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EDITORIAL COMMENT

Where Are the Boundaries for Transcatheter Valve Therapy?*

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It is inherently human to explore and innovate. These desires may be born simply out of curiosity, altruism, or the need for survival, and they have spurred the ongoing revolution in valvular heart disease. Symptomatic valvular disease is a life-threatening disorder, with poor survival that resembles that of advanced malignancy, yet many of these patients go untreated in contemporary practice. Transcatheter valve therapy, through rapid evolution, has continued to traverse boundaries previously considered treacherous or unfathomable, enabling the treatment of hundreds of thousands of patients worldwide. These advancements are important, as they are elementary to the field of medicine, in which the mantra is to repeatedly practice to improve patients' lives.

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Mitral annular calcification (MAC) is a common, vexing clinical challenge for cardiovascular specialists and surgeons. Prevalence is age dependent, with 15% to 30% of those older than 70 years afflicted, and it is more frequent in patients with kidney disease, genetic abnormalities of the fibrous skeleton (e.g., Marfan syndrome), hypertension, and chronic inflammatory disorders (1). Although MAC is an incidental finding in many patients, significant calcific mitral stenosis or regurgitation can occur, arising from impairment of diastolic annular dilation and restriction of mitral leaflet opening. Patients with MAC can be difficult to treat surgically because of the risk for atrioventricular groove disruption, a complication that is nearly universally fatal when it occurs. Other significant complications include ventricular rupture and injury to the left circumflex coronary artery. Moreover, the surgical risk can be high or prohibitive because of the morbidities that frequently accompany MAC, such as coronary atherosclerosis, vascular disease, and renal insufficiency. Thus, mitral valve surgery generally is reserved for only select patients. Even in clinical trials of transcatheter mitral valve replacement (TMVR) or repair, in which novel approaches are being studied, the presence of MAC, even that of only a modest degree, is an exclusion criterion.

It is in this light that we must consider the study of Guerrero et al. (2). The investigators examined 64 patients who had aortic balloon-expandable valves (SAPIEN, SAPIEN XT, SAPIEN 3 [Edwards Lifesciences, Irvine, California], or Inovare [Braile Biomédica, São José do Rio Preto, Brazil]) adapted to treat high- or prohibitive-risk patients with clinically significant MAC. Patients were predominantly women, with frequent morbidities. The mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 14.4 ± 9.5%; this elevated risk is particularly noteworthy because the presence of MAC is not part of the Predicted Risk of Mortality score calculation and therefore must be considered in addition to the risk factors already examined in that algorithm. Key findings of the analysis were: 1) technical success using Mitral Valve Academic Research Consortium criteria was achieved in 46 patients (72%), with an additional 11 patients (17%) receiving a second valve; 2) significant left ventricular outflow tract (LVOT) obstruction occurred in 6 patients (9%); 3) residual mitral gradients were low (mean 4.4 ± 2.2 mm Hg), with mild or no paravalvular regurgitation in all implanted patients; 4) 5 patients had malpositioning requiring additional valve replacement, and there were 4 additional embolizations; and 5) consistent with the high-risk nature of these patients, there was high 30-day mortality (29.7%). Among survivors with 30-day follow-up data, 84% were minimally symptomatic or asymptomatic.

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The emergence of this therapeutic option and the findings of this registry are pioneering, and Guerrero et al. (2) are to be commended for developing a procedure for patients who had few, if any, surgical options. Although the use of these aortic prostheses for mitral valve-in-valve procedures has been well described, their application in MAC has been markedly limited because of challenging technical considerations. The shape of the mitral annulus is markedly irregular, subject to varying degrees of calcification and compliance in its body, with an anterior segment that is devoid of annular tissue and is contiguous with the posterior aortic root. Moreover, this irregularity poses significant challenges for determining an appropriate landing zone, which is a key technical consideration not only for the stability of the prosthesis but also to minimize the risk for LVOT obstruction. The operators achieved their clinical results through circularization of the irregular and potentially noncompliant mitral annulus; the incidence of paravalvular regurgitation was reduced through some degree of oversizing to maximize apposition of the prosthesis to the mitral annulus. There were no instances of annular rupture or perforation in the entire cohort, there was no moderate or severe residual mitral regurgitation in those with follow-up echocardiography (n = 22), and the procedure was performed without the coaxial support and added safety of transcatheter rails in most patients. These results are notable, as this procedure was novel for nearly all of the operators in this registry, with experience at each participating institution being markedly limited (64 patients treated at 32 sites) and with little or no guidance on technical considerations, including patient selection, annular sizing, prosthesis positioning, and complication management.

Although this registry demonstrates the feasibility of this novel approach for these challenging patients, notable unanswered questions remain. Patient selection is a key element to the success of any surgical procedure. Although the investigators describe criteria in general terms, there is limited insight into favorable and unfavorable characteristics for the landing zone. The pathology of MAC in the general population is highly variable, ranging from local to circumferential, with varying degrees of annular compliance. A subset of patients had significant LVOT obstruction, yet details on strategies to avoid this dreadful complication are not provided. Among these expert operators, many different technical approaches were used: transapical, transatrial with direct visualization, or transseptal access; placement of a rail or a wire free in the left ventricle; balloon predilation or not, and so on. Anecdotally, and not described in this registry, some operators also have sutured the prosthesis to the mitral annulus directly during the transatrial approach, sometimes with additional sealing material applied. In addition, there is scant detail on prosthesis sizing and positioning, and no imaging data on the post-procedural configuration of the prostheses or leaflet motion that could provide insight into the suitability of this therapy for the mitral position. These technical considerations must be addressed further while going forward, with the ultimate goal being to reduce the rate of complications, which, even when seemingly minor, can be catastrophic when they occur in high-risk patients.

On the whole, it is important to recognize the remarkable progress in the field of TMVR that is evident in this global, multicenter registry. The feasibility in this study was demonstrated with a circular prosthesis that is neither retrievable nor repositionable and is without a sealing cuff or an anchoring mechanism specifically designed to overcome with wide cyclic pressures in the left ventricle. Also, the cohort included treatment of women and those with preserved left ventricular function, 2 patient subsets that may be particularly predisposed to LVOT obstruction and that frequently have been excluded from clinical TMVR trials to date. A new boundary was crossed with successful TMVR therapy for severe MAC, which previously was considered to be hostile, through the adaptation of an off-label prosthesis for the procedure. One can therefore consider, with enthusiasm, the potential possibilities for success once dedicated prostheses become available, and how the unmet needs of many patients with mitral regurgitation will be finally addressed.

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KEY WORDS calcification, mitral valve, transcatheter