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Commentary: Bicuspid aortic valve endocarditis—a different disease?

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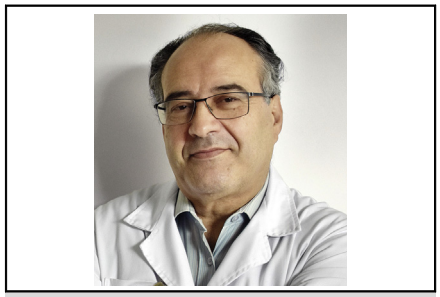

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CENTRAL MESSAGE

Aortic valve endocarditis remains a serious surgical problem. Infection is more frequent and may be more destructive in bicuspid than tricuspid valves. Hence, those patients require closer attention.

Native infective endocarditis (IE) is not a rare complication of aortic valve diseases. Its incidence is estimated at 3 to 10 cases per 100,000 persons per year. It is more often caused by *Streptococcus viridans* and *Staphylococcus aureus*, but other agents, including fungi, are also frequently involved.

All infective agents demonstrate particular potential for destruction of the valve components, including leaflets, annulus, aortic root, sometimes even extending to the aortic–mitral curtain. Except in drug-addicted or immunosuppressed individuals, the infection usually occurs in structutally-deteriorated valves, either stenotic or regurgitant. Although medical therapy can cure the disease in more incipient cases, hospital mortality may reach 20%. Often, however, the disease is very destructive, requiring aortic valve replacement. Indications for surgery include extensive destruction of the valve components, which results in treatment-refractory congestive heart failure, persistent sepsis, fungal endocarditis, repeat septic emboli, rupture of sinus of Valsalva and/or aneurysm, and conduction defect due to septal abscess.

Particularly susceptible to infection appear to be the congenital bicuspid aortic valves (BAVs). This is the most common congenital cardiac malformation, affecting 0.5% to 2% of the population. Almost one half of subjects with a BAV develop different degrees of valvular dysfunction during their lifetimes.[1] The Mayo Clinic Group estimates that the incidence of BAV-IE cases is approximately 14 per 10,000 patient-years, 11 times greater than that of the general population.[2] Kiyota and colleagues[3] also found that patients with BAV are at a markedly increased risk of IE and aortic root abscess than patients with tricuspid aortic valves (TAVs), that is, the incidence of IE in the BAV population ranges from 10% to 30%. Increased risk of IE in patients with BAV indicates they may be a candidate group for long-term trials of antibiotic prophylaxis of IE. This has become a source of controversy in recent times.

According to most series, there do not appear to be significant differences in the infecting agents between the BAV and TAV groups. Patients who have bicuspid are usually younger than those who have tricuspid valves and more often have periannular complications.[4] In contrast, extension to the mitral valve appears to be more common in patients with tricuspid valves. Most probably because of the younger age, the in-hospital mortality rate in the bicuspid is lower than that in the tricuspid group. However, the differences in behavior between bicuspid and tricuspid valve endocarditis are, again, subjected to a great degree of controversy.

In a work published in this issue of the *Journal*, Le and colleagues[5] set to determine the long-term survival and need for reoperation after surgical treatment of IE in 51 patients with BAV (24%) and 159 patients with TAV operated on at their institution from 1997 to 2017. This is a well-written article, but the numbers are relatively small. However, the outcomes are well described. They found that "while only 2% of the population has a BAV, 24% of

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patients with IE had BAV. The disproportionate incidence of IE in patients with BAV is observed despite significantly fewer preoperative risk factors relative to those with TAV-IE, such as prior cardiac surgeries, which are well-known risk factors for IE."

They found that the surgical incidence of IE in BAV did not change significantly following the 2007 American Heart Association guideline changes for antibiotic prophylaxis, which was one of the aims of their study. The TAV-IE group was significantly older, with greater incidences of hypertension, coronary artery disease, and congestive heart failures. There was no significant difference in postoperative stroke, sepsis, pacemaker requirement, or in-hospital mortality between groups. Liver disease was a risk factor for operative mortality. Ten-year survival rate was significantly better for BAV (64% vs 46%), although the authors admit that this might be due to the small size sample. Significant risk factors for long-term mortality were intravenous drug use and preoperative renal failure requiring dialysis. They thus concluded that "BAV patients develop infective endocarditis requiring surgery at a younger age than TAV patients, but have significantly better long-term survival. We should detect BAV early to prevent endocarditis and treat BAV endocarditis aggressively with surgery."

I am not sure that this conclusion is sufficiently supported by the data presented. After all, the BAV group was relatively small (51 patients). One important, positive point—the percent completion of follow-up for survival was 100%. While it is apparent that patients with BAV treated surgically for IE do well and have good long-term survival, these data do not actually influence the debate regarding antibiotic prophylaxis and should not be used to support or refute American Heart Association guidelines on this topic. Still, this paper may contribute to the discussion of this topic. I'll come back to that later. Nevertheless, there does not appear to be major differences attributable to the type of valve. The longer-term survival of patients with BAV almost certainly is due to the younger patients' age, but the small population size may also have had an impact.

In this series, the authors found that *Enterococcus* species were more often the causative organism of IE in patients with TAV (22% vs 3.9%), whereas *Streptococcus* were more often the causative organism in patients with BAV (51% vs 29%). This difference was not found in other series by other authors, but Le and colleagues could not provide a convincing explanation for this difference. They feel that in their population "infections *by Streptococcus* species are associated with dental procedures and poor oral hygiene" and speculate that "BAV patients seemed to be more susceptible to oral bacterial flora, due to the damage of BAV from valvulopathy and hemodynamics." This issue merits further study.

Finally, there remains the question of prophylaxis in patients with BAV versus TAV following the publication of the newer guidelines, actually not very dissimilar from European Guidelines.[6,7] After prophylactic antibiotic restriction, there was no significant increase in surgical BAV IE incidence, and patients with BAV had better long-term survival. The authors findings "supported continued restriction (of prophylaxis) for BAV patients." Nonetheless, they defend that "we should detect the BAV condition early in patients to provide recommendations for prevention of BAV endocarditis, and surgically treat BAV endocarditis aggressively."

In conclusion, there still is a degree of controversial information about IE in BAV. I agree with the authors' conclusion in that considering the mounting evidence that patients with BAV are at greater risk of developing IE despite being younger in age and having fewer comorbidities than those with TAV, it is important to identify patients with BAV early. Hence, although this may vary significantly from population to population, earlier identification of BAV allows for earlier patient education regarding the importance of maintaining proper oral hygiene and routine dental follow-up. Curiously, the incidence of IE has increased rapidly in England, although no change was detected in trends directly following the updated National Institute for Health and Care Excellence guidelines for antibiotic prophylaxis, in the United Kingdom (2008), either overall or in cases associated with oral *Streptococci*. The differences were attributed to "inclusion criteria."[8] However, in a new version, currently under discussion, "the committee recommended that people with bicuspid aortic valve disease of any severity (including mild disease) should be offered specialist referral as it differs in terms of its progression to other types of valve disease."[9]

References

1. Della Corte A, Lo Presti F. Latest advances in the treatment of bicuspid aortic valve. *Surg Technol Int*. 2020;37:177-82.
2. Michelena HI, Katan O, Suri RM, Baddour LM, Enriquez-Sarano M. Incidence of infective endocarditis in patients with bicuspid aortic valves in the community—Letter to the Editor. *Mayo Clin Proc*. 2016;91:122-3.
3. Kiyota Y, Della Corte A, Vieira VM, Habchi K, Huang CC, Della Ratta DD, et al. Risk and outcomes of aortic valve endocarditis among patients with bicuspid and tricuspid aortic valves. *Open Heart*. 2017;4:e000545.
4. Kahveci G, Bayrak F, Pala S, Mutlu B. Impact of bicuspid aortic valve on complications and death in infective endocarditis of native aortic valves. *Tex Heart Inst J*. 2009;36:111-6.
5. Le T, Graham NJ, Naeem A, Clemence J Jr, Caceres J, Wu X, et al. Aortic valve endocarditis in patients with bicuspid and tricuspid aortic valve. *J Thorac Cardiovasc Surg Open*. 2021;8:228-36.
6. Baddour LM, Wilson WR, Bayer SA, Fowler VG Jr, Tleyjeh IM, Rybak MJ, 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.
7. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, 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). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J*. 2015;36:3075-128.

8. QuanTP, Muller-Pebody B, Fawcett N, Young BC, Minaji M, Sandoe J, et al. Investigation of the impact of the NICE guidelines regarding antibiotic prophylaxis during invasive dental procedures on the incidence of infective endocarditis in England: an electronic health records study. *BMC Med*. 2020;18:84.

9. National Institute for Health and Care Excellence–guideline heart valve disease presenting in adults: investigation and management–draft for consultation, March 2021. Available at: https://www.nice.org.uk/guidance/GID-NG10122/documents/draft-guideline. Accessed September 21, 2021.