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Paul Nona
Shazil Mahmood
Alejandro Lemor
Mohammed Qintar
Brian P. O'Neill

See next page for additional authors

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Incidence of acquired ventricular septal defect after transcatheter aortic valve replacement: A large single center experience

Paul Nona MD | Shazil Mahmood MD | Alejandro Lemor MD, MSc | Mohammed Qintar MD | Brian O'Neill MD | James Lee MD | Tiberio Frisoli MD | Dee Dee Wang MD | Marvin Eng MD | William W. O'Neill MD | Pedro A. Villablanc MD, MSc

Division of Cardiology, Henry Ford Health System, Detroit, Michigan, USA

Correspondence
Pedro A. Villablanc, Division of Cardiology, Center for Structural Heart Disease, Henry Ford Hospital, Henry Ford Health System, 2799 West Grand Boulevard, CFP 4th floor, Detroit, MI 48202, USA.
Email: pvillab1@hfhs.org

Abstract

Objective: To determine the rate and clinical outcomes of post-TAVR VSD.

Background: Transcatheter aortic valve replacement (TAVR) is a safe and established procedure for patients with severe symptomatic aortic stenosis. Ventricular septal defect (VSD) is a rare complication of TAVR. The rate of post-TAVR VSD and patient outcomes are not well known.

Methods: A retrospective record review of VSD cases occurring after all TAVRs performed between January 2012 and September 2020 at one urban US tertiary hospital. VSD rate and early- and long-term outcomes were analyzed. Computed tomography images taken before TAVR and transthoracic echocardiograms done before and after each procedure were analyzed.

Results: Of the 1908 patients who underwent TAVR in the study period, 7 patients (0.37%) had post-procedure VSD. The average patient age was 77 ± 11 years with average society of thoracic surgeons short-term risk score of 6%. All 7 implanted valves were balloon-expandable. Of the 7 TAVR procedures, 5 were performed on a native tricuspid valve, 1 was performed on a native bicuspid valve, and 1 was done as a “valve-in-valve” procedure on a prior surgical bioprosthetic valve. All VSDs were small and restrictive in nature. Right heart failure in a patient with preexisting right ventricular dysfunction occurred in 1 (13%) patient who died. The remaining 6 patients (86%) were discharged. All 6 patients (86%) were alive and stable at 1 year follow-up, reporting improvement in symptoms (NYHA class I-II), with no evidence of right ventricular dysfunction.

Conclusion: VSD is a rare complication of TAVR. Hemodynamic and clinical sequelae in majority of the patients in this study did not result in mortality. Proper imaging techniques and appropriate pre-procedure planning are needed to decrease the incidence of VSD formation post-TAVR.
INTRODUCTION

Transcatheter aortic valve replacement (TAVR) is an established alternative treatment option to surgical aortic valve replacement in patients with severe aortic stenosis (AS). With the increasing evidence regarding positive outcomes with TAVR, the popularity of the procedure continues to grow, and with increasing popularity, more data are available regarding adverse outcomes. Several TAVR-related complications have been previously reported, some of which are relatively common, including vascular access complications, conduction abnormalities, and paravalvular aortic regurgitation. Rarer complications include aortic root rupture, obstruction of a main coronary artery, and formation of membranous ventricular septal defect (VSD). Development of VSD is a rare complication of TAVR, and scarce literature exists regarding the incidence, risk factors, imaging analysis, and prognosis for this complication. In this study we aimed to assess the occurrence of iatrogenic membranous post-TAVR VSD in a single large, tertiary hospital; we considered incidence, clinical manifestations, imaging characteristics, and prognosis.

MATERIAL AND METHODS

In this retrospective study, medical records of all patients who underwent TAVR at a single, US-based tertiary medical center between January 2012 and September 2020 were included in the analysis. Demographic data, diagnosis, and imaging modalities performed before and after the TAVR were reviewed. The appearance of VSD by pre- and post-procedural transthoracic echocardiography was reviewed. Echocardiography was performed after all TAVR procedures to assess integrity of the bioprosthetic valve and to grade severity of any residual aortic stenosis. Computed tomography (CT) imaging was obtained before each procedure. With the exception of 1 patient who had the CT completed early in the TAVR program, all CT scans were gated. All CT images were reviewed for annular and left ventricular outflow tract (LVOT) dimensions, valve calcification severity, and distribution and leaflet morphology. Annulus and LVOT measurements were performed on CT imaging. Valve oversizing in relationship to annulus and LVOT dimensions was calculated based on nominal valve area in relationship to measured annulus and LVOT area.

RESULTS

A total of 1908 patients underwent TAVR in our hospital between January 2012 and September 2020. VSD was not reported in any of the pre-procedural echocardiography studies. A total of 7 (0.37%) patients had confirmed VSD in their post-procedural echocardiogram study. The baseline demographic features of the patient cohort are given in Table 1. The average patient age was 77 ± 11 years, 3 (43%)
were women, 4 (57%) were men, and the average Society of Thoracic Surgeons score for isolated AVR was 6%. All 7 patients were symptomatic with NYHA class 3–4 symptoms prior the procedure and after the procedure they majority were NYHA class 1–2 despite the creation of a VSD.

All procedures were performed electively in the cardiac catheterization laboratory with patients under conscious sedation. No mechanical hemodynamic support was used during any procedure. All procedures were performed transfemoral except for one, which was done via axillary route. Given the degree of stenosis and calcification of the valvular apparatus, 1 patient required transseptal puncture to cross the valve antegrade. No patient required pre-dilation of the aortic valve prior to TAVR deployment.

All VSDs were small and restrictive in nature. The average mean Doppler gradient across the aortic valve was 45 mm Hg with a left ventricular ejection fraction of 37% ± 15.6. Of the 7 patients with VSD, 5 (71%) had a native tricuspid valve, 1 (14%) had bicuspid valve, and 1 (14%) had a surgical 21 mm Edwards Sapien bovine bioprosthetic valve that had been previously implanted (see echocardiographic characteristics in Table 2).

Pre-TAVR CT characteristics of annulus and LVOT are given in Tables 3 and 4. The average systolic annulus/LVOT area ratio was 1.07 ± 0.05, and the absence of annular and LVOT calcium was seen in only 3 (43%) native valves. All VSD were membranous with restrictive characteristics and average velocity of 4.3 m/s ± 0.59. VSD characteristics are given in Table 5.

The implanted valves were all balloon-expandable from Edwards Sapiens (Edwards Lifesciences, Irvine, CA). Types of implanted valves included the following: 4 patients (57%) received the Sapien 3 valve, 1 patient (14%) received the Sapien valve, 1 patient (14%) received the Sapiens XT, and 1 patient (14%) received the Sapient Ultra. Aside from the valve-in-valve procedure, all TAVR valves were oversized at an average of 11.6% ± 5.55 to their native annulus. While this average is less than the standard 20% threshold with risk of annular rupture, we speculate that the majority of these cases resulted in a VSD not due to the degree of oversizing however rather due to the extent and location of calcification (Table 6).
Procedure and valve deployment were performed successfully in all cases. Post-dilatation was performed in 1 patient. For 1 patient, a VSD was diagnosed immediately after aortogram post TAVR deployment. Complete heart block, occurring immediately after TAVR deployment, requiring permanent pacemaker placement developed in the only patient that ultimately died. In-hospital mortality was 13%, accounting for 1 patient who developed right heart failure due to previous right ventricular dysfunction. The remaining 6 (86%) patients were alive and discharged and reported NYHA class I-II symptoms at 1-year follow-up with no subsequent hospitalizations for acute heart failure or right ventricular dysfunction (see Table 7).

### DISCUSSION

To our knowledge, this is the largest case series reporting the incidence of iatrogenic VSD formation after TAVR procedure. In our study, we identified 7 cases of post-procedural VSD (0.37% incidence) in a cohort of 1908 patients who underwent TAVR in a single, urban hospital within an approximately 8-year timespan. Four main findings were observed. First, the incidence of post TAVR iatrogenic VSD was very low. Second, despite the VSD complication, most patients were asymptomatic post-procedure and reported minimal symptoms at 1 year follow-up. Third, outcomes were poor for the one patient who developed right-side heart failure in the setting of pre-existing RV dysfunction. Fourth, all our cases of VSD occurred within the context of balloon-expandable valves in which the TAVR valve was oversized to the annulus.

As TAVR procedures gain in popularity, the occurrence of rare complications becomes more apparent. VSDs are classified as types 1 through 4 according to their location within the ventricular septum. All iatrogenic VSDs observed in our study were type 2, occurring around the membranous septum. While we obtained an incidence rate of VSD of 0.37%, it must be noted that the true rate of iatrogenic VSD in the wider population is unknown. Our findings may be an underestimate of the true rate since transthoracic echocardiography to visualize VSDs has limited sensitivity. The main limitation of this method is that the degree to which the interventricular septum can be visualized with color Doppler is limited due to poor acoustic window. Also, given these limitations, it is possible that VSD may be pre-procedurally misdiagnosed, thus causing false over-diagnosis of “iatrogenic” VSD.
Aside from echocardiography, other imaging modalities for diagnosing VSD include CT angiography and cardiac MRI. The advantages of echocardiography for diagnosing VSD include its ready availability and its ability to interrogate the VSD with Doppler assessment. The main disadvantage of echocardiography, as mentioned above, is that limited acoustic windows could lead to suboptimal imaging, potentially leading to false negative diagnosis. CT angiography and cardiac MRI both provide imaging modalities that can diagnose a VSD without the acoustic window imposed by echocardiography. CT angiography is a more rapid test compared to cardiac MRI and provides better spatial resolution (see Figure 1: CT images of VSD from patient 2). We want to note, however, that our patient in this study did not have post-procedural CT angiography. Conversely, cardiac MRI offers better temporal resolution, allows for anatomic and physiologic evaluation of the VSD, and does not emit ionizing radiation. Cardiac MRI allows for velocity mapping for flow quantification; thus, it can be used in the setting of a VSD to assess flow ratio.

Several hypotheses have been suggested for the mechanism of VSD formation during TAVR.

One such hypothesis is that VSD occurs from injury to the proximal part of the ventricular septum during balloon dilation or valve deployment. Another possible mechanism for the pathogenesis of VSD is the possibility of guide wire injury to the distal ventricular septum. Another hypothesis suggests direct trauma caused by the bioprosthetic valve that leads to excessive pressure placed on the left ventricular outflow tract and the membranous part of the septum. Still, others speculate that the degree and location of calcium concentration within the aortic annulus and LVOT play a role in the development of VSD (see Table 6). Heavy and asymmetric calcification of the aortic valve, elliptical shaped aortic annulus, and oversizing of the bioprosthetic valve have all been suggested as risk factors of the development of VSD during TAVR.

While the pathogenesis of VSD during TAVR is unclear and may be multifactorial, the clinical manifestations of this complication depend on the characteristics of the VSD in regard to size, location, and degree of outflow resistance. Understanding of the potential mechanism of VSD formation after TAVR can help prevent this complication by implementing systematic and thorough pre-procedure planning. In routine pre-procedure planning, accurate evaluation of the aortic valve annulus and the calcifications should be evaluated before TAVR to minimize the risk for VSD development.

There is a limited amount of literature showing the clinical significance of iatrogenic VSD formed during TAVR and while there is data to support percutaneous intervention in symptomatic patients, it is unclear how to proceed in patients who are asymptomatic. In the majority of cases that have been described, the VSDs were shown to be small and restrictive. At 1 year follow-up, no patient who survived to discharge, reported symptoms suggestive of RV dysfunction due to VSD creation. Proper imaging techniques after the procedure, when clinically indicated, is critical. Appropriate imaging and accurate positioning of the bioprosthetic valve may be helpful in preventing periprocedural VSD formation.

### 5 | LIMITATIONS

Many limitations exist for this study. First, is important to note that this is a retrospective study which provides its own sets of limitations given the study design. Second, our center has an institutional bias and predominantly uses balloon-expandable valves over self-expandable valves, and thus this data may not be able to be applied to other centers that have an increased utility of self-expandable valves. Third, most patients did not receive a post-procedural CT so details on anatomy and VSD defect are lacking. Forth, the lack of standard quantification methods for calcium distribution in the annulus and LVOT leads to limitations in reporting this information and thus we elected to provide the readers with CT images for them to review. Finally, an additional limitation is the lack of comparison to matched patients.

### 6 | CONCLUSIONS

Iatrogenic VSD formation during TAVR appears to be a rare complication. Nonetheless, at an incidence of 0.37%, being aware of VSD in patients who present with persistent symptoms after TAVR is crucial.
Most iatrogenic post-TAVR VSDs are small and restrictive; they should be considered in the differential diagnosis of patients with continued dyspnea after TAVR.

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CONFLICT OF INTEREST
Dr. Marvin Eng is a clinical proctor for Edwards Lifesciences, Medtronic and Boston Scientific. Dr. Tiberio Frisoli is a clinical proctor for Edwards Lifesciences, Abbott, Boston Scientific, and Medtronic. Dr. Brian O’Neill has served as a consultant and received research support from Edwards Lifesciences. Dr. James Lee is a consultant for HeartFlow. Dr. William W. O’Neill has served as a consultant for Abiomed, Edwards Lifesciences, Medtronic, Boston Scientific, Abbott Vascular and St. Jude Medical; and serves on the Board of Directors of Neovasc Inc. Dr. Dee Dee Wang is a consultant to Edwards Lifesciences, Boston Scientific, receives research grant support from Boston Scientific assigned to employer Henry Ford Health System, is a member of the Edwards CLASP IITR Steering Committee, and Abbott PARADIGM Steering Committee. All other authors report no relevant financial disclosures.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to patient privacy.

ORCID
Paul Nona  https://orcid.org/0000-0002-4758-7211
Brian O’Neill  https://orcid.org/0000-0001-5206-1639
Dee Dee Wang  https://orcid.org/0000-0002-5784-9924
Marvin Eng  https://orcid.org/0000-0002-0334-6504

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