Endocarditis is on the rise. Between 15,000 to 20,000 new cases are diagnosed each year, exposing patients to a high risk of morbidity and mortality. The diagnosis, therapy and prognosis of endocarditis also seem to be moving targets, as new options for imaging and treatment come into clinical practice. Early precise diagnosis and identification of clinically significant complications is critical to best patient management. The last decade has seen tremendous advances in early diagnosis, based largely on the increasing sensitivity and specificity of transesophageal echocardiography (TEE). The Duke criteria for the diagnosis of infective endocarditis (IE) (1) have formalized the role of echocardiographic findings into the diagnostic strategy for IE. Although our clinical reliance on echocardiographic methods has increased, it remains a vexing problem that echocardiographic findings are not perfect predictors of some of the most clinically dangerous complications of IE, particularly embolization and perivalvular extension of infection.

Perivalvular extension of endocarditis is associated with more complications, including heart failure and need for surgery, and poorer outcome of patients with endocarditis (2–4). Recognition of abscesses, fistulous tracts and perivalvular leaks is much better with TEE compared to transthoracic echocardiographic approaches and continues to improve as echocardiographic technology advances. Higher spatial and temporal resolution, better near-field visualization and multiple planes all assist in defining anatomy and avoiding confusion from artifacts and interference. However, technology-based advances are incorporated into general clinical practice over time in an unpredictable fashion. Many of the most important clinical studies on patients with IE have been based on retrospective data. It is sometimes difficult to extrapolate data from those studies—collected often over many years using a broad range of echocardiographic equipment and methods—to current clinical practice based on ever-improving echocardiographic technology. Prospective data acquired over relatively short time intervals is highly valuable, because it narrows the range of equipment and technique and minimizes the effects of variable sensitivity and specificity due to imaging practice over time.

The study reported in this issue of the Journal, by Graupner et al. (5) at five centers in Spain and Argentina, is both large and prospective. Perivalvular extension of infection (PVEI) was sought prospectively in 211 patients with left-sided endocarditis using current transthoracic and transesophageal echocardiographic methods. Their data include a mix of imaging approaches performed with single, biplane and multiplane probes on a variety of echocardiography machines; the data are applicable to the common current spectrum of equipment in current clinical use. With that relatively current equipment and approach, they documented eight perivalvular abscesses that were missed with TEE but confirmed at surgery. The use of single, biplane or multiplane probes did not seem to relate to the incidence of these false-negative TEE studies. Review of the false-negative cases showed that three of eight missed abscesses were recognizable as periannular thickening, which fell short of the investigators’ cutoff value of 10 mm of reduced echocardiographic density for diagnosis of an abscess. While their data do not clarify whether this may relate to imaging at an early stage of infection, it is increasingly common to do TEE very early on in the clinical course, since initial TEE in patients with Staphylococcus bacteremia has been suggested to be cost-effective (6). In general, TEE has had good but not perfect sensitivity and specificity for PVEI (76% to 100%), with positive and negative predictive values of 87% and 89%, respectively (7–9). Future study will be needed to clarify whether very early TEE may create some increased risk of missed PVEI. Progression of an abscess to pseudoaneurysm may improve reliability; in the present study (5) no pseudoaneurysms were missed, likely because the characteristic flow pattern in those regions increases their ease of detection.

Prosthetic valves are strongly associated with perivalvular infection (10), and they present many technical challenges to both transthoracic and transesophageal imaging. Interference from prosthetic materials, pledgets around the annular ring, and the complicated distribution of closing jets, particularly from mechanical prostheses, provide a large number of potentially confusing artifacts and findings. The best approach is thorough interrogation from as many planes as possible, and having skilled operators with experience in visualizing these prostheses. Many prosthetic valves have small, stable perivalvular leaks originating at or between suture sites at the sewing ring, which are visible on TEE from the time of implantation. Without baseline postoperative images, it may be very difficult to tell these from small perivalvular leaks related to infection. Similarly, regions of the coronary sinuses may appear in some views to be periannular spaces, and their flow misinterpreted as flow in a pseudoaneurysm. Avoiding these imaging pitfalls is important. Low confidence views and studies may need to be repeated, particularly if the patient is doing well in other regards.

The reliability of our clinical tools and effectiveness of our treatment strategies may vary depending upon the specific
The incidence of underlying immunodeficiency, bacteriology, underlying substrate for infection, and the location and extent of the endothelial infection in each patient. The patients in the present study were middle-aged or older, and they had a very low incidence of intravenous (IV) substance abuse. They also had a low incidence of underlying immunodeficiency. This is very different from the demographics of many endocarditis populations and is in clear distinction from the inner-city mix of patients, which includes a much greater proportion of IV drug users, and a significant proportion of patients with underlying HIV, chronic hepatitis and uncontrolled medical co-morbidities. The extent to which those clinical characteristics increase the frequency of PVEI and modify the clinical course cannot be extrapolated from these data, but other studies have shown active IV drug use to be positively associated with PVEI in multivariate analysis.

One of the most striking findings of the Graupner et al. (5) study is that patients who required surgery generally had congestive heart failure (CHF) or persistent signs of infection in addition to their perivalvular infection. Perivalvular infections in the absence of CHF, persistent infection or severe valvular insufficiency alone accounted for surgery in only three patients. These complications often coexist. The perioperative mortality among the patients with PVEI in this series was quite high (36.1%). The mortality among patients with PVEI who did not undergo surgery was not different (35.3%).

Do these results imply that we should develop a “wait and see” attitude toward PVEI? Data from several surgical groups suggest that operative survival is heavily influenced not only by CHF but also by advanced age and other medical co-morbidities, including renal failure and cerebrovascular events. Operative mortality of patients with IE has been estimated to increase threefold in the presence of heart failure from younger, more high-risk populations. The observation of heart failure are associated with poorer outcomes. For some patients with high risk for surgery—for example, owing to coexisting medical illnesses, repetitive prosthetic infection or ongoing IV drug use—medical therapy of PVEI has some possibility of success. Whether there is a safe strategy for nonsurgical management in patients with PVEI who would otherwise be surgical candidates remains to be proven, although it would clearly be restricted to cases without heart failure, severe valvular insufficiency or extensive infections. In cases where medical management is elected for whatever reason, serial transesophageal imaging can be used to closely follow valvular and ventricular function and abscess size. The long-term sequelae of unoperated abscesses or pseudoaneurysms, including progression, heart failure or reinfarction, must await future study.

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