Evaluating and Optimizing Outcomes of Surgery for Endocarditis

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The mortality rate for infective endocarditis remains high—too high. In the preantibiotic era, death was inevitable for anyone unfortunate enough to develop this disease. Penicillin changed this dismal picture. By 1951, based on more than 1000 cases of endocarditis compiled from several reports, Hunter estimated that the overall cure rate was about 70%. A half-century later, despite the advent of valve replacement surgery and the development of many more antibiotics, the “global cure rate” for infective endocarditis remains about the same. For example, Hasbun et al recently reported a 6-month survival rate of 74% among 513 patients with endocarditis in the United States. Similarly, for 208 patients in England the cure rate at 6 months was 73%. Mortality in a large tertiary-care hospital in the United States was about 35%. When more favorable rates have been reported, for example from France by Hoen et al, the follow-up period often was relatively short. The mortality for patients who have been microbiologically “cured” continues to increase over years. In sum, it appears that little progress has been made.

This remarkable fact merits further explanation. Since 1951, much has been learned about the management of endocarditis and patients have benefited from important therapeutic advances, chief among which is valve replacement surgery. It is clear that the ability to remove infected valves and replace them with metal, plastic, or tissue prostheses has saved the lives of many patients. At the same time, availability of a broad range of new, more powerful antibiotics has made it easier to achieve microbiological cure; these advances have clearly improved outcomes in some patient groups. For example, cure rates for patients infected with penicillin-sensitive viridans streptococci are expected to be well above 90%. For this reason, when a clinical series includes a fairly high proportion of cases caused by streptococci, the reported cure rate tends to be more favorable—around 85%.

Why, then, is the global mortality much worse? The primary explanation lies in the steadily evolving epidemiology of infective endocarditis. Major trends include more valvular prostheses and prosthetic valve endocarditis; more intravascular devices and device-related endocarditis; more antibiotic resistance among the etiologic organisms; more patients with major comorbid conditions, such as diabetes, dialysis-dependent renal failure, drug abuse, or AIDS; more patients with hospital-acquired endocarditis; and more patients with staphylococcal infections. The mortality rates in most of these subgroups continue to be high, as evidenced in recent reports: 56% at 1 year among patients receiving hemodialysis, up to 46% in patients with prosthetic-valve endocarditis, and up to 68% in nosocomial cases.

The steeply rising proportion of cases of endocarditis due to staphylococci is a major contributing factor to these high mortality rates. Staphylococcus aureus (whether antibiotic-sensitive or resistant), coagulase-negative staphylococci, Staphylococcus lugdunensis—all are more difficult to treat and more difficult to cure than relatively less severe streptococcal infections.

The end result of this complicated combination of factors is that the current global mortality rate for endocarditis is still about 30%, much the same as in 1951. Disappointing, and challenging. What can be done?

While further incremental advances in prevention, diagnosis, and antibiotic therapy are expected, optimization of surgical approaches seems to offer the best immediate opportunity to reduce mortality. The high value of surgery for selected cases of endocarditis is taken for granted, based on extensive clinical experience. However, the evidence to support its value remains empirical, not based on randomized controlled trials. The reason is simple—sicker patients are selected for surgery. This source of bias is unavoidable because management for these complex, varied, and seriously ill patients must be individualized; it seems ethically unacceptable to randomize them prospectively to surgical vs nonsurgical treatment.

In this issue of THE JOURNAL, Vikram and colleagues approach this difficult issue in a novel way. After defining a large cohort of patients with endocarditis, the authors developed and applied a propensity score that predicts the quantitative likelihood that surgery would be recommended for an individual patient. Patients who actually underwent surgery were matched with controls, patients with identical or similar propensity scores who (for whatever reason) did not undergo surgery. This technique, previously described and validated in other settings, largely eliminates the confounding effect of selection bias and can be expected to yield results comparable with those of randomized controlled trials.

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The main finding was that surgery was associated with about a 50% reduction in mortality at 6 months in the subgroup of 109 patients who could be matched by propensity scores to 109 controls. Demonstration of such a substantial benefit, while not surprising, helps to validate the belief that surgery is valuable. Likewise, it was not surprising that benefit was greatest in patients with significant heart failure, a complication long associated with higher mortality in endocarditis.\textsuperscript{16}

Thus, the major contribution of this study is not so much its immediate findings, but its implications for future studies. The authors point the way for application of a powerful statistical technique to some previously intractable problems in research on endocarditis. Use of propensity scores to evaluate outcomes among patients in large databases, such as that now being assembled by the International Collaboration on Endocarditis (ICE),\textsuperscript{17} should be productive.

In this study, the lack of demonstrated benefit for patients with indications for surgery other than moderate to severe heart failure (eg, septic embolism; refractory infection, including intracardiac abscess; large vegetations) is surprising and provocative. Is it possible that the presumed benefits of surgery are overestimated for patients who do not have significant heart failure? This is one of many pressing questions about surgical management that still require clarification and explanation. Others include: What interval between diagnosis and surgery is associated with the lowest mortality? Is earlier intervention better? If so, how early? How can patients best be selected for this major intervention? Is the presence of a large vegetation per se an adequate indication for surgery? If so, what size is considered large in this context?

A better understanding of how and when to intervene surgically offers the best opportunity to overcome the central challenge in endocarditis management today—how to reduce mortality. The approach described by Vikram and colleagues\textsuperscript{15} can help to reach the heart of this matter.

REFERENCES

The SARS Response—Building and Assessing an Evidence-Based Approach to Future Global Microbial Threats

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ON FEBRUARY 21, 2003, AN ILL PHYSICIAN TRAVELING from China’s Guangdong Province spent 1 night on the ninth floor of a Hong Kong hotel. During the next 24 hours, this individual would infect more than a dozen other hotel guests and visitors.\textsuperscript{3} Within days, these guests would transmit their infections to health care workers and family members in Hong Kong, Vietnam, Singapore, and Canada, providing a vivid illustration of the rapidity and ease with which infectious diseases can spread and marking the start of the global outbreak of severe acute respiratory syndrome (SARS). One of the first persons to recognize the potential gravity of the situation was Carlo Urbani, an infectious disease physician working for the World Health Organization (WHO) in Hanoi. Urbani observed that a patient who had recently arrived from Hong Kong had a highly transmissible form of atypical pne-

See also pp 3215, 3222, and 3229.

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