HHS Public Access

Author manuscript

Catheter Cardiovasc Interv. Author manuscript; available in PMC 2024 July 29.

Ventricular Arrhythmias Following Balloon-Expandable Transcatheter Pulmonary Valve Replacement in the Native Right Ventricular Outflow Tract

Spencer B. Barfuss, M.D.[a], **Juan Carlos Samayoa, M.D.**[b], **Susan P. Etheridge, M.D.**[a], **Thomas A. Pilcher, M.D.**[a], **S. Yukiko Asaki, M.D.**[a], **Zhining Ou, M.S.**[c], **Dana M. Boucek, M.D.**[a], **Mary Hunt Martin, M.D.**[a], **Robert G. Gray, M.D.**[a], **Mary C. Niu, M.D.**[a]

[a]Department of Pediatrics, Division of Cardiology, University of Utah and Primary Children's Hospital, Salt Lake City, UT, USA

[b]Department of Pediatrics, Division of Cardiology, University of Washington and Seattle Children's Hospital, Seattle, WA, USA

[c]Department of Internal Medicine, Division of Epidemiology, University of Utah, Salt Lake City, UT, USA

Structured Abstract:

Background: Ventricular arrhythmia incidence in children and adolescents undergoing transcatheter pulmonary valve replacement (TPVR) within the native right ventricular outflow tract (nRVOT) is unknown. We sought to describe the incidence, severity, and duration of ventricular arrhythmias and identify associated risk factors in this population.

Methods: This was a retrospective cohort study of 78 patients < 21 years of age who underwent TPVR within the nRVOT. Patients were excluded for pre-existing ventricular arrhythmia or antiarrhythmic use. Study variables included: surgical history, valve replacement indication, valve type/size, and ventricular arrhythmia. Univariable logistic regression models were used to evaluate factors associated with ventricular arrhythmias, followed by subset analyses.

Results: Non-sustained ventricular arrhythmia occurred in 26/78 patients (33.3%). Median age at procedure was 10.3 years (IQR 6.5, 12.8). Compared with other nRVOT types, surgical repair with transannular patch was protective against ventricular arrhythmia incidence: OR 0.35 (95% CI, 0.13 to 0.95). Patient weight, valve type/size, number of pre-stents, and degree of stent extension into the RVOT were not associated with ventricular arrhythmia occurrence. Beta blocker was started in 16/26 (61.5%) patients with ventricular arrhythmia. One additional patient was lost to follow-up. Median beta blocker duration was 46 days (IQR 42, 102). Beta blocker was discontinued in 10 patients by 8-week follow-up and in the remaining 4 by 9 months.

Corresponding Author: Address: 81 N. Mario Capecchi Drive, Salt Lake City, Utah, 84113, Telephone: 801-662-1000, Fax: 801-213-7778, spencer.barfuss@hsc.utah.edu.

Disclosures:
The authors of this study have no conflicts of interest to disclose.

The Authors have no financial relationships to disclose.

This study was prepared and performed without any relationship with industry.

Conclusions: Though common after balloon-expandable TPVR within the nRVOT, ventricular arrhythmias were benign and transient. Antiarrhythmic medications were successfully discontinued in the majority at 6 to 8-week follow-up, and in all patients by 20 months.

Condensed Abstract:

In children and adolescents undergoing transcatheter pulmonary valve replacement within the native right ventricular outflow tract (nRVOT), ventricular arrhythmia occurred in 26/78 patients (33.3%). Compared with other nRVOT types, surgical repair with transannular patch was protective against ventricular arrhythmia incidence: OR 0.35 (95% CI, 0.13 to 0.95). Patient weight, valve type/size, number of pre-stents, and degree of stent extension into the RVOT were not associated with ventricular arrhythmia occurrence. Beta blocker was started in 16/26 (61.5%) patients with ventricular arrhythmia. Median therapy duration was 46 days (IQR 42, 102). Beta blocker was successfully discontinued in all patients by 20 months.

Keywords

Transcatheter pulmonary valve replacement; ventricular arrhythmia; congenital heart disease; adult congenital heart disease

Introduction:

Due to technical advances and the availability of large diameter transcatheter bioprosthetic valves, the use of transcatheter pulmonary valve replacement (TPVR) has expanded beyond treatment of surgically implanted dysfunctional right ventricle to pulmonary artery (RV-PA) conduits and bioprosthetic pulmonary valves to include treatment of severe pulmonary insufficiency within native right ventricular outflow tracts (nRVOTs)[1–4]. One known complication associated with non-nRVOT TPVR is ventricular arrhythmia, with reported incidences ranging from 3.4–9%[5–8]. Within nRVOTs, outcome data from TPVR have been derived from adult, or combined adult and pediatric, cohorts in which post-intervention ventricular arrhythmia incidences ranged from 0.4–40%[5–10]. Ventricular arrhythmia incidence and sequelae in children and adolescents undergoing TPVR within the nRVOT are unknown. The time course for resolution of these arrhythmias remains unclear. Some studies suggest this is a transient phenomenon, yet some patients are treated indefinitely[8]. A recent cohort study reported late occurrence of severe ventricular arrhythmias following TPVR in this population[11]. This underscores the need for additional pediatric data to inform guidelines and protocols for ventricular arrhythmia surveillance and management following TPVR.

Currently, two types of balloon-expandable transcatheter valves are approved by the US Food and Drug Administration (FDA) for use within dysfunctional, previously surgically implanted RV-PA conduits and bioprosthetic pulmonary valves: the Melody valve (Medtronic Inc., Minneapolis, MN, USA) – a trileaflet bovine jugular venous valve – and the Edwards SAPIEN XT and 3 valves (Edwards Lifesciences Inc., Irvine, CA) – trileaflet bovine pericardial valves originally designed for use in the aortic position[12, 13]. Although both the SAPIEN XT and S3 valves are FDA approved for use within dysfunctional RVOT conduits and surgical bioprosthetic pulmonary valves[14, 15], use of these balloon-expandable

valves in the nRVOT has been off-label. Furthermore, while both the Melody and SAPIEN valves have been well studied within surgically implanted RV-PA conduits and bioprosthetic pulmonary valves, few studies have investigated clinical factors associated with ventricular arrhythmia incidence and persistence, particularly in patients treated for severe pulmonary insufficiency within the nRVOT.

The primary purpose of this study was to describe the incidence, severity, and duration of ventricular arrhythmia and identify associated risk factors in a pediatric population undergoing balloon-expandable TPVR within the nRVOT. Adult patients were excluded to provide a clearer picture of the risk in this understudied population. The ability to identify patients susceptible to post-procedure ventricular arrhythmia will allow clinical providers to develop patient specific monitoring and treatment protocols. In addition, outcomes data regarding ventricular arrhythmia duration, its response to treatment, and its likelihood for recurrence will be useful in informing clinical practice guidelines for children and adolescents undergoing TPVR in the nRVOT.

Methods:

This was a single center, retrospective cohort study of pediatric patients <21 years of age at the time of valve replacement who underwent TPVR in the nRVOT at Primary Children's Hospital between November 2010 through June 2020. Valve type and size, as well as the techniques used for valve implantation, were at the discretion of the interventional physician. All patients were monitored with continuous telemetry during the associated hospitalization. Arrhythmia data was based on extraction from the medical record since telemetry data is not stored at our institution following hospital discharge. The study protocol was approved under a waiver of consent by the institutional review boards at Primary Children's Hospital and the University of Utah.

Patients were excluded for any of the following: 1) pre-existing ventricular arrhythmia, 2) treatment with any antiarrhythmic medication prior to TPVR, and 3) TPVR within a surgically implanted RV-PA conduit or bioprosthetic pulmonary valve. Pre-existing arrhythmias prompting exclusion were defined as: 1) accelerated ventricular rhythm, 2) non-sustained ventricular tachycardia (VT) (≥ 3 beats and < 30 seconds in duration at a rate 20% faster than the preceding sinus rhythm), or 3) sustained VT 30 seconds in duration at a rate 20% faster than the preceding sinus rhythm.

Patients were identified through our institutional catheterization database. Data were collected from the electronic medical record and included: underlying diagnosis, RV function on pre-procedure echocardiogram, valve replacement indication, type of valve (Melody vs. SAPIEN), size of valve, pre-stenting prior to valve implantation, degree of stent or valve extension into the RVOT as measured on stored angiographic images, and indexed right ventricular volumes by MRI where available. Stent extension into the RVOT was measured using lateral projections of angiography within the RVOT. Pre-implant images were used to identify the RVOT/MPA border by determining the limit of contractile tissue. Landmarks were then used to measure this area to the furthest point of stent extension within the RVOT. This technique was performed by SB and a subset verified

by MHM. Medical records, including narrative and procedural history, ECGs, inpatient telemetry, Holter monitors, and event monitors, were reviewed for post-TPVR ventricular arrhythmia and confirmed by an electrophysiologist. RVOT type was categorized as: 1) prior transcatheter pulmonary valve intervention (e.g. balloon valvuloplasty), 2) surgical repair with transannular patch, and 3) surgical repair without transannular patch (e.g. valvotomy).

A post-TPVR ventricular arrhythmia was defined as any ventricular arrhythmia occurring within the first 24 hours following TPVR that either 1) met criteria for a significant ventricular arrhythmia (as previously defined for exclusion criteria) or 2) resulted in any antiarrhythmic treatment. Arrhythmia treatment included invasive antiarrhythmic therapy received during hospitalization (e.g. electrical cardioversion, temporary pacing), and/or discharge on a new antiarrhythmic medication. The primary outcome was occurrence of a post-TPVR ventricular arrhythmia (as defined above).

Descriptive data were reported as medians with interquartile ranges (IQR) for continuous variables, and as counts with percentages for categorical variables. Categorical variables were evaluated using χ^2 and Fisher exact tests as appropriate. Univariable logistic regression models were fitted to evaluate factors associated with post-procedure ventricular arrhythmia, followed by subset analyses. A multivariate model was considered, but later abandoned given the small numbers and univariable results. Wilcoxon signed-rank test was used to compare pre and post TPVR QRS duration. All tests were 2-sided and p-value < 0.05 was considered significant. Statistical analyses were implemented using R v. 4.0.3 (R Core Team, 2020).[16]

Results:

During the study period, there were 439 TPVR patient candidates at our center. Of the 104 patients who underwent successful TPVR within the nRVOT, 78 met study criteria (Figure 1). Patient demographic and clinical data are displayed in Table 1. Median age at procedure was 10.3 years (IQR 6.5, 12.8). The most common underlying diagnosis was Tetralogy of Fallot (45 patients, 58%) followed by congenital valvar pulmonary stenosis (14 patients, 18%) and pulmonary atresia with intact ventricular septum (12 patients, 15%). The most common intervention preceding TPVR was a surgical repair with a transannular patch (54 patients, 69%). The vast majority of patients underwent TPVR for treatment of pulmonary regurgitation (71 patients, 91%). MRI data was available for 53 of the 78 patients (68%). Subjective RV function by echocardiogram was normal at baseline in 75 of the 76 patients in whom pre-operative echo data were available – there were no significant differences in RV function in those with and without ventricular arrhythmia.

Non-sustained ventricular arrhythmia occurred in 26 patients (33.3%). The most common arrhythmia was non-sustained VT which occurred in 24 patients (31%). Frequent premature ventricular contractions leading to antiarrhythmic medication initiation occurred in 2 patients, and no patients had accelerated ventricular rhythm (Figure 2). No patients had sustained VT following TPVR. Compared with other types of nRVOT, prior surgical transannular patch repair was associated with lower incidence of ventricular arrhythmia with an odds ratio of 0.35 (95% CI, 0.13 to 0.95). Other types of preceding interventions, patient

weight, TPVR valve type/size, number of pre-stents, degree of stent or valve extension into the RVOT, post-implant valve performance, pre-procedure QRS duration, and pre-procedure QTc were not associated with the occurrence of ventricular arrhythmia (Tables 1 and 2). Notably, no valves were placed in the supra-annular position. All had some degree of stent extension into the muscular RVOT.

Of the 26 patients with ventricular arrhythmias, 16 (61.5%) were treated pharmacologically. At the discretion of the treating physician, the other 10 were observed without medication; all had improvement in their arrhythmia burden prior to discharge. For those started on medication, the initial treatment of choice was oral beta blocker (with atenolol as first-line therapy) in all 16 patients. The mean atenolol dose was 0.9 mg/kg/day with a median of 0.8 mg/kg/day typically divided into twice daily dosing. One patient had persistent non-sustained VT and was transitioned to propranolol which resulted in successful rhythm control. Another patient did not respond to beta blocker therapy and was transitioned to amiodarone for persistent non-sustained VT. This patient was lost to follow-up. No patient required electrical cardioversion and no patient underwent ablation for treatment of their arrhythmia during the study period. The mean time to discharge was longer for patients started on antiarrhythmic therapy (1.8 vs 1.2 days) but this was not statistically significant ($p=0.29$).

Fifteen patients had ectopy recorded on ECG, Holter and/or catheterization rhythm recordings. In 14 patients, the morphology of ventricular ectopy was consistent with an RVOT origin; rhythm tracings from the remaining patient could not definitely be localized to a specific location. Following hospital discharge, outpatient ambulatory rhythm monitors were performed on 17 of the 26 patients with post-procedure ventricular arrhythmias (65%). Of the subset of 16 patients treated for their arrhythmia, 2 were lost to follow-up. Thirteen of the 16 patients (81%) had a 24-hour Holter monitor obtained in follow-up. Full ambulatory monitoring information can be found in Table 3. Median therapy duration was 46 days (IQR 42, 102). Beta blocker therapy was discontinued in 10 patients by 6 to 8-week follow-up and in the remaining 4 by 9 months per provider discretion (Figure 3). Two patients had their beta blocker discontinued without subsequent Holter evaluation.

Of the 13 evaluated following discontinuation, there were two recurrences of ventricular arrhythmia (both accelerated ventricular rhythm with a maximum of 5 beats in duration, at a maximum rate of 112 beats per minute in one and 140 beats per minute in another) detected on Holter obtained after beta blocker discontinuation. For one, therapy was restarted and later discontinued at 20 months with no evidence of recurrence on subsequent ambulatory monitoring. The other patient remained off beta blockade.

Of the 17 Holter monitors obtained in treated and untreated patients following hospital discharge, only one demonstrated a ventricular ectopy burden > 1%. This was the same patient with accelerated ventricular rhythm in whom beta blockade was re-started. All other patients had a ventricular ectopy burden < 1%. Three patients had Holters available for comparison from before TPVR and all 3 had an ectopy burden of < 1% at that time.

Discussion:

In our single center study of patients ≤21 years of age undergoing balloon-expandable TPVR within the nRVOT, post-procedure ventricular arrhythmias were common, occurring in 33% of patients. Those with post-procedural ventricular arrhythmias had a benign course. All patients with institutional follow up were successfully weaned off antiarrhythmic therapy; by 6 weeks for most patients, and by 20 months for the remainder (Figure 1). In our cohort, surgical transannular patch repair was the only implantation related factor significantly associated with ventricular arrhythmia incidence, decreasing its likelihood of occurring (OR 0.35, p = 0.04, Table 2). The finding that prior transannular patch was protective against ventricular arrhythmia has not been described previously. We hypothesize that this may be due to the presence of electrically inert material in the stent landing zone, leading to less overall potential for arrhythmia in stent contact areas.

This study represents the first and largest study to describe the natural history and temporal duration of ventricular arrhythmias in children and adolescents undergoing balloon-expandable TPVR in the nRVOT. The incidence of ventricular arrhythmia in our cohort was higher than reported incidences from prior studies evaluating TPVR within non-nRVOTs (3.4–9%)[5, 6, 7, 8]. This may be due in part to this study's focus on arrhythmia outcomes – the granularity of our study's arrhythmia data likely improved our ability to identify ventricular arrhythmias not previously identified by multicenter cohorts focused on non-arrhythmia outcomes. Notwithstanding, prior studies of TPVR in the nRVOT have also reported higher incidences of ventricular arrhythmias, ranging from 11.5% - 29%[5, 7]. Simmons et al. found that in children and adults with implanted transcatheter pulmonary valves, nRVOT was a risk factor for ventricular arrhythmia occurrence. Indeed, their reported ventricular arrhythmia incidence of 29% was comparable to ours[7]. This increased incidence of arrhythmia is likely due to mechanoelectrical stimulation and inflammation that occur when the stented valve apparatus interfaces with native myocardial tissue. This is consistent with the RVOT origin of ventricular ectopy identified in our study. Over time, resolution in inflammation at these contact zones may lead to the reported decrease in arrhythmia burden; scarring at these contact areas may also generate electrical quiescence[7].

One important finding of our study was that valve type/size, number of pre-stents, and degree of stent extension into the RVOT were not associated with the occurrence of ventricular arrhythmias. We hypothesize that larger valve size was not associated with increased arrhythmia burden because the larger valves were placed within larger nRVOTs. In the absence of significant RVOT obstruction, the selected valve size was the minimum size required to ensure valve stability rather than an oversized valve that would stretch or widen the RVOT. Although we expected the degree of stent extension into the RVOT to be positively associated with ventricular arrhythmia burden, our study did not find a significant association. We did, however, demonstrate a protective effect of prior transannular patch placement. It is possible that the valves placed were confined to patched areas, limiting interaction with right ventricular myocardium. This suggests circumferential contact with RVOT myocardium may be more important than length of stent extension into the RVOT[6]. This protective effect may not apply in cases of novel TPVR devices that address larger

RVOT diameters, as these are likely to be associated with myocardial interactions below the transannular patch from vertical and, perhaps more importantly, circumferential contact[10].

While ventricular arrhythmia occurrence is common following TPVR in the nRVOT, our data suggest that this is a benign and transient phenomenon. The periprocedural ventricular arrhythmias evaluated in this study likely have a different mechanism from the late occurring severe ventricular arrhythmias reported recently in this population[11]. Only 61.5% of patients with ventricular arrhythmia were treated. This suggests that for many patients, the arrhythmia (typically accelerated ventricular rhythm or non-sustained VT) resolves prior to the need for therapy. Most of the remaining patients were placed on a standard protocol of beta blockers with planned discontinuation at 6 weeks, followed by an outpatient Holter monitor. There were two arrhythmia recurrences, both identified by surveillance Holter monitoring. Practice variability accounted for the longer duration of treatment in other patients. Of note, no patient underwent a pre-procedure EP study to evaluate for a slow conducting isthmus, and our practice has not changed in this respect since data collection terminated.

The arrhythmias we identified were not life threatening and resolved with time. Therefore, one could consider avoiding antiarrhythmics altogether in this population. However, the short course of beta blockade was well tolerated in all patients. Therefore, our institution has chosen to continue to treat patients with ventricular arrhythmias (as defined above) in this setting. Based on our data we propose a novel management algorithm for patients with ventricular arrhythmias following balloon-expandable TPVR within the nRVOT (Figure 4). For patients requiring antiarrhythmic therapy, we suggest initial treatment with beta blockade for 6 weeks – in our study atenolol proved to be a low-cost and effective option for arrhythmia suppression. Patients are monitored on telemetry following beta blocker initiation to establish 12 or more hours without NSVT. At 6 weeks post procedure, beta blockade is discontinued if the patient does not have any symptoms of ongoing arrhythmia and a follow-up Holter is obtained to evaluate for recurrence off therapy. This time point was chosen for convenience as it corresponds with the typical post-procedure follow-up schedule at our institution. Implementation of this algorithm at our institution has simplified the communication regarding post-TPVR arrhythmias. If ongoing arrhythmia is documented, beta blockade should be resumed. If the patient remains asymptomatic, discontinuation may be re-attempted every 6 months followed by Holter surveillance for arrhythmia recurrence.

We anticipate that the results of this study will be helpful in guiding management of ventricular arrhythmias associated with ongoing balloon-expandable and new TPVR applications. As innovations in transcatheter pulmonary valve therapies evolve to include self-expanding stents, the length and circumference of these stents may make them more arrhythmogenic and increase the arrhythmia burden for susceptible patients. Implementing a feasible arrhythmia surveillance and treatment algorithm will be important to optimize patient safety and outcomes.

Limitations:

This was a single center retrospective cohort study and as such has certain limitations. No standard screening for arrhythmia occurred pre-procedurally. Because our institution does not store telemetry data following hospital discharge, periprocedural arrhythmias were not available for more granular analysis. Loss of follow-up due to patient relocation and/or resumption of care by referral centers meant incomplete capture of arrhythmia data, particularly in those who were treated for ventricular arrhythmias. Additionally, owing to practice variability, arrhythmia management and surveillance were not uniform – not all patients followed our typical management of 6 weeks of treatment followed by Holter surveillance after beta blocker discontinuation. This limits our analysis of the adequacy of this timeline. Finally, as this is a single center study, the outcomes we describe may not be generalizable to other centers. A prospective study evaluating the effectiveness of our proposed management algorithm would provide stronger evidence for its use. Additionally, despite our relatively large TPVR cohort, a larger multicenter cohort would provide more clarity regarding factors associated with ventricular arrhythmias that our study was not sufficiently powered to identify.

Conclusions:

Non-sustained ventricular arrhythmias were common in pediatric patients after balloon-expandable TPVR within the nRVOT, with an incidence of 33%. However, these arrhythmias were benign, did not require electrical cardioversion or invasive therapies, and were transient, with nearly 40% resolving without the need for medication at the time of discharge. In those patients who were pharmacologically treated, antiarrhythmic medications were successfully discontinued in most patients at 6-week follow-up, and in the remainder of patients not lost to follow-up by 20 months, with no subsequent arrhythmia recurrence. Valve type/size, number of pre-stents, and degree of stent extension into the RVOT were not associated with the occurrence of ventricular arrhythmia. Patients surgically repaired with a transannular patch in the RVOT had overall lower ventricular arrhythmia burden.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The authors would like the acknowledge the efforts of the catheterization lab staff and research staff whose work made this manuscript possible.

Sources of Funding:

This investigation was supported by the University of Utah Study Design and Biostatistics Center, with funding in part from the National Center for Research Resources and the National Center for Advanced Translational Sciences, National Institutes of Health, through Grant 8UL1TR000105 (formerly UL1RR025764).

Abbreviations List:

RVOT	right ventricular outflow tract

TPVR	transcatheter pulmonary valve replacement
RV-PA	right ventricle to pulmonary artery
nRVOT	native right ventricular outflow tract
FDA	Food and Drug Administration
VT	ventricular tachycardia
IQR	interquartile range

References:

1. Holzer RJ, Hijazi ZM. Transcatheter pulmonary valve replacement: State of the art. Catheter Cardiovasc Interv. 2016 Jan 1;87(1):117–28. doi: 10.1002/ccd.26263. Epub 2015 Oct 1. [PubMed: 26423185]
2. Cabalka AK, Asnes JD, Balzer DT, Cheatham JP, Gillespie MJ, Jones TK, Justino H, Kim DW, Lung TH, Turner DR, McElhinney DB. Transcatheter pulmonary valve replacement using the melody valve for treatment of dysfunctional surgical bioprostheses: A multicenter study. J Thorac Cardiovasc Surg. 2018 Apr;155(4):1712–1724.e1. doi: 10.1016/j.jtcvs.2017.10.143. Epub 2017 Dec 6. [PubMed: 29395214]
3. Haas NA, Carere RG, Kretschmar O, Horlick E, Rodés-Cabau J, de Wolf D, Gewillig M, Mullen M, Lehner A, Deutsch C, Bramlage P, Ewert P. Early outcomes of percutaneous pulmonary valve implantation using the Edwards SAPIEN XT transcatheter heart valve system. Int J Cardiol. 2018 Jan 1;250:86–91. doi: 10.1016/j.ijcard.2017.10.015. Epub 2017 Oct 6. [PubMed: 29017776]
4. Morgan GJ, Sadeghi S, Salem MM, Wilson N, Kay J, Rothman A, Galindo A, Martin MH, Gray R, Ross M, Aboulhosn JA, Levi DS. SAPIEN valve for percutaneous transcatheter pulmonary valve replacement without “pre-stenting”: A multi-institutional experience. Catheter Cardiovasc Interv. 2019 Feb 1;93(2):324–329. doi: 10.1002/ccd.27932. Epub 2018 Oct 23. [PubMed: 30351525]
5. Esmaeili A, Khalil M, Behnke-Hall K, Gonzalez Y Gonzalez MB, Kerst G, Fichtlscherer S, Akintuerk H, Schranz D. Percutaneous pulmonary valve implantation (PPVI) in non-obstructive right ventricular outflow tract: limitations and mid-term outcomes. Transl Pediatr. 2019 Apr;8(2):107–113. doi: 10.21037/tp.2019.04.02. [PubMed: 31161077]
6. Wadia SK, Lluri G, Aboulhosn JA, Shivkumar K, Reemtsen BL, Laks H, Biniwale RM, Levi DS, Salem M, Moore JP. Ventricular arrhythmia burden after transcatheter versus surgical pulmonary valve replacement. Heart. 2018 Nov;104(21):1791–1796. doi: 10.1136/heartjnl-2017-312769. Epub 2018 Apr 10. [PubMed: 29636402]
7. Simmons MA, Elder RW, Shabanova V, Hellenbrand W, Asnes J. Ventricular arrhythmias immediately following transcatheter pulmonary valve implantation: A cause for concern? Catheter Cardiovasc Interv. 2018 Apr 1;91(5):920–926. doi: 10.1002/ccd.27454. Epub 2017 Dec 27. [PubMed: 29280541]
8. Loar RW, Qureshi AM, Miyake CY, Valdes SO, Kim JJ, De la Uz CM. Percutaneous Pulmonary Valve Implantation-Associated Ventricular Tachycardia in Congenital Heart Disease. J Interv Cardiol. 2016 Dec;29(6):639–645. doi: 10.1111/joic.12344. Epub 2016 Sep 26. [PubMed: 27670128]
9. Martin MH, Meadows J, McElhinney DB, Goldstein BH, Bergersen L, Qureshi AM, Shahanavaz S, Aboulhosn J, Berman D, Peng L, Gillespie M, Armstrong A, Weng C, Minich LL, Gray RG. Safety and Feasibility of Melody Transcatheter Pulmonary Valve Replacement in the Native Right Ventricular Outflow Tract: A Multicenter Pediatric Heart Network Scholar Study. JACC Cardiovasc Interv. 2018 Aug 27;11(16):1642–1650. doi: 10.1016/j.jcin.2018.05.051. Epub 2018 Aug 1. [PubMed: 30077685]
10. Taylor A, Yang J, Dubin A, et al. Ventricular arrhythmias following transcatheter pulmonary valve replacement with the harmony TPV25 device. Catheter Cardiovasc Interv. 2022;100(5):766–773. doi:10.1002/ccd.30393 [PubMed: 36198126]

11. Veillette PO, Miro J, Khairy P, Abadir S, Le Bloa M. Ventricular Arrhythmias and Sudden Death Following Percutaneous Pulmonary Valve Implantation in Pediatric Patients [published online ahead of print, 2022 Apr 8]. Pediatr Cardiol. 2022;10.1007/s00246-022-02881-5. doi:10.1007/s00246-022-02881-5

12. Baron SJ, Thourani VH, Kodali S, Arnold SV, Wang K, Magnuson EA, Pichard AD, Babaliaros V, George I, Miller DC, Tuzcu EM, Greason K, Herrmann HC, Smith CR, Leon MB, Cohen DJ; PARTNER 2 Investigators. Effect of SAPIEN 3 Transcatheter Valve Implantation on Health Status in Patients With Severe Aortic Stenosis at Intermediate Surgical Risk: Results From the PARTNER S3i Trial. JACC Cardiovasc Interv. 2018 Jun 25;11(12):1188–1198. doi: 10.1016/j.jcin.2018.02.032. Epub 2018 May 30. [PubMed: 29860075]

13. Baron SJ, Arnold SV, Wang K, Magnuson EA, Chinnakondepali K, Makkar R, Herrmann HC, Kodali S, Thourani VH, Kapadia S, Svensson L, Brown DL, Mack MJ, Smith CR, Leon MB, Cohen DJ; PARTNER 2 Investigators. Health Status Benefits of Transcatheter vs Surgical Aortic Valve Replacement in Patients With Severe Aortic Stenosis at Intermediate Surgical Risk: Results From the PARTNER 2 Randomized Clinical Trial. JAMA Cardiol. 2017 Aug 1;2(8):837–845. doi: 10.1001/jamacardio.2017.2039. [PubMed: 28658491]

14. Kenny D, Rhodes JF, Fleming GA, Kar S, Zahn EM, Vincent J, Shirali GS, Gorelick J, Fogel MA, Fahey JT, Kim DW, Babaliaros VC, Armstrong AK, Hijazi ZM. 3-Year Outcomes of the Edwards SAPIEN Transcatheter Heart Valve for Conduit Failure in the Pulmonary Position From the COMPASSION Multicenter Clinical Trial. JACC Cardiovasc Interv. 2018 Oct 8;11(19):1920–1929. doi: 10.1016/j.jcin.2018.06.001. [PubMed: 30286853]

15. Kenny D, Hijazi ZM, Kar S, Rhodes J, Mullen M, Makkar R, Shirali G, Fogel M, Fahey J, Heitschmidt MG, Cain C. Percutaneous implantation of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position: early phase 1 results from an international multicenter clinical trial. J Am Coll Cardiol. 2011 Nov 15;58(21):2248–56. doi: 10.1016/j.jacc.2011.07.040. [PubMed: 22078433]

16. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

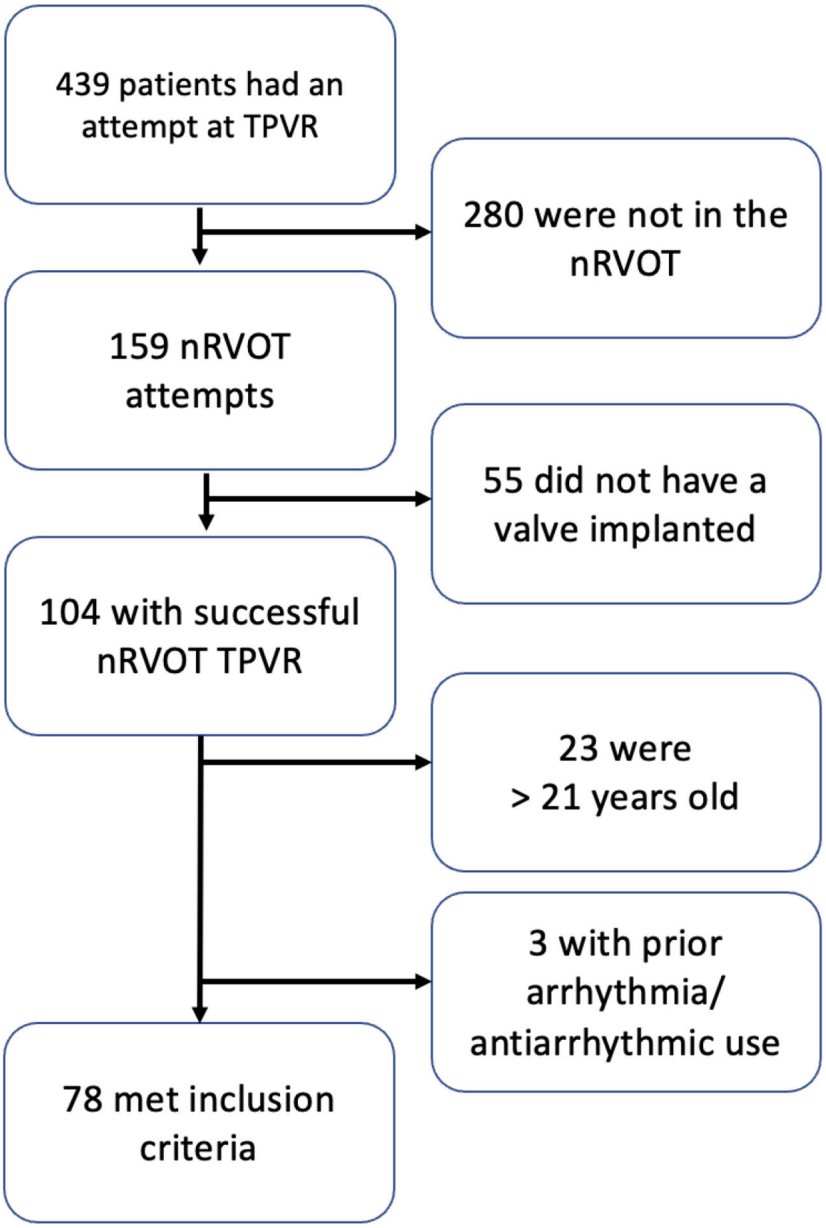


Figure 1:
Patient Eligibility and Inclusion Flow Chart

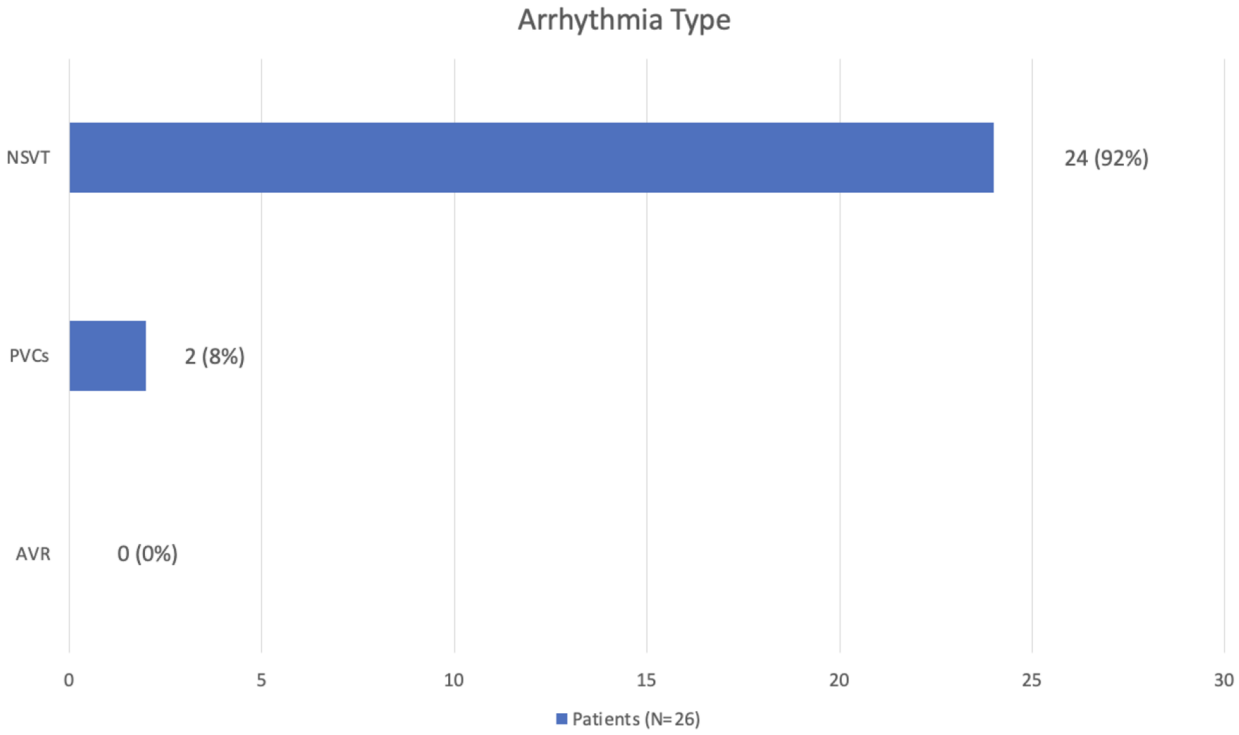


Figure 2:

Ventricular Arrhythmias by Type

NSVT = non-sustained ventricular tachycardia; PVCs = premature ventricular contractions; AVR = accelerated ventricular rhythm

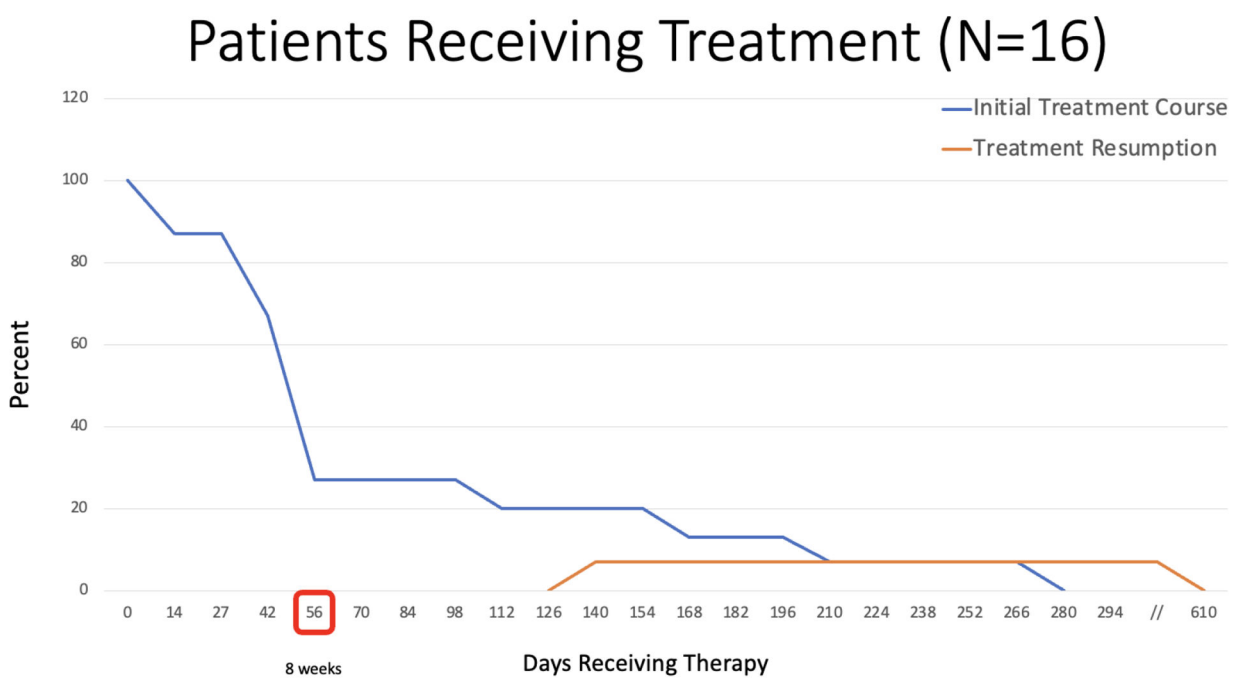


Figure 3:

Patients Receiving Treatment for Post-Procedure Ventricular Arrhythmias by Time

Percentage of patients receiving pharmacologic treatment for ventricular arrhythmias as a function of time since TPVR. The 6-week endpoint is highlighted by the red box. The blue line represents patients remaining on treatment from the time of valve implantation. The orange line represents patients for whom therapy was resumed due to persistent arrhythmia after discontinuation.

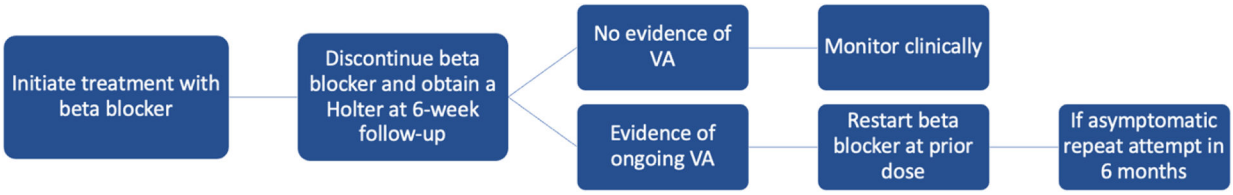


Figure 4:

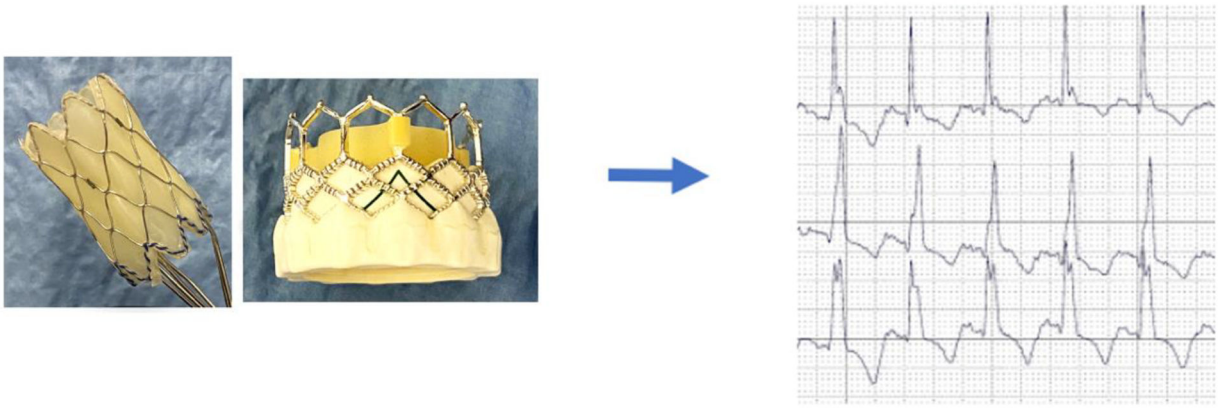
Suggested Management Algorithm for Clinically Significant Ventricular Arrhythmias

VA = ventricular arrhythmia

*Patients are monitored on telemetry to assure at least 12 hours without NSVT following beta blocker initiation.

Central Illustration:

Ventricular arrhythmias are common following TPVR in the native RVOT with an incidence of 33%.



Many patients don't require antiarrhythmic treatment; for those who do, 6 weeks is usually sufficient.

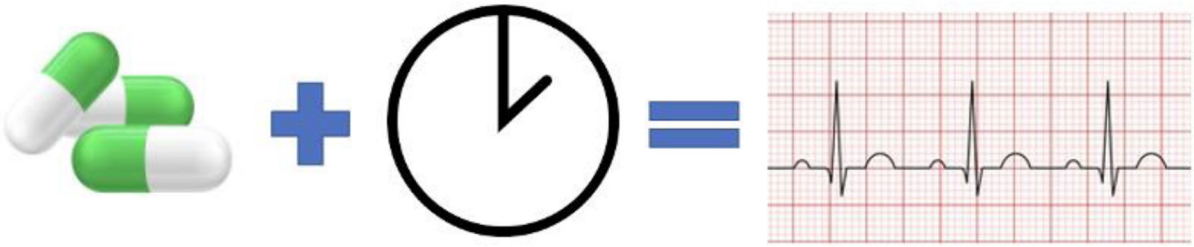


Table 1:

Patient Cohort Characteristics of Patients With and Without Ventricular Arrhythmias After TPVR in the Native Right Ventricular Outflow Tract

Variable	All Patients (N = 78)	VA (N=26)	No VA (N=52)	P-value
Age at TPVR (years)	10.3 (6.5, 12.8)	9.9 (6.2, 12.7)	10.4 (6.6, 12.8)	0.61[a]
Female	37 (47.4%)	13 (50%)	24 (46.2%)	0.75[b]
Weight at procedure (kg)	29.0 (19.3, 49.4)	29.0 (21.9, 49.4)	29.9 (19.1, 48.6)	0.93[a]
BMI at procedure	16.3 (14.6, 19.6)	16.3 (14.9, 19.1)	16.3 (14.5, 19.9)	0.95[a]
Indexed end diastolic RV volume by MRI (mL/m2)	129.0 (107.0, 157.0)	137.0 (118.0, 158.0)	128.5 (99.2, 153.5)	0.45[a]
Annulus measurement by MRI (mm)	22.4 (20.2, 24.5)	21.9 (20.0, 26.3)	22.4 (20.6, 23.5)	0.68[a]
Transannular patch repair:	54 (69.2%)	14 (53.8%)	40 (76.9%)	-
History of other surgical repair:	5 (6.4%)	2 (7.7%)	3 (5.8%)	-
Prior transcatheter intervention:	19 (24.4%)	10 (38.5%)	9 (17.3%)	0.09[c]
Pre-procedure ECG:				
QRS duration	117 (90.5, 135.5)	106 (92, 136)	118 (88, 143)	0.98[a]
QTc duration	440 (426, 462)	448 (427, 460)	438 (426, 462)	0.81[a]
Primary Indication:				
Mixed disease	7 (9%)	3 (11.5%)	4 (7.7%)	0.68[c]
Pulmonary insufficiency	71 (91%)	23 (88.5%)	48 (92.3%)	-
Pulmonary stenosis	0 (0%)	0 (0%)	0 (0%)	-
Valve Type:				
Melody	34 (43.6%)	13 (50%)	21 (40.4%)	-
SAPIEN	44 (56.4%)	13 (50%)	31 (59.6%)	-
Valve labelled size (mm)	23 (18, 26)	22.5 (18, 29)	23 (18, 26)	0.94[a]
Number of Pre-stents:				
0	29 (37.2%)	7 (26.9%)	22 (42.3%)	0.34[c]
1	45 (57.7%)	17 (65.4%)	28 (53.8%)	-
2	4 (5.1%)	2 (7.7%)	2 (3.8%)	-
Stent extension into RVOT (mm):	11.2 (8.4, 13.2)	11.6 (9.2, 13.4)	11.1 (8.4, 12.9)	0.68[a]
Degree of pulmonary insufficiency:				
≥ Moderate	0 (0%)	0 (0%)	0 (0%)	1.00[c]
Mild	1 (1.3%)	0 (0%)	1 (1.9%)	-
≤ Trace	77 (98.7%)	26 (100%)	51 (98.1%)	-
Peak gradient, mmHg	11.5 (8.0, 17.0)	10.5 (8.2, 13.0)	12.5 (7.8, 17.2)	0.23[a]
Days from TPVR to discharge	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	0.13[a]

Values are median (IQR) or n (%)

[a]Exact Wilcoxon rank sum test;

[b]Chi-squared test;

[c] Fisher's exact test

VA = ventricular arrhythmia; TPVR = transcatheter pulmonary valve replacement; IQR = interquartile range; kg = kilogram; BMI = body mass index; RV = right ventricle; MRI = magnetic resonance imaging; RVOT = right ventricular outflow tract

Table 2:

Univariable Analysis* of Clinical and Procedural Variables Associated with Ventricular Arrhythmia Incidence (N=78)

Variables	OR (95% CI)	P-value
Age at TPVR	0.98 (0.87, 1.1)	0.71
Male	0.86 (0.33, 2.21)	0.75
Weight at procedure	1 (0.97, 1.02)	0.98
BMI at procedure	0.98 (0.87, 1.07)	0.62
Valve type = SAPIEN	0.68 (0.26, 1.75)	0.42
Valve size	0.99 (0.89, 1.11)	0.91
Primary indication - Pulmonary insufficiency	0.64 (0.13, 3.46)	0.58
Indexed end diastolic RV volume (ml/m2)	1.01 (0.99, 1.03)	0.29
Annulus measurement by MRI (mm)	1.07 (0.93, 1.24)	0.37
Number of pre-stents	1.84 (0.79, 4.51)	0.16
Transannular patch repair	0.35 (0.13, 0.95)	**0.041**
Stent extension into RVOT (mm)	1.02 (0.88, 1.17)	0.83
Pre-procedure QRS duration	1 (0.98, 1.02)	0.87
Measurements on First Echo Post-Procedure:		
Peak Instantaneous Gradient Across the Valve (mmHg)	0.95 (0.87, 1.02)	0.16
*Pulmonary Valve Insufficiency ≤ Trivial	1.54 (0.08, 228.46)	0.79

* Firth's logistic regression used due to small sample size

OR = odds ratio; other abbreviations as in Table 1

Table 3:

Ambulatory Monitoring[a] in those with Ventricular Arrhythmia (N=26)

Variables	N (%)
Total Holter monitors obtained in follow up	17 (65%)
Patients treated for ventricular arrhythmia	16 (62%)
Holter monitors obtained in those treated with antiarrhythmics	13 (81%)
Holter monitors obtained in those untreated	4 (40%)
Recurrence of arrhythmia on Holter after treatment cessation[b]	2 (12.5%)
Recurrence of arrhythmia on Holter in those untreated	0 (0%)

[a]All were 24-hour Holter monitors;

[b]Both had accelerated ventricular rhythm

Table 5:

Univariable Analysis* of Clinical and Procedural Variables Associated with NSVT Incidence (N=78)

Variables	OR (95% CI)	P-value
Age at TPVR	0.97 (0.86, 1.1)	0.67
Male	1.1 (0.42, 2.92)	0.85
Weight at procedure	1 (0.97, 1.02)	0.91
BMI at procedure	0.97 (0.86, 1.07)	0.53
Valve type = SAPIEN	0.54 (0.20, 1.42)	0.21
Valve size	0.98 (0.87, 1.09)	0.66
Primary indication - Pulmonary insufficiency	0.56 (0.11, 3.05)	0.47
Indexed end diastolic RV volume (ml/m2)	1.01 (0.99, 1.03)	0.21
Annulus measurement by MRI (mm)	0.98 (0.84, 1.14)	0.82
Number of pre-stents	2.03 (0.86, 5.17)	0.12
Transannular patch repair	0.49 (0.18, 1.36)	0.17
Stent extension into RVOT (mm)	2.24 (0.17, 313.41)	0.58
Pre-procedure QRS duration	1 (0.98, 1.02)	0.77
Measurements on First Echo Post-Procedure:		
Peak Instantaneous Gradient Across the Valve (mmHg)	0.96 (0.89, 1.04)	0.32
*Pulmonary Valve Insufficiency ≤ Trivial	1.37 (0.07, 203.43)	0.84

* Firth's logistic regression used due to small sample size

OR = odds ratio; other abbreviations as in Table 1