Iatrogenic Atrial Septal Defect
Mohamad Alkhouli, MD; Mohammad Sarraf, MD; David R. Holmes, MD

The number of left atrial transcatheter procedures performed via a transseptal (TS) approach has grown exponentially over the last 2 decades. Persistent iatrogenic atrial septal defects (iASD) after structural TS interventions are not uncommon especially when larger TS sheaths are used (25%–50% with 22 Fr sheaths). The optimal management strategy of postprocedural iASD is currently unknown. In the absence of societal recommendations with regards to iASD, the decision to close iASD and the timing of the closure pose a clinical dilemma to the Interventionalist caring for these patients. We present 2 cases of iASD after TS transcatheter mitral valve repair/implantation and discuss the challenges in the management of such patients.

Case Presentation
Two patients were seen in consultation by the Mayo Clinic structural heart service:

Ms K: An 81-year-old female admitted with decompensated biventricular heart failure. She had hypertension, atrial fibrillation, systolic heart failure (left ventricular ejection fraction=42%), a permanent pacemaker, and a history of mitral valve replacement with a 33 mm St Jude EPIC prosthesis and tricuspid valve repair. On examination, she was a slender woman (5’0″, 49 kg). Heart rate was 72 bpm, blood pressure was 129/83 mm Hg, and oxygen saturation was 92% on room air. Auscultation revealed a prominent thrill at the apex radiating across her chest and a loud 4/6 apical holosystolic murmur. Jugular veins were distended, and rales were heard at both lung bases. Moderate peripheral pitting edema was also noted. Echocardiography showed a degenerative mitral prosthesis with a flail leaflet and severe mitral regurgitation (MR). It also showed severe right ventricular enlargement with moderately depressed right ventricular function. No thrombus or evidence of endocarditis was present. The heart team concluded that the patient was at high risk for redo mitral valve replacement (Society of Thoracic Surgeons [STS] score=10%). She then underwent a successful antegrade TS mitral valve in valve implantation with a 29-mm Sapien S3 valve. To facilitate delivery of the S3 valve, the septum was dilated with a 15 mm Z-Med Balloon (B. Braun Inc, Melsungen, Germany; Figure 1A). After the procedure, the left atrial V wave decreased from 51 to 26 mm Hg (Figure 1D), and there was no residual MR. However, there was a residual atrial septal defect measuring 7×5 mm by transesophageal echocardiography (TEE) with a predominant left to right shunt (Figure 1B and 1C).

Mr J: An active 89-year-old male who was evaluated in the outpatient setting for worsening dyspnea. He has history of hypertension, remote deep venous thrombosis, anemia, and chronic kidney disease stage 3 (estimated glomerular filtration rate=31 mL/min per 1.73 m2). On examination, the patient was obese (5’5″, 103 kg), had bradycardic (49 bpm), and had a normal blood pressure 126/78 mm Hg. There was a 4/6 holosystolic apical murmur. Echocardiography documented normal left ventricular ejection fraction of 62% and a flail mitral valve posterior leaflet with severe MR. The right ventricle was mildly dilated with mildly reduced systolic function. Because of his age and renal insufficiency, he was not deemed to be a candidate for mitral valve surgery. He underwent a successful transcatheter mitral valve repair (TMVR) with one MitraClip (Abbott Vascular, Santa Clara, CA). After the procedure, the MR decreased from severe to mild–moderate, and the left atrial V wave decreased from 60 to 40 mm Hg (Figure 2C). A small residual atrial septal defect measuring 3×4 mm with left to right shunt was noted (Figure 2A and 2B).

Discussion
Dr Sarraf: Both patients are left with an iASD after a successful mitral valve therapeutic procedure. Should we be concerned about these residual defects, or do they usually close spontaneously?

Dr Holmes: Historically, the majority of residual iASD following transcatheter TS interventions have been thought to close spontaneously and therefore have not been routinely closed. However, there is growing evidence that iASDs which have resulted from placement of larger diameter devices could persist beyond 6 months after TS procedures (Table 1). With the substantial increase in the number of patients with valvular and arrhythmic disorders who are being treated with transcatheter TS procedures (Table 2), persistent iASDs are an increasing concern.

Dr Sarraf: Are these residual iASD associated with adverse clinical outcomes?

Dr Alkhouli: The available data are scarce and inconclusive. There are multiple case reports of the deleterious effects of iASD (hypoxemia, heart failure, and systemic embolization). There is only one single-center prospective study that suggested a possible negative impact of persistent iASD on right ventricular function, dyspnea, and mortality after TMVR.
with MitraClip. However, in this study, patients with persistent iASD had longer procedures (82.4±39.7 versus 68.9±45.5 minutes; \( P = 0.05 \)) and had somewhat higher degrees of residual MR (95.5% versus 88.5% with residual MR grade >II; \( P = 0.35 \)) compared with those who had spontaneous closure of the iASD. The iASD might have been related to a more challenging anatomy/procedure or might have been a marker of a higher degree of residual MR and left atrial pressure. An association between higher residual MR and persistent iASD after MitraClip procedures has been suggested by Smith et al. Other studies have evaluated the effect of iASD on clinical outcomes, but were underpowered due to the very low incidence of adverse events (Table 1).

**Dr Sarraf:** In the absence of an immediate deterioration requiring urgent iASD closure (eg, right to left shunt with hypoxemia), when should we consider iASD closure?

**Dr Holmes:** Unfortunately, there are currently no guidelines to aid with the management of iASD. Desaturation due to right to left shunting is probably the strongest indication to close an iASD during the index procedure. If oxygen desaturation is noted after removing the TS sheath, and is found to be related to the iASD, then immediate closure is indicated. The causal relationship between oxygen desaturation and the iASD can be confirmed with the improvement in oxygen saturation with balloon occlusion of the defect and sometimes even with readvancement of the large TS sheath across the defect.

Besides this indication, it is reasonable to consider elective iASD closure in selected patients who are at high future risk for right ventricular overload and/or systemic embolization (paradoxical thrombus). It is also clinically reasonable to consider iASD closure in patients who suffer a cryptogenic stroke and are found to have persistent iASD. In our first case, Ms K was at particularly high risk for right ventricular overload given her large left to right shunt and her baseline severe right ventricular dysfunction. In addition, she also has permanent pacemaker leads which may increase her risk for paradoxial embolism. I would therefore consider percutaneous iASD closure in this patient. A suggested algorithm for the assessment and management of iASD is illustrated in Figure 3.

**Dr Sarraf:** Is there a role for routine invasive hemodynamic assessment of iASD in the cath lab?

**Dr Alkhouli:** A detailed hemodynamic study at baseline and after the intervention would be very helpful when considering iASD closure for several reasons: (1) calculation of baseline pulmonary vascular resistance would aid in avoiding closure in patients with irreversible severe pulmonary hypertension (pulmonary vascular resistance \( >2/3 \) systemic vascular resistance), (2) shunt volume/fraction calculations after the intervention could identify patients with very large left to right shunts (Qp/Qs \( >2 \)) who might require a more aggressive follow up and in whom a lower threshold for iASD closure should be considered. (3) When continuous left atrial pressure monitoring is not available, pulmonary capillary wedge...
pressure measurement before and after the TS procedure would identify those patients with high postprocedural pulmonary capillary wedge pressure that might be better served with conservative management of the iASD. Given the low incidence of iASD after TS with sheath <12 Fr in diameter, I would reserve this comprehensive assessment for patients who undergo TS procedures with large-bore sheathsguides (>12 Fr).2

Dr Sarraf: The issue of closure of the iASD is complex. Some data suggest an increased risk of serious acute left ventricular dysfunction leading to pulmonary edema immediately after closure of left to right shunts from an ASD in elderly patients with significant LV diastolic dysfunction.20,21 Should we be concerned about this risk in our patients?

Dr Alkhouli: Congenital defects are different than iASD. With the former, the heart is subject to a life-long conditioning

Table 1.  A Summary of Studies on Persistent iASD Following Transseptal Structural Heart Procedures

<table>
<thead>
<tr>
<th>Study</th>
<th>Procedure</th>
<th>Sheath Size, Fr</th>
<th>iASD Incidence</th>
<th>Follow Up, m</th>
<th>Detection Method</th>
<th>Diameter, mm</th>
<th>Echo Parameters</th>
<th>Clinical Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshida et al5</td>
<td>PBMV</td>
<td>14</td>
<td>3/15 (20%)</td>
<td>6</td>
<td>TEE</td>
<td>1.1</td>
<td>NR</td>
<td>None</td>
</tr>
<tr>
<td>Ishikura et al7</td>
<td>PBMV</td>
<td>14</td>
<td>2/46 (4.4%)</td>
<td>12</td>
<td>2D TTE</td>
<td>NR</td>
<td>NR</td>
<td>None</td>
</tr>
<tr>
<td>Devarakonda et al6</td>
<td>PBMV</td>
<td>14</td>
<td>21/110 (19%)</td>
<td>12</td>
<td>3D TTE</td>
<td>5.4±3.1</td>
<td>NR</td>
<td>None</td>
</tr>
<tr>
<td>Singh et al4</td>
<td>LAA Closure</td>
<td>14</td>
<td>14/253 (7%)</td>
<td>12</td>
<td>2D TEE</td>
<td>&lt;3 (50%)</td>
<td>NR</td>
<td>No Δ in stroke</td>
</tr>
<tr>
<td>Smith et al2</td>
<td>TMVR</td>
<td>22</td>
<td>8/30 (27%)</td>
<td>12</td>
<td>2D TTE</td>
<td>6.6±3.1</td>
<td>No Δ in RVD</td>
<td>None</td>
</tr>
<tr>
<td>Schueler et al3</td>
<td>TMVR</td>
<td>22</td>
<td>33/66 (50%)</td>
<td>6</td>
<td>2D TEE</td>
<td>4.3±3.8</td>
<td>↑ RVSP, RAD, RVD</td>
<td>↑ Death, HF</td>
</tr>
</tbody>
</table>

Δ indicates change; 2D, 2-dimensional; 3D, 3-dimensional; Fr, french; HF, heart failure; iASD, iatrogenic atrial septal defects; LAA, left atrial appendage; NR, not reported; PBMV, percutaneous balloon mitral valvuloplasty; RAD, right atrial dimension; RVD, right ventricular dimension; RVSP, right ventricular systolic pressure; TEE, transesophageal echo; TMVR, transcatheter mitral valve repair; and TTE, transthoracic echo.
process, and hence, sudden closure of these defects may lead to acute decompensation in patients with significant diastolic dysfunction and/or elevated left-sided filling pressures. iASDs are more acute phenomena, and therefore, the risk of decompensation upon their closure should be much less. However, if there is any concern about clinical deterioration after iASD closure, a balloon occlusion test may help to identify high-risk patients for postclosure heart failure. This procedure involves temporary closure of the defect with a soft AMPLATZER Sizing Balloon (AGA Medical, Plymouth, MN). During this time, pulmonary capillary wedge pressure or left atrial pressures are monitored. If temporary occlusion of the iASD with the sizing balloon result in significant elevation in mean left atrial pressures (>10 mmHg), closing the defect is not recommended. Mr J has severely elevated left atrial pressure despite the reduction in his MR (Figure 2C). The iASD in this patient might be a useful pop-off route for his elevated filling pressures. In addition, his residual iASD is small and his right ventricular function is preserved, minimizing the risk of right-sided overload if the left to right shunt is not closed. In this patient, I would not close the iASD immediately at the time of the index procedure but would repeat a transthoracic echocardiography (TTE) in 3 to 6 months.

Dr Sarraf: Are there any procedural or patient’s characteristics that are associated with a higher chance of having a persistent iASD?

Dr Holmes: The available data do not provide strong evidence that any particular patient factor is associated with higher probability of iASD persistence. Elevated left atrial pressure was suggested as a negative predictor of spontaneous closure after left atrial appendage closure with the Watchman device and after TMVR with the MitraClip device. In terms of procedural characteristics, the size of the TS sheath seems to be a key factor in determining the likelihood of iASD...
perfusion versus spontaneous closure. Structural heart interventions that utilize TS sheaths ≤14 Fr are associated with a very high rate of spontaneous closure (80%–90%), while those that utilize TS >20 Fr are associated with lower rates of spontaneous closure (50%–75%: Table 1).

**Dr Sarraf:** Does the access location on the interatrial septum predict the likelihood of spontaneous iASD closure?

**Dr Holmes:** Pulmonary vein isolation procedures that are performed via an inferior limbus puncture are associated with lower incidence of acute iASD compared with those performed via a fossa ovalis puncture.23,24 However, many structural interventional procedures require a specific access location on the septum for successful execution of the procedure. For example, TMVR requires a TS puncture that is located posteriorly and superiorly on the fossa ovalis about 4 cm above the mitral valve annulus. Similarly, TS mitral valve in implantation and left atrial appendage closure require posterior and inferior fossa ovalis puncture site. Therefore, the possibility of utilizing a non–fossa ovalis access may be limited to a small number of specific structural procedures.

**Dr Sarraf:** A certain percentage of these patients may require a second TS procedure. Would the need to recross the septum be hampered with the presence of septal occluder device?

**Dr Alkhouli:** Certainly. The presence of a septal occluder device will complicate recrossing attempts and this issue should be considered before closing an iASD. In most cases, a second TS puncture can be performed adjacent to the ASD closure device. However, in some patients, puncture through the ASD closure device might be necessary which while possible is technically challenging and associated with significantly longer procedure time.25,26

**Dr Sarraf:** What are your preferred septal occluder device for iASD closure?

**Dr Holmes:** There are 2 commercially available atrial septal defect closure devices: The GORE Cardioform Septal Occluder (WL Gore and Associates, Flagstaff, AZ) and the AMPLATZER Atrial Septal Occluder (AGA Medical, Plymouth, MN). I prefer the Cardioform device because it is softer and more compliant than the AMPLATZER device and because there have not been any reports of cardiac erosion with this device. However, the Cardioform septal occluder is limited to treating defects <15 to 18 mm. Although uncommon, larger iASD would need to be treated with an AMPLATZER. There are also emerging bioabsorbable septal occluders that could potentially be utilized in these cases in the future. The CARAG septal occluder (CARAG-S Engineering, Baar, Switzerland) showed promising acute and early follow-up results in a small first-in-man series.27 A clinical trial is currently ongoing to evaluate the safety and effectiveness of this device (https://www.clinicaltrials.gov: NCT01960491). If bioabsorbable septal occluders are proven safe and effective, they may become the occluders of choice for iASD closure as they might preserve future access to the left atrium.

**Dr Sarraf:** Are there any technical considerations specific to closing iASD?

**Dr Alkhouli:** Sizing iASD is not always straightforward as these defects often have irregular borders and/or edge tearing, and their true dimensions may be underestimated with 2D imaging.28 We prefer to obtain 3D imaging of the septum when possible to avoid undersizing or oversizing of the defect. Balloon sizing is also an option in equivocal cases. Otherwise, the iASD closure procedure is performed in a similar manner to congenital ASD closure.

**Dr Sarraf:** If the decision is to not close the iASD, how often do we image these patients and what imaging tools do we choose?

**Dr Holmes:** The ideal test for postoperative surveillance of iASD should be noninvasive or minimally invasive and should provide an accurate assessment of the iASD size and the interatrial shunt. TTE is readily available and noninvasive but has limited accuracy in detecting and measuring iASD.29 Studies that used TTE for the follow up of iASD yielded lower rates of persistent iASD compared with those that used TEE.3,35 Real-time 3D technology has proven to be superior to 2D imaging in accurately assessing the dimensions of iASD with both TTE and TEE.6,28 I would start with an enhanced TTE (ie, TTE with agitated saline contrast and valsva means ±3D). If the study is negative and I am still concerned (for example, in case of unexplained worsening heart failure), I would then proceed to TEE ± right heart catheterization.

### Outcomes

Ms K: Following her successful mitral valve in valve implantation, the patient underwent percutaneous closure of the iASD (Figure 1E). A 25-mm Cardioform septal occluder device was placed with trivial residual shunt seen on TEE. She was discharged home on day 2 and has done very well at 2-month follow-up.

Mr J: After undergoing TMVR with the MitraClip device, the decision was made to observe the iASD clinically and with a follow-up TTE at 6 months. At 1 month follow up, Mr J increased his 6-minute walk distance from 213 m to 278 m and had only mild residual exertional dyspnea.

###Disclosures

None.

### References

6  Alkhouli et al  Iatrogenic ASD


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Circ Cardiovasc Interv. 2016;9:
doi: 10.1161/CIRCINTERVENTIONS.116.003545
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7640. Online ISSN: 1941-7632

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