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EDITORIAL COMMENT

Avoiding a Repeat Sternotomy in Recurrent Carcinoid Heart Disease*

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In this issue of *JACC: Case Reports*, Luthra et al. (1) provide an important contribution, illustrating the application of evolving percutaneous cardiac valve replacement techniques to the troubling phenomenon of recurrent serotonin-induced valvulopathy in carcinoid heart disease. First, a few comments about the problem of recurrent carcinoid valvulopathy on newly implanted bioprosthetic valves.

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In 2014, in an abstract at the annual meeting of the European Neuroendocrine Tumor Society, we presented an abstract that reported a 46% early recurrence of carcinoid valvulopathy on newly implanted bioprosthetic valves in patients with carcinoid heart disease (2). One year later, at the annual European Neuroendocrine Tumor Society meeting, the Jerusalem group led by Simona Glasberg presented, in abstract format, a similar patient series demonstrating an even higher rate of early recurrence (3). At that time, both abstracts concluded that serious consideration should be given to the use of mechanical prosthetic valves in light of the high frequency of recurrent fibrosis attributable to serotonin and possibly other tumor-derived amines as well. In 2017, the Food and Drug Administration approved the use of telotristat ethyl (a tryptophan hydroxylase inhibitor that blocks the first step in the conversion of tryptophan to serotonin); the drug was approved for use in the treatment of diarrhea associated with carcinoid syndrome (4). It is the first oral medication that blocks the primary causative agent of carcinoid heart disease and, although logic would suggest its likely efficacy, data are lacking concerning its success at halting the occurrence or progression of carcinoid heart disease. Therefore, the decision of which valve prosthesis should be used in patients with carcinoid valvulopathy has remained a major debate with the neuroendocrine experts split between the desire to use bioprosthetic (tissue) valves because of the increased safety of valves that do not require anticoagulation in patients frequently requiring tumor-reductive invasive procedures and the option of mechanical valves that eliminate the propensity of serotonin to cause recurrent valve fibrosis on newly implanted valves but that require anticoagulation with warfarin. The current case report illustrates what carcinoid heart disease experts had hoped would eventually be a therapeutic option for recurrent valvulopathy in those cases in which, despite all tumor-reductive modalities tried, serotonin remains elevated, contributing to recurrent carcinoid valve disease. In our series of 27 patients, despite the hope that after valve replacement antitumor drugs and procedures would reduce serotonin to normal levels, only 1 patient ultimately achieved a normal serotonin level. Until the transcatheter valve replacement option became a reality, the plight of those with recurrent valve fibrosis on newly implanted bioprosthetic valves was progressive heart failure unless a repeat open-heart operation was performed. However, the success of the transcatheter valve-in-valve technique has provided new hope that tissue valves can be used in these patients without the fear of an open-chest reoperation. This innovation and the employment of a patch enlargement of the right

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ventricular outflow tract with bovine pericardium (5) to enable the use of a larger pulmonic valve prosthesis set the stage for a less invasive intervention for the problem of recurrent serotonin-related valvulopathy on bioprosthetic valves.

In addition, it is hoped that telotristat ethyl will provide an added therapeutic tool in the attempt to prevent carcinoid fibrosis of the transcatheter bioprosthetic valves. This is a topic begging for a study aimed at elucidating the efficacy of telotristat in achieving such protection. It is in this context that the current report demonstrates the appropriate and successful use of transcatheter bioprosthetic valve replacement for recurrent carcinoid valvulopathy.

We would make 1 constructive comment regarding the authors' statement "Right heart disease develops only with hepatic metastasis because the vasoactive substances are degraded in the liver, lung, and brain." Although liver metastases are the usual proximate source of a high concentration of serotonin, which stimulates serotonin receptors on the right-heart endocardium, in the absence of liver metastases, one should search for an ovarian carcinoid among other rare sources of a high concentration of serotonin draining via the inferior vena cava into the right heart (6).

The authors should be commended for this contribution. Already, the availability of the transcatheter valve-in-valve replacement option has begun to positively impact the discussion with patients contemplating surgery for carcinoid valvulopathy.

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