

EDITORIAL COMMENT

Early Surgery in Infective Endocarditis

Can it Be Too Early?*



Michael J. Mack, MD,^a Patrizio Lancellotti, MD^{b,c}

Approximately 50% of patients with infective endocarditis (IE) will require early surgery (i.e., during the initial hospitalization before the completion of a full therapeutic course of antibiotics) (1). With early surgery, there are concerns that performing the procedure during an active infection, before the valve is completely sterilized, may lead to an increase in post-operative complications. However, recently it has been suggested that early surgical intervention with <7 days of pre-operative antibiotic therapy is associated with a lower risk of mortality in comparison with surgery performed between 8 and 20 days after the initiation of antibiotics (2). Indeed, in general, clinical practice has moved more aggressively toward earlier surgical intervention.

The decisions on the timing of surgical intervention in IE are complex and depend on many clinical factors. It is generally agreed that those decisions on both the indication and timing of surgical intervention should be determined by a multispecialty team with expertise in cardiology, imaging, cardiothoracic surgery, and infectious diseases (3). Among those

factors that mitigate decisions toward early surgery are the infecting organism; the size of the vegetation; the presence of perivalvular infection, embolism, or heart failure; patient age; noncardiac comorbidities; and available surgical expertise (Table 1). Current guideline Class of Recommendations (COR) I; Level of Evidence (LOE): B, are that early surgery is indicated in patients with IE who present with valve dysfunction resulting in symptoms or signs of heart failure or in patients with IE caused by fungi or highly resistant organisms (e.g., vancomycin-resistant *Enterococcus*, multidrug-resistant Gram-negative bacilli) (4). Other COR I, LOE: B recommendations include patients with IE complicated by heart block, annular or aortic abscess, or destructive penetrating lesions with evidence of persistent infection (manifested by persistent bacteremia or fever lasting >5 to 7 days, provided that other sites of infection and fever have been excluded) after the start of appropriate antimicrobial therapy. COR IIa, LOE: B indications for early surgery include patients who present with recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy, severe valve regurgitation, and mobile vegetations >10 mm, particularly when involving the anterior leaflet of the mitral valve.

The timing of surgery is based on balancing the urgency of indications for surgery versus the risks of complications occurring afterward. However, there is a paucity of robust evidence available to define the optimal timing of valve surgery. Over several decades, the guideline recommendations have all relied on data from observational studies regarding the indications for early surgery. The problems with all studies examining the benefit of early surgery in IE is that they are subject to survivor bias. The correlation between longer survival and surgery may be wrongly interpreted as evidence that surgical treatment improves survival. In fact, when published studies are

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the ^aBaylor Scott & White Health, Dallas, Texas; ^bUniversity of Liege Hospital, GIGA Cardiovascular Sciences, Department of Cardiology, CHU Sart Tilman, Liege, Belgium; and the ^cGruppo Villa Maria Care and Research, Maria Cecilia Hospital, Cotignola, and Anthea Hospital, Bari, Italy. Dr. Mack has served as a trial co-principal investigator for Edwards Lifesciences and Abbott; and is a study chair for Medtronic. Dr. Lancellotti has reported that he has no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [JACC author instructions page](#).

TABLE 1 Factors That Mitigate Toward Early Surgery in Infective Endocarditis

Infesting organism
Fungus
Enterococcus (vancomycin-resistant)
Staphylococcus
Multidrug resistant Gram-negative bacilli
Size and mobility of vegetation
>10 mm
Enlarging on antibiotics
Anterior leaflet mitral valve
Paravalvular infection
Heart block
Annular/periaortic abscess
Recurrent embolism
Severe valve regurgitation
Heart failure

adjusted for survivor bias, which occurs because patients who live longer are more likely to undergo surgery than those who die early, there may be a loss of benefit from early surgery (2).

SEE PAGE 31

With this background in mind, Gisler et al. (5) in this issue of the *Journal*, examined the impact of pre-operative antibiotic treatment duration on valve culture results in an attempt to determine the incidence and significance of specimen culture positivity on outcomes. They included 231 patients with IE and surgical specimens over an 11-year period of which 153 (66%) were native valve IE. In total, 58 (25%) patients had positive specimen cultures and 173 (75%) were culture negative. Infection with *Staphylococcus* species and *Enterococcus* species were significantly associated with a positive valve specimen culture, and there was not a

direct linear correlation between the length of pre-operative antibiotic duration and reduction in culture positivity. More specifically, the greatest impact was within the first few days, with very little impact from treatment >7 to 9 days and no impact from >19 to 21 days of pre-operative antibiotic treatment. Furthermore, IE caused by *Staphylococcus* and *Enterococcus* species demonstrated a high risk of positive specimen cultures, irrespective of the length of pre-operative antibiotic treatment. The authors conclude that results of this study indicate that, in particular in staphylococcal and enterococcal IE, the aim for a negative valve culture should not primarily influence the decision making on the timing of valve surgery. They also demonstrated diminishing returns the longer antibiotics are used.

So, what useful information does this study provide to help direct clinical practice? All retrospective, observational studies including this one are subject to survivor bias and lack of insight as to the rationale for the clinical decisions that were made. Nonetheless, the present study does provide some additional evidence in support of early surgery, especially when staphylococcal or enterococcal bacteria are the causative organisms. If an urgent indication for early surgery is present, the multidisciplinary clinical decision-making team should err on the side of early surgery. To delay surgery to “get more antibiotics on board” is likely not going to lead to any additional patient benefit.

ADDRESS FOR CORRESPONDENCE: Dr. Michael J. Mack, Baylor Scott & White Health, 1100 Allied Drive, Plano, Texas 75075. E-mail: Michael.mack@bswhealth.org. Twitter: [@Mmack555](https://twitter.com/Mmack555).

REFERENCES

1. Chu VH, Park LP, Athan E, et al. Association between surgical indications, operative risk, and clinical outcome in infective endocarditis: a prospective study from the International Collaboration on Endocarditis. *Circulation* 2015;131:131-40.
2. Anantha Narayanan M, Mahfood Haddad T, Kalil AC, et al. Early versus late surgical intervention or medical management for infective endocarditis: a systematic review and meta-analysis. *Heart* 2016;102:950-7.
3. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J* 2015;36:3075-128.
4. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation* 2015;132:1435-86.
5. Gisler V, Dürr S, Irincheeva I, et al. Duration of pre-operative antibiotic treatment and culture results in patients with infective endocarditis. *J Am Coll Cardiol* 2020;76:31-40.

KEY WORDS cardiac valve cultures, infective endocarditis, pre-operative antibiotic treatment