solid registry with a detailed database. Level A evidence can only be achieved by multiple randomized, controlled trials corroborated by high-quality registry studies.⁶ For these international leadership bodies, it is time to work on building the infrastructure for randomized, controlled trials and an IE registry to go beyond the existing guidelines.

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RANDOMIZED CLINICAL TRIALS OF SURGERY FOR INFECTIVE ENDOCARDITIS: REALITY VERSUS EXPECTATIONS!

Supplemental material is available online.

Reply to the Editor:

Lack of randomized clinical trials (RCTs) to provide level A evidence is particularly evident in guidelines for infective endocarditis (IE).^{1,E1-E5} Although it is fashionable to dismiss information, inferences, and comparisons of outcomes derived from observational experiences, much of the information used to manage patients with cardiac disease is derived from nonrandomized studies.² It is sobering to know that only

11% of American College of Cardiology/American Heart Association guidelines are based on level A evidence.³

To date, only 1 RCT has been published for IE.^{E6} It included 76 patients in 2 centers during a 4.5-year enrollment period to answer a specific question about the timing of surgical intervention for left-sided IE with large vegetations and important valve regurgitation: Should surgery be performed within 48 hours, or should one wait until heart failure symptoms occur? The attention paid to and the effect of this small study underscore the value of RCTs for evidence-based medicine.

Managing patients with IE involves a multispecialty team, and IE operations are difficult, with the highest reported mortality of any valve surgery.^{E1} Establishing an international registry and conducting an RCT, as proposed by Bando,¹ would be ideal, but there are still limitations and pitfalls.^{2,4,5} Current outcomes are variable, and not every surgeon or center can be included, because experience with and mastery of the technical aspects of these operations are essential. This must be recognized so that appropriate referrals are made to centers of excellence.^{E1} Even then, there would remain many impediments to clinical trials of IE. Because IE operations are uncommon even at centers of excellence, low enrollment and underpowered studies would be a challenge.^{2,4,5} Equipoise is also challenging: The better the surgical judgment and experience, the more likely that equipoise will be lacking.^{2,4,5}

The challenges in organizing an international registry are apparent when one considers the experience of ICE-PCS (International Collaboration on Endocarditis Prospective Cohort Study group), a multicenter international (64 sites from 28 countries) registry of patients with IE.^{E7} ICE-PCS recently published results of early surgery for *Staphylococcus aureus* prosthetic valve IE.^{E7} During a 6-year period, only 168 patients who qualified for the study were enrolled, and in-hospital and 1-year mortalities were high, probably because of the wide variability in expertise among contributing centers. The CTSN (Cardiothoracic Surgery Clinical Trials Network) includes only select surgical programs and highly experienced operators.⁴ Despite the efforts of the CTSN to control site-to-site variability in technique, however, the surgical procedures are subject to modifications. Both technical expertise and procedural variation affect the actual treatment delivered in ways that may not be apparent.^{2,4}

Ultimately, the primary goal is to improve patient outcomes, and it is imperative that there is transparency in reporting outcomes of IE operations by all centers. Clinical trials may serve to identify and disseminate more effective therapies. Because of the complexity, variability, and high-risk nature of IE surgery, trials must be designed with very specific questions and must ensure a standardized team approach to patient selection,

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surgical indication, timing of operation, and conduct of the operation by an experienced high-volume surgeon and surgical team. Even then, however, the results will never be generalizable to centers that average too few patients with IE to achieve the experience necessary for excellent outcomes.

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**KEEP FUMBLING AROUND
IN THE DARK WHEN IT
COMES TO INFECTIVE
ENDOCARDITIS, OR
PRODUCE NEW, RELIABLE
DATA TO REDESIGN THE
GUIDELINES?**

Reply to the Editor:

We thank Dr Bando¹ for his valuable comments and we share his view regarding the construction of an infrastructure for randomized controlled trials and a registry of endocarditis. The scarcity of data emerging from the few available randomized trials significantly restricts our ability to draw conclusions on the most appropriate treatment of complex endocarditis or define a line of demarcation between allogenic tissue and mechanical or xenograft prostheses. The benefit of early surgery over medical treatment remains established,² and a randomized study revealed better long-term survival and lack of thromboembolic complications with the use of allograft over conventional prostheses.³ Additionally, several studies are insisting on the biomechanical and hemodynamic advantage provided by allogeneic and autologous substitutes, which is reflected in the favorable long-term outcomes in terms left ventricular function.⁴

We agree with Bando¹ about the potential unavailability of allogenic substitutes in certain parts of the world. In Africa and Asia, the limitation to their use is exacerbated by other factors, such as lack of specific training and rules imposed by social and religious education. However, when thinking of a revision of the current guidelines on infective endocarditis,⁵ several factors need to be taken into account. First of all, over the past 15 years, infective endocarditis has seen a substantial change in its etiology and pathogenesis. Changes in the characteristics of the patient population—in the geographic distribution of infective endocarditis as well as the selection of antibiotic-resistant germ strains—have significant implications in regard to surgical strategy and approach. An international registry to collect information on the epidemiology, etiology, drug resistance, and geographic distribution is of paramount importance in this context. Also, data on the actual trend of use of synthetic or autologous tissues around the world for the reconstruction of extensive lesions of the annulus and related cardiac structures, along with the data on their long-term outcomes, would be extremely valuable to shed light on a field that is still dominated by expert consensus rather than evidence from adequate trials.

Another important point to consider is the morphology of the vegetation, which represents a discriminatory criterion

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