalence of device-related infection especially with S. aureus has amplified and recently been reported in 0.8–19.9% of patients.6,8 Mortality rates of up to 66% for untreated patients have been observed compared with 18–19% in treatment with antibiotics and subsequent complete device removal.8,9

Vegetations on intracardiac leads present as echogenic, oscillating, irregularly formed masses, which should be confirmed in multiple views due to possible artifact generation of metallic leads.6 Off-axis views, particularly during subcostal imaging, should be performed for evidence of device endocarditis. The differential diagnosis of masses on leads also includes thrombus and fibrous casts; however, the presence of infection can be difficult to exclude despite negative blood cultures. TEE usually offers better visibility of right-sided intracardiac lead vegetations, but metallic reverberations can impede the identification of small vegetations or strands, and a right atrial Rete Chiari can also be confounded with vegetations.

Patients with large device-related intracardiac vegetations >10 mm have historically been managed with extraction through an open surgical thoracotomy due to the potential risk of septic, especially pulmonary, embolization. Recently, lead extraction by percutaneous technique has been reported to be a feasible alternative even in the case of large vegetations (up to 4 cm8,9).

**When should surgery be performed: role of imaging**

Up to 50% of patients with infective endocarditis require cardiac surgery, primarily due to heart failure, increasing destruction of the valve in uncontrolled infection, and prevention of recurrent
Therapy considerations and outcome

For antibiotic treatment, it is crucial to differentiate methicillin-susceptible or methicillin-resistant *S. aureus* (MRSA). The duration of treatment is longer in prosthetic than native valve endocarditis, and in MRSA infection. Vancomycin is recommended in MRSA endocarditis treatment regimens; for vancomycin-resistant strains newer antimicrobials such as daptomycin or linezolid are suggested. The duration of bacteraemia with persistently resistant strains newer antimicrobials such as daptomycin or linezolin MRSA endocarditis treatment regimens; for vancomycin- and left or right ventricular function.

Pre-operatively, multi-slice computed tomographic (CT) imaging provides non-invasive assessment of the coronary arteries and simultaneous evaluation of the cardiac valves. Recently, the complementary value of CT was confirmed in infective endocarditis. Compared with TEE, the sensitivity of CT was 97% and specificity 88%. CT depicted the extent of perivalvular complications such as abscess or pseudoaneurysm, and perioperative planning in view of the vicinity of the coronary arteries or coronary sinus was superior to TEE. However, valvular leaflet perforation was missed in CT due to lack of flow information.

As technical resolution further improves, three-dimensional (3D) real-time echocardiography can provide further spatial understanding of the full extent of valvular and perivalvular involvement in infective endocarditis. Especially in perivalvular abscess or pseudoaneurysm, surgical aspects can be directly addressed by 3D echo.

Cardiac magnetic resonance imaging may supplement information regarding, for example, the extent of valvular regurgitation, accompanying myocarditis (by applying gadolinium enhancement) and left or right ventricular function.

Predictors of poor outcome in endocarditis are persistent infection, older age, and co-morbidities (e.g. diabetes, renal failure). *S. aureus* endocarditis patients developing heart failure and/or perianular complications are at highest risk of death and need for surgery, as patients with *S. aureus* prosthetic valve endocarditis, who often require early valve replacement. In high-risk patients, close echocardiographic follow-up is mandatory.

In conclusion, echocardiography screening by TTE and TEE should be routinely performed in all patients with *S. aureus* bacteremia in view of the high prevalence and mortality of endocarditis, especially in high-risk patients with prosthetic valves or pre-existing valve disease. It is time to get to the heart of this common severe infection.

References