Percutaneous paravalvular leak closure with their outcomes: A single center experience

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ABSTRACT
Background: Transcatheter paravalvular leak (PVL) closure in recent times has emerged as a safe and effective alternate to redo-surgical repair. We sought to examine the clinical efficacy and safety of percutaneous PVL closure at our center.

Methods and Results: A retrospective study from August 2012 to December 2019 of 19 patients who underwent 21 procedures for PVL closure. The mean age was 49.25 ± 14.72 years. The target valve was mitral in 11 (57%) and aortic in 7 (36%) cases. One (5%) patient had prosthetic valve in left atrioventricular valve with congenitally corrected transposition of great arteries. Majority of the cohort presented with heart failure without hemolysis (89%), with most of them being in NYHA functional class III (57%) or class IV (21%). A procedural success of 85% was achieved. Post procedure severity of regurgitation reduced from severe in thirteen patients and moderate in six patients to moderate in two patients and mild in fourteen patients. Symptomatic improvement was observed in all cases who had successful closure with NYHA functional class improving from 3 ± 0.64 to 1.6 ± 0.94. The mean follow-up duration was 21 ± 13 months (median 24 months). There was one (4.7%) mortality with cumulative survival from all-cause mortality of 95%.

Conclusion: The results of percutaneous PVL closure appear encouraging in our series with modest number of patients and offers a promising alternative to redo-surgery in this high-risk cohort.

Keywords: Closure, paravalvular leak, single center, transcatheter

INTRODUCTION

Paravalvular leak (PVL) is an infrequent but a well-known, potential complication after implantation of prosthetic valve. Incidences ranges from 2 to 12% after mitral valve replacement and 1-5% after aortic valve replacement.[1-3] It originates because of the incomplete apposition of the prosthetic valve ring and the native valve annulus,[4] owing to friability of tissues which may result from infection, suture technique, significant calcification or fibrosis of annulus.[5]

Hemodynamically significant PVL presents with congestive heart failure and/or refractory hemolytic anemia which can be dealt both surgically or via transcatheter approach. Surgical re-intervention although has traditionally been considered as a standard approach for management of PVL, it is associated with high early morbidity, mortality and is technically more demanding.[6-7] Percutaneous closure of PVL was first reported in 1992,[8] since then transcatheter occlusion of paravalvar leaks has emerged as a safe, effective and less invasive alternative.[8,9] Considerable refinement in catheter based techniques and imaging modalities...
(specially 3D Trans esophageal echocardiography) have improved clinical results of this complex procedure with high success rate and low procedure mortality. Here we describe our single center experience with 19 patients who underwent percutaneous PVL closure.

MATERIAL AND METHODS

This was retrospective study comprising of 19 patients who underwent PVL device closure at our center from August 2012 to December 2019. Clinical data and procedural details were retrieved from the previous medical records.

Procedure

All interventions were performed under general anesthesia, with fluoroscopy and TEE guidance. One dose of antibiotic was given prior to the procedure. During the procedure unfractionated heparin was given to maintain an activated clotting time >250s.

Aortic PVL

A retrograde femoral approach was employed in all aortic PVL cases (n = 7). A diagnostic catheter was used to support an angled hydrophilic wire guide wire (Terumo Cardiovascular, Tokyo) which was passed retrogradely from the aorta then through the PVL. Following this a delivery sheath or a guiding catheter of appropriate size was passed into left ventricle, through which the occluder was delivered and deployed across the PVL [Figure 1a].

Mitral PVL

Majority of the mitral PVL were closed by antegrade approach (n = 11) after performing a transeptal puncture under TEE and fluoroscopy guidance. The location of the transeptal puncture was decided according to the location of leak (i.e., posterior and superior puncture for medial defects and inferior puncture for lateral defects). After accessing the left atrium a deflectable sheath (8.5F Agilis steerable sheath, St Jude medical, Minnesota) was introduced into the left atrium through which a diagnostic catheter was then introduced making a telescopic coaxial system. Real time 3D transeophageal echocardiography (TEE) (surgeon's view) was used to accurately position the steerable sheath over the defect [Figure 1b]. PVL was then crossed using an angled hydrophilic wire guide wire through the diagnostic catheter guided by the real time 3D TEE and fluoroscopy. 3D TEE and fluoroscopy both were used to confirm the position of the wire. After crossing the defect, the angled hydrophilic wire was then either exchanged with a stiff wire or an arterio-venous loop [Figure 2a] was formed. A sheath or guide catheter was then introduced and the occluder was delivered and deployed across the PVL [Figure 2b]. One patient underwent PVL closure retrogradely via femoral artery access using a diagnostic catheter in the left ventricle to cross the defect [Figure 3a].

For defects requiring multiple devices either a simultaneous or a sequential approach was utilized. In simultaneous method two guidewires were crossed across the leak and

Figure 1: (a) Fluoroscopic image of retrograde closure of Aortic PVL showing occluder and guide wire across the defect. (b): Real time three-dimensional echocardiogram of mitral prosthetic valve as viewed from left atrial side (surgeon’s view) showing steerable sheath (white arrow) directed across the PVL located at 10-11 O’clock position.

Figure 2: (a) Fluoroscopic image of antegrade closure of mitral PVL showing sequential delivery. First device (blue arrow) attached to delivery cable has been deployed across the defect and exteriorized; additional second device (white arrow) is also delivered across the defect loaded into the sheath over the buddy wire (yellow arrow). The hydrophilic wire (yellow arrow) is seen forming an arterio-venous loop facilitating delivery of device. (b) Three-dimensional echocardiogram of mechanical valve prosthesis from left atrial side showing two occluder (white arrow) across the PVL at 9-10 O’clock position.

Figure 3: (a) Fluoroscopic image of antegrade closure of PVL located at left atrioventricular region in a congenitally corrected transposition of great arteries showing two occluders across the defect. (b) Fluoroscopic image of retrograde closure of aortic PVL showing simultaneous delivery of two occluders (white arrow) through delivery system. Hydrophilic wire (blue arrow) is seen across the defect forming arterio-arterial loop facilitating delivery of device.
two separate delivery sheaths or one large delivery sheath were tracked on two guidewires. Selected occluders were then deployed at the same time using two separate sheaths or a large delivery system [Figure 3b]. For sequential technique one hydrophilic guidewire was kept across the defect into the left ventricle over which delivery sheath was tracked. The occluder was thereafter deployed while retaining one hydrophilic guidewire (buddy wire) across the leak. This buddy wire maintained access into left ventricle allowing deployment of second or a third device. After deploying the occluder, the sheath was then removed and reloaded over the guidewire leaving the device attached to the delivery cable exteriorized [Figure 2a]. Subsequently this sheath facilitated the delivery of additional devices.

Before releasing the occluder, TEE and fluoroscopy imaging was used to carefully assess the interaction of device and the prosthetic valve leaflets. In case of interference with the prosthetic valve leaflets or appearance of significant regurgitation through the prosthetic valve, the occluder was retrieved and an alternate strategy was then employed.

Statistical methods
Statistical analyses were carried out using the SPSS statistical software version 25. Continuous data was presented as mean ± SD or median. Paired t-Test was applied for comparing changes in NYHA class and severity of regurgitation before and following intervention. A P value of less than 0.05 was considered as significant. Estimates of overall survival and of freedom from reoperation were obtained by means of the Kaplan-Meier method with 95% confidence interval.

RESULTS
A total of 19 patients amongst which, two underwent two procedures each cumulating into a total of 21 procedures [Table 1 and 2].

Patient factors
Baseline demographics and comorbidities of the study group are shown in Table 1. The mean age of the cohort was 49.25 ± 14.72 years with male preponderance (73%). The most common indication for PVL closure was heart failure without hemolysis (89%), with majority of the cohort presenting in NYHA functional class III (57%) and class IV (21%). Prosthetic valve requiring intervention were dominantly in mitral location (57%), whereas 36% had aortic PVL. One case (5%) had congenitally corrected transposition of great artery with prosthetic valve replacement in left atrioventricular position. The mean ejection fraction of the cohort was 43.3 ± 13.17%. Thirteen patients had mechanical prosthetic valve (68%), whereas six patients had bioprosthetic valve (31%) at the time of intervention. Pre-procedure PVL was severe in 68% of patients and 31% had moderate regurgitation. The median duration from surgery to intervention was 65.5 ± 67.2 months (range 3-276 months, median 36.5 months).

Table 1: Baseline characteristics
| Patient treated | n= 19 |
|-----------------|-------|
| Age (years)     | 49.25±14.72 |
| Sex (M:F)       | 14:5   |
| Valve location  |       |
| Aortic valve    | 7/19 (36%) |
| Mitral valve    | 11/19 (57%) |
| Left AV Valve in CTGA | 1/19 (5%) |
| NYHA functional class |       |
| NYHA class IV   | 4/19 (21%) |
| NYHA class III  | 11/19 (57%) |
| NYHA class II   | 4/19 (21%) |
| NYHA class I    | 0/19 (0%)  |
| Type of valve   |       |
| Bioprosthetic   | 6/19 (31%) |
| Mechanical valve| 13/19 (68%) |
| Number of previous surgery | 1.15±0.36 |
| Severity of Regurgitation |       |
| Severe          | 13/19 (68%) |
| Moderate        | 6/19 (31%) |
| Mild            | 0/19 (0%)  |
| Heart failure   | 17/19 (89%) |
| Heart failure and Hemolysis | 2/19 (10%) |
| Hemolysis alone | 0/19 (0%)  |
| Ejection fraction | 43.3±13.17 |
| Previous PVL closure | 2/19 (10%) |
| Interval after surgery (months) | 65.5±67.2 |

Table 2: Procedure characteristics
| Patient treated | n= 21 |
|-----------------|-------|
| Number of procedures | 21 |
| Number of defects |       |
| One             | 15/19 (78%) |
| Two             | 4/19 (21%)  |
| Number of procedures |       |
| One             | 17/19 (89%) |
| Two             | 2/19 (10%)  |
| Procedure success | 18/21 (85%) |
| Number of devices implanted |       |
| One             | 12/19 (63%) |
| Two             | 4/19 (21%)  |
| Three           | 3/19 (15%)  |
| Staged procedure | 2/19 (10%)  |
| Type of device (n=24) |       |
| Amplatzer vascular plug II | 18/24 (75%) |
| Amplatzer duct occluder I | 4/24 (16%)  |
| Amplatzer septal occlude | 1/24 (4%)   |
| Amplatzer vascular plug III | 1/24 (4%)  |
| Post procedure regurgitation |       |
| Severe          | 3/19 (15%)  |
| Moderate        | 2/19 (10%)  |
| Mild            | 14/19 (73%) |
| Complications   | 2/21 (9.5%) |
| Periprocedural death (within 48 hours) | 1/21 (4.7%) |
| Procedure duration (minutes) (median) | 110 (90-180) |

CTGA: Corrected transposition of great arteries
Two patients had double prosthetic valve replacement and rest of the study group had prior single prosthetic valve implantation. One PVL was present in 15 (78%) whereas 4 (21%) patients had two PVL which were closed. Comorbidities included atrial fibrillation (26%), prior coronary artery bypass grafting (10%), chronic renal failure (10%) and type 2 diabetes mellitus (5%).

Procedure factors
Procedural characteristics are depicted in Table 2. None of the patients had infective endocarditis at the time of intervention. Seventeen patients had a single attempt at PVL closure which was technically successful in fourteen of them, whereas two patients underwent two staged procedures both of which were successful. Procedural success was achieved in 85% of cohort. Patients who had a bioprosthetic valve implanted required a mean of 2 ± 0.8 (median 2) devices whereas those with mechanical valve required a mean of 1.25 ± 0.62 (median 1) devices for successful leak closure. The mean number of PVL treated per patient were 1.2 ± 0.41 and the mean of 1.5 ± 0.73 ocluders were used per patient. A variety of ocluders were used to close PVL, including AVP II (75%), PDA occlude (16%), ASD device (4%) and AVP III (4%).

Outcome
Procedural success amongst the cohort resulted in significant improvement in severity of PVL from severe in thirteen patients and moderate in six patients to moderate in only two patients and mild in fourteen patients (P < 0.05). Patients in whom PVL could not be closed successfully (n = 3) persisted with severe regurgitation in one patient and moderate in two patients. 84% (16/19) of the cohort achieved clinical success. Clinical success was accomplished in all aortic PVL except one patient, whereas two patients with mitral PVL could achieve clinical improvement. Symptomatic improvement was witnessed in all patients who had successful closure of PVL immediately after the procedure and at the latest follow up, with none of them requiring reintervention. The mean NYHA function class improved from 3 ± 0.64 pre procedure to 1.6 ± 0.94 after attempted PVL closure (P < 0.05). The mean follow-up duration was 21 ± 13 months (median 24 months).

Complications
A cumulative survival from all-cause mortality of 95% was observed. Two of the mitral PVL and one aortic PVL could not be closed and were referred for surgery (15%). Amongst failed procedures, there was one mortality (4.7%) within 48 hours of attempted PVL closure. This was a 66-year-old male patient who had undergone triple vessel coronary artery bypass grafting and bio prosthetic mitral valve replacement. He presented with complains of dyspnea on exertion (NYHA class IV) with severe mitral valve regurgitation and moderate left ventricular dysfunction (EF = 45%) within 3 months of surgery. He was very high-risk surgical candidate with a Euro score II of 7.76, and was undertaken for attempt at transcatheter PVL closure. Multiple failed attempts at occluding the defects in this patient resulted in increase in severity of mitral PVL as compared to the pre-procedural level. This was most likely due to catheter manipulation and excess tissue friability leading to suture giving way which was evident on TEE. Being a very poor surgical candidate, he was managed conservatively but he succumbed within 48 hours of the procedure. No mortality was witnessed in the remaining cohort at the latest follow-up (21 ± 13 months [median 24 months]). Two patients (9.5%) developed minor complication including contained retroperitoneal hematoma and acute renal failure, both were managed conservatively.

DISCUSSION
Paravalvular leak occurs in about 5 to 17% of the implanted prosthetic valves,[10] with 1-5% being symptomatic and requiring intervention.[5] Surgical closure of the dehiscence has traditionally been considered as the gold standard approach, as it repairs the defect under direct vision. However, following redo surgical repair in PVL, morbidity is high, and recurrence is quite common, due to immanent annular calcification and tissue friability.[6,7] With considerable modifications and incorporation of multimodality imaging, transcatheter closure of PVL has emerged as a less invasive and effective alternative to repeat surgery.[8] The American Heart Association guidelines for valvular heart disease provides level IIa recommendation for percutaneous PVL closure at experienced centers.[11] Although, percutaneous PVL closure is complicated and technically demanding, at experienced centers, good procedural success rate can be accomplished.

This is our single center experience with PVL device closure with a modest number of patients. A procedural success rate of 85% was achieved in our study which is in accordance with previously reported results of series (range 60-90%).[6,12,13] An acceptable alleviation of leak was demonstrated in majority of the patients (85%) post procedure. Multidisciplinary approach should be employed while undertaking PVL closure starting from its diagnosis, procedure planning and post procedure follow up. In our experience using real time 3D TEE was quite valuable in profiling the defect and crossing the
defect during intervention. Using a clockwise approach for defining the defect helped in a better understanding between the echocardiographer and the interventionist.

Successful PVL closure lead to at least one functional NYHA class improvement in the cohort after the procedure, which correlates with the previous reports.\textsuperscript{[10,12]} This underscores the fact that successful reduction of the leak is the required key factor for clinical improvement in these patients.\textsuperscript{[8]} Despite having a fair clinical success, 2 (9.5%) patients developed minor complications, which is slightly higher than the reported rates in other series.\textsuperscript{[10,13]} Access site related complications are the most formidable complications encountered after interventional procedures and are commonly experienced because of large delivery system being used. Both vascular complications were managed with conservative strategies in the series. A 30 day mortality of 4.7% was seen in the group, which compares fairly with the larger published series with transcatheter PVL closure.\textsuperscript{[18]} Only mortality was a poor surgical candidate with high Euro II score who presented very early (3months) after prosthetic valve implantation. Multiple attempts at occluding the defect failed and lead to further increase in severity of regurgitation. This particular case highlights the risks of procedure failure in addressing a paravalvar leak early in the natural history. Tissue friability is one of the key causes of PVL development particularly in immediate or early follow up. These friable tissues are prone to damage by tension in guidewires specially during transcatheter rail road formation.

A variety of devices can be used to close PVL, however vascular plugs (specially AVP II and AVP III) are the most favored devices because of their low profile, multi-segment shape, and ability to deliver multiple devices at the same area, which is often essential in percutaneous PVL closure.\textsuperscript{[10,14]} Several occluders were used to close paravalvular dehiscence in this series of which AVP II was used in almost two-thirds of the patients, as AVP III is not commercially available in our country.

The anatomy of defects in PVL is heterogeneous, often complex and the leaks are often multiple in number.\textsuperscript{[10,12]} Majority of PVL are not circular in shape and because of the absence of a custom made occluder, successful closure may hence, require multiple devices. Almost one third of our cohort required more than one device for successful reduction of regurgitation. Bioprosthetic valves as compared to mechanical valves tend to accommodate larger and higher number of devices by virtue of their providing less interference of the occluder to the valve leaflets. Transcatheter PVL closure are complex and relatively longer procedures. Knowledge of a broad range of interventional skills is required while undertaking this complex procedure. The average time applied in the cohort was close to two hours, which correlates well with the work by previous authors.\textsuperscript{[10,13]} A number of techniques were utilized in the cohort, including rail road, buddy wire or sequential delivery of multiple occluders, and have become our preferred approach in recent times. Interposing a hydrophilic wire across the PVL while releasing the occluder prevented the need for recrossing the defect in patients requiring multiple devices reducing the procedural time significantly.

**CONCLUSION**

Our limited series demonstrates the acceptable safety and efficacy of transcatheter PVL closure in a single center, as a reasonable management strategy of this high-risk cohort of patients. Reduction in regurgitation post procedure is the most important factor leading to symptomatic improvement in these group of patients.

**Limitation**

This was single center experience with a limited number of patients preventing the generalization of results.

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