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EDITORIAL

What Is Blocking Transcatheter Ventricular Septal Defect Closure?

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Ventricular septal defects (VSDs) are among the most common congenital heart defects, with an incidence rate of 3 to 3.5 per 1000 live births.[1] VSDs range in size from tiny pinholes to the near absence of the ventricular septum. Perimembranous VSDs (pmVSDs) account for 80% of VSDs, involving the membranous septum. The membranous septum is adjacent to the septal leaflet of the tricuspid valve on its right ventricular aspect and to the aortic valve on its left ventricular aspect, while its inferoposterior margin closely relates to the bundle of His and bundle branches.

See Article by Tang et al.

Spontaneous VSD closure is common, but invasive closure is indicated in a subset.[2]Although surgery has long been the standard approach, transcatheter options have been available for decades. The first human experience of transcatheter closure (of muscular VSDs) was reported in 1988 by Lock et al.[3] Investigators have since explored various approaches and devices for transcatheter device VSD closure, with widely varying rates of success and risk of complications.[4]With improvements in device technology and techniques, transcatheter VSD closure is increasingly appealing, given the associated shorter hospital stay and faster recovery. Despite this, the US Food and Drug Administration has yet to approve any device for the indication of transcatheter closure of a pmVSD.

Successful transcatheter closure of pmVSD requires detailed anatomic delineation of the defect and its relation to surrounding cardiac structures. Because of the proximity of the conduction system and the aortic and atrioventricular valves, devices designed for other applications are often unsatisfactory. Careful defect sizing and device selection are important to minimize the risk of complications. Undersized devices are associated with device embolization and residual shunt. Oversized devices may damage adjacent structures, causing cause complete atrioventricular block (CAVB) or aortic or tricuspid valvular injury. The presence of a ventricular septal "aneurysm," a frequent finding, can help reduce the effective orifice size, allowing a smaller device and attenuating the likelihood of direct compression of conduction tissue; however, they can also be associated with multiple fenestrations, leading to incomplete closure.[5]

The first device designed specifically for transcatheter pmVSD closure had an asymmetrical design aimed to prevent aortic valve distortion and tricuspid valve injury. Following the initial use of an Amplatzer pmVSD occluder in 2003, several reports described reasonably high efficacy.[6,7] However, these early experiences were associated with a high incidence of CAVB, around 5% (and up to 20%).[8,9] The mechanism was presumed to be direct compression, trauma, or inflammatory

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reaction of conduction tissue, in the context of stiff disks often oversized to prevent embolization. Because of the high rate of CAVB, the original Amplatzer pmVSD occluder was not clinically acceptable, and there was a search for other devices with less risk of complications. Several devices have been developed for this purpose, with varied outcomes, and a-generation Amplatzer pmVSD occluder (St. Jude Medical, St. Paul, MN) is being studied in clinical trials. Multiple devices are also currently used off label for pmVSD closure, most commonly the Amplatzer Vascular Plug II and Amplatzer Duct Occluder first generation (St. Jude Medical). Both of these devices depend on stiffer delivery sheaths that can make the procedure challenging, especially in younger children.[8,10] Importantly, most experience has been outside the United States.

The Amplatzer Duct Occluder II (St. Jude Medical), a modification of the Amplatzer Duct Occluder first generation, indicated for small to moderate-sized patent ductus arteriosus closure, is made of soft, fabric-free, multilayered Nitinol wire mesh with low-profile retention disks; these characteristics are expected to minimize clamp force on the septum and radial stress on the conduction system, hopefully reducing the occurrence of postprocedural conduction abnormalities. Since the initial report of off-label use of Amplatzer Duct Occluder II to close a pmVSD in 2010, there have been several published studies. In addition to ease of use with the ability to deliver the device via antegrade or retrograde approach, potential advantages include fewer constraints based on age and weight given the lower profile of the delivery system (4F and 5F) and lower incidence of postprocedural electrophysiologic complications.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Tang et al describe the outcome of transcatheter VSD closure using the Amplatzer Duct Occluder II device as part of their routine clinical management.[11] Their stated goal was to describe the overall risk of complete left bundle-branch block (CLBBB), and to identify risk factors for CLBBB. The cohort consisted of 276 patients with a median age of 34 months and a median weight of 13.5 kg, who successfully underwent VSD closure. Follow-up was obtained in 244 patients. Postprocedural arrhythmias were identified in 87 patients (35.7%). Most of the arrhythmias were transient, whereas 15 patients (6.2%) were deemed to have persistent arrhythmias (duration not noted). No patient developed CAVB, but CLBBB occurred in 8 (early onset in 6 patients and late onset in 2 patients). All but 2 patients recovered normal conduction. Longer procedure time was the only risk factor identified. The investigators concluded that transcatheter closure of pmVSD using Amplatzer Duct Occluder II was technically effective, with several advantages, and suggest it should be considered a suitable device for transcatheter pmVSD closure despite the off-label use.

The report by Tang et al is a research letter, precluding the presentation of detailed procedural data, information that might be relevant to understanding the risk factors for left bundle-branch block.[11] Given that left bundle-branch block was transient in most, one wonders if some of the long procedures caused reversible injury to the His bundle (eg, because of multiple attempts at device positioning or difficulty with advancing the catheter across the lesion). In a more detailed previous report by the same group in a more heterogeneous cohort closed with various devices, the incidences of CAVB and CLBBB were 0.6% and 2.7%, respectively. On univariate analysis, the delivery sheath diameter and occluder size were risk factors for CLBBB. Given concern for the late occurrence of CLBBB, there is a need for long-term follow-up. Previous studies of both surgical and device closure of pmVSDs have raised concern about late atrioventricular block, requiring appropriate counseling about this potential complication. To compare outcomes across different devices, we will need to delve into the procedural details; this may also help identify whether the reported low rate in this series may have been attributable to patient selection.

Other challenges to further streamline transcatheter closure of pmVSDs are the diversity of indications and patient selection. A large number of patients in this cohort did not meet conventional indications for VSD closure based on symptoms, left ventricular volumes, pulmonary-to-systemic blood flow (Qp/Qs), aortic regurgitation, or sequelae of overcirculation. The concern with offering any invasive procedure in the absence of compelling clinical indication is that the consequence of a complication can be severe for an individual, even though the absolute risk of an adverse outcome is low.

How might a referring cardiologist use all the numbers discussed pertaining to complications of transcatheter pmVSD closure? The absence of CAVB and low incidence of CLBBB are encouraging Surgical studies focus on CAVB and need for permanent pacemaker placement, with most surgical literature reporting an incidence of around 1%, with contemporary results under 1%.[12,13] In a large single-center study of 848 patients with pmVSD by Yang et al, who used Amplatzer and Shanghai (LEPU Medical Technology Co, Ltd, Beijing, China) pmVSD occluders, pacemaker placement for CAVB was required in only 2 patients (0.24%) after a median follow-up of 3.1 years.[14] Other studies have similarly reported low rates of CAVB, permanent pacemaker placement, and other complications, such as aortic regurgitation.[15] Meta-analysis of surgical versus transcatheter device closure has described similar rates of procedural success and complications, such as clinically relevant residual shunt,

heart block requiring pacemaker placement, and significant valve regurgitation; and catheter closure is associated with less need for blood transfusion and shorter length of stay.[16]

Yet, as described below, most pmVSDs are closed surgically in the United States. This brings us back to the most remarkable aspect of this story: there were 276 pmVSD closed transcatheter using a single device at a single center. Given the incidence of pmVSD and extensive published evidence supporting that the safety and efficacy of percutaneous VSD closure are equal to or better than surgical closure, one might expect this procedure would be among the most common catheter procedures in pediatric cardiology. Indeed, many transcatheter procedures have been adopted broadly without evidence of equivalence or noninferiority to an existing conventional surgical approach. Yet, this procedure is rarely performed in the United States.

One reason for such regional differences may relate to distinct perspectives on appropriate clinical indications for VSD closure. On the margin, some differences of opinion between countries in specific situations would be expected. For example, one might understand a preference for surgery in the presence of aortic valve prolapse, where there might be a long-term risk of aortic regurgitation or erosion.[17]

But the difference is not marginal. Most of these patients included in this report would not meet indications for VSD closure in the United States. Of the 276 patients, only 51 had appreciable left ventricular dilation, and only 10 had a left ventricular end-diastolic dimension *Z*-score >3. Many more, about half (n=136), underwent closure because of “patient preference or social pressure.” We cannot imagine closing a VSD in the United States for this reason.

In fact, the reported US experience suggests that catheter-based VSD closure is a rare procedure in the United States. We queried HCUPNet (https://hcupnet.ahrq.gov), which uses data from the Healthcare Cost and Utilization Project to provide US national estimates of health care statistics for hospital inpatient, emergency department, and ambulatory settings, as well as US population-based health care data. Transcatheter VSD closure (*International Classification of Diseases, Ninth Revision* [*ICD-9*], procedure code 35.55) was performed ≈57±12 times in children in 2012. Taken at face value, putting aside the substantial caveats appropriate for the use of administrative data,[18] this suggests the current report from a single center includes about as many children as undergo catheter VSD closure in the United States over 5 years.

Our experience is that the vast majority of pmVSD closure is still performed surgically in the United States, and this aligns with HCUPNet data. In 2012, ≈3145 surgical VSD closures were performed in children (*ICD-9* procedure codes 35.62 [with tissue graft] and 35.53 [with device/synthetic material]; 1707±230 and 1438±191 cases, respectively). That is, according to these data, VSD closure is performed surgically ≈98% of the time in the United States (≈3200 operations versus 60 catheter-based closures annually).

There may be path-specific factors driving distinct evolution of practice in different countries; for example, if there was a major difference in surgical outcomes, the appeal of catheter closure would rightly differ. Likewise, it may be easier to rationalize a catheter procedure than an open operation in the setting of borderline or questionable indications. The broader indications for VSD closure in the Chinese context also confound interpretation when considering how these data apply to the United States and other countries because it is plausible that those with small shunts (eg, attributable to partial closure by tricuspid valve tissue) have a lower risk of complications, and the risk for the cohort who would undergo closure in the United States could be substantially higher. But with recent data, including the current report, it is increasingly believable that the risks of transcatheter closure are likely to be about the same or lower than for surgery in many scenarios.

As always, "questions remain." Why has catheter VSD closure not been more widely adopted in the United States and, presumably, elsewhere in the Americas and Europe? What would be required to shift views? Would any amount of data from Asia convince US clinicians? Are there other factors incentivizing observed patterns of care? When should data on a catheter procedure from one region be accepted to apply to others? When are local data necessary? When might persistent regional differences be appropriate?

These questions are remarkable because they relate less to empiric data and science than to history, sociology, and epistemology. Nevertheless, these considerations will be fundamental to achieving our shared goal: reconciling the widely divergent clinical care provided in different geographic regions to identify the safest and most effective approach to pmVSD closure.

ARTICLE INFORMATION

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Disclosures

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