Commentary: How many times are enough? Infective endocarditis in drug users

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The incidence of infective endocarditis (IE) has increased in parallel with the current opioid crisis across North America.^{1,2} The relationship between active drug use (DU) and concomitant IE is shaping into a formidable societal problem. For the cardiac surgeon, drug-related IE constitutes not only a technical challenge but also an ethical one when facing reoperation for reinfection of prosthetic valves secondary to recurrent DU. Few studies have investigated large numbers of patients with DU undergoing valve surgery for IE and its outcomes in the current era, and current peer-reviewed guidelines have little to contribute with respect to patient management.³

In this issue of the *Journal*, Mori and colleagues⁴ attempt to assess the incidence and early outcomes of first valve surgery (FVS; n = 652) versus reoperative valve surgery (RVS; n = 273) in patients with DU and infective endocarditis in a large contemporaneous cohort of patients. This retrospective study encompasses 925 patients with a median age of 37 years and a history of DU who underwent valve surgery for IE at 8 university-affiliated US centers during the course of 5 years. Data were gathered by interrogating each center's Society of Thoracic Surgeons database. Mori and colleagues⁴ found that the overall case volume and the proportion of RVS during the study period increased significantly, from 19% to 28%. As expected, patients undergoing RVS have higher operative risk and higher unadjusted 30-day mortality than those undergoing FSV. Multivariate analysis, including number of reoperations as a covariate, showed that reoperation was an independent risk factor for 30-day mortality; however, RVS was not associated with an increased risk of composite major adverse events. Multiple reoperations were not shown to be associated with increased early mortality, but this could be a type II error resulting from patient attrition. Active IE, a history of dialysis, shock at the time of surgery, and number of valves operated on were other independent risk factors for 30-day mortality.

Siamak Mohammadi, MD, FRCSC (left), and Dimitri Kalavrouziotis, MD, FRCSC (right)

Central Message

Reoperations can be performed safely for drug-related endocarditis. Prognosis in these young patients may be influenced more by concerted rehabilitation programs than by progress in surgical technique.

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Mori and colleagues⁴ are to be congratulated on this collaborative effort to study this timely problem in the setting of a current opioid crisis in a young population with a potentially high functional life expectancy. The younger age and lower burden of baseline morbidity among these patients may partly explain the lower mortality (8.1%) among patients with RVS, despite higher markers of surgical acuity, than in previous reports,^{5,6} which show a greater than 20% mortality for patients with prosthetic valve IE without a history of DU. Notably, the study by Mori and colleagues⁴ does not have a comparator group consisting of patients with IE but without DU. Furthermore, the lower mortality could be explained by the high prevalence of right-sided IE (34%), which is thought to have better prognosis than left-sided IE. One of the major limitations of the study by Mori and colleagues⁴ is the potential for misclassification bias, and, as a result, the data need to be analyzed cautiously. Any history of DU allows the inclusion of patients without intravenous injection DU and those with recreational DU, including the use of cannabinoids, which is common among young patients and has not been shown to be pathophysiologically linked to IE. This definition of a DU may “dilute” the target population of the study and thus contribute to the improved outcomes reported. The absence of a clear distinction between a remote and a recent history of DU is also another drawback of the study of Mori and colleagues.⁴ A history of recent DU

had not been reported in 25% of patients undergoing FVS and 46% of those undergoing RVS, and was limited to patients in later Society of Thoracic Surgeons iterations, which included DU timing information in relation to valvular surgery.

The study shows us that RVS in drug-associated IE patients is technically feasible in expert centers, with acceptable early mortality and morbidity rates. That RVS is associated with worse outcomes than FVS and that the second reoperation is worse than the first in terms of early mortality are not novel concepts. The real missing piece of the puzzle concerns late outcomes after FVS and RVS, with the major concern being the risk of reinfection associated with persistent DU in this population. Stated differently, there is little reason to believe that the early surgical outcomes of the patients with both IE and DU should be any different from those of patients with IE but without a history of DU. What is the risk of recurrent DU and recurrent prosthetic valve IE in patients after FVS? How many reoperations should be performed in the patients undergoing RVS before the risks become prohibitive? Is operative risk the only element that should be considered when offering reoperation to a patient with DU after FVS? These questions unfortunately remain unanswered. Late follow-up for evaluating the risk of mortality and recurrent infection from continued DU is the compelling unknown. Shedding some light on this question may help the surgical community to confront precisely this issue, which is more ethical than technical. The results of the current study by Mori

and colleagues⁴ underline the increasing burden of drug-associated IE, which primarily affects young patients, and the urgent need to focus our efforts to reduce recurrent DU in this population. This study identifies a significant opportunity to create specialized multidisciplinary IE teams, dedicated to providing rehabilitation from substance addiction and the social support required after valve surgery. Future studies should examine the effects of such programs after valvular surgery for drug-associated IE and should focus exclusively on patients with active intravenous DU to allow us to make informed decisions in this challenging area of cardiac surgery.

References

1. Rudasill SE, Sanaiha Y, Mardock AL, Khoury H, Xing H, Antonios JW, et al. Clinical outcomes of infective endocarditis in injection drug users. *J Am Coll Cardiol*. 2019;73:559-70.
2. Copper HL, Brady JE, Ciccarone D, Tempalski B, Gostnell K, Freidman SR. Nationwide increase in the number of hospitalization for illicit injection drug use-related infective endocarditis. *Clin Infect Dis*. 2007;45:1200-3.
3. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Fleisher LA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2017;70:252-89.
4. Mori M, Bin Mahmood SU, Schranz AJ, Sultan I, Axtell AL, Sarsour N, et al. Risk of reoperative valve surgery for endocarditis associated with drug use. *J Thorac Cardiovasc Surg*. 2020;159:1262-8.e2.
5. Kim JB, Ejiofor JI, Yammine M, Ando M, Camuso JM, Youngster I, et al. Surgical outcomes of infective endocarditis among intravenous drug users. *J Thorac Cardiovasc Surg*. 2016;152:832-41.e1.
6. Leontyev S, Borger MA, Modi P, Lehmann S, Seeburger J, Walther T, et al. Redo aortic valve surgery: influence of prosthetic valve endocarditis on outcomes. *J Thorac Cardiovasc Surg*. 2011;142:99-105.