JACC: CASE REPORTS VOL. 2, NO. 6, 2020

MINI-FOCUS ISSUE: TRANSCATHETER INTERVENTIONS

INTERMEDIATE

CASE REPORT: CLINICAL CASE SERIES

Transcatheter Pulmonary Valve Performance During Pregnancy and the Postpartum Period

Valeria E. Duarte, MD,[a,b,c,*] Julia A. Graf, BS,[a,*] Audrey C. Marshall, MD,[d] Katherine E. Economy, MD, MPH,[e] Anne Marie Valente, MD[a,b]

ABSTRACT

Increasing numbers of women with congenital heart disease are undergoing pregnancy after transcatheter pulmonary valve replacement (TPVR). We present the course of 9 pregnancies in 7 women with TPVR, noting pre-pregnancy, antepartum, and postpartum gradients, as well as maternal cardiac, obstetric, and neonatal outcomes. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:847–51) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Women with congenital heart disease (CHD) are at increased risk for adverse cardiovascular events during pregnancy (1). Many women with CHD undergoing pregnancy have had right ventricular outflow tract (RVOT) reconstruction and live with some level of RVOT obstruction and pulmonary regurgitation (PR). Pulmonary valve replacement (PVR) is commonly performed in this population to address both of these hemodynamic burdens. Due to inevitable time-dependent valve dysfunction, some patients may require serial PVRs over a lifetime (2,3). Over the past decade, development and dissemination of transcatheter therapies have allowed patients with CHD to benefit from PVR without undergoing reoperation. Transcatheter pulmonary valve replacement (TPVR) relieves RVOT obstruction, reduces PR, and yields favorable hemodynamic and clinical outcomes at 7-year follow-up (4,5).

Women with prior RVOT interventions are able to complete pregnancy with low risk of mortality, but with increased risk for arrhythmias and heart failure (6). There is a paucity of published data regarding the performance of TPVR in pregnant women (7). The

LEARNING OBJECTIVES

- To document the outcomes of pregnant women with TPVR.
- To contextualize changes in echocardiographic peak gradients for TPVRs during pregnancy and the postpartum period.

From the [a]Department of Cardiology, Boston Children's Hospital, and Department of Pediatrics, Harvard Medical School, Boston, Massachusetts; [b]Division of Cardiology, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts; [c]Houston Methodist DeBakey Heart and Vascular Center, Houston, Texas; [d]Harvard T.H. Chan School of Public Health, Boston, Massachusetts; and the [e]Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Brigham and Women's Hospital, Boston, Massachusetts. *Dr. Duarte and Ms. Graf contributed equally to this work. This work was supported by the Brigham and Women's Hospital Watkins Discovery Award, the Barton and Weinberg Family Fund, the Connors Center for Women, the Boston Adult Congenital Heart Disease Program Dunlevie Fund, and the Sarah Marie Liamos Fund for Adult Congenital Heart Disease Research. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received January 2, 2020; accepted February 26, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.02.029

ABBREVIATIONS AND ACRONYMS

CHD = congenital heart disease

PR = pulmonary regurgitation

PS = pulmonary stenosis

PVR = pulmonary valve replacement

RVOT = right ventricular outflow tract

TPVR = transcatheter pulmonary valve replacement

increased cardiac output associated with pregnancy would be expected to result in higher gradients across the fixed pulmonary valve. Given that pregnancy is a high-risk time to intervene on obstructed valves, it is important to understand the natural history of gradients during pregnancy.

We describe a single center's experience with regard to maternal cardiac, obstetric, and fetal outcomes among women with repaired CHD and TPVR, with attention to valve function before, during, and after pregnancy.

METHODS

Pregnant women enrolled in the STORCC (Standardized Outcomes in Reproductive Cardiovascular Care) registry from 2012 to 2018 who had undergone TPVR prior to pregnancy were included (8). Data harvested for this report included baseline demographics, cardiac anatomy, TPVR and surgical history, comorbid conditions, and medications. Although multiple devices were available during this period, all STORCC patients had received a Melody valve (Medtronic Inc., Minneapolis, Minnesota). Information on new cardiac or obstetric symptoms, changes in clinical status, medications, and cardiac and obstetric outcomes were collected prospectively at each clinic visit, during all admissions, and for up to 1 year following delivery, as previously described. Women with incomplete cardiac imaging or who did not complete pregnancy were excluded. All women provided informed consent, and the Institutional Review Boards at the Brigham and Women's Hospital and Boston Children's Hospital approved this protocol.

Echocardiograms were performed at 3 time points as per STORCC protocol: baseline (within 18 months prior to conception or in the first trimester), during the third trimester (except in 1 patient who delivered prematurely at 29 weeks, the echocardiogram was obtained at 20 weeks), and postpartum (4 to 6 weeks after delivery). Measurements included pulmonary valve peak and mean gradients as well as qualitative assessment of PR, tricuspid regurgitation, and right ventricular systolic function. A single investigator (V.E.D.) reviewed all echocardiograms.

Medical records were reviewed for outcomes of pregnancy. Adverse pregnancy outcomes were classified as cardiovascular, obstetric, and fetal as established in the STORCC protocol.

RESULTS

In total, 7 women and 9 pregnancies were analyzed (2 subjects had 2 pregnancies included). Clinical characteristics of these women are summarized in **Table 1**. The mean age at delivery was 32.1 years (range 26 to 38 years), and the mean time post-TPVR implantation at delivery was 4.4 years (range 1.0 to 9.4 years). Underlying anatomical diagnoses included repaired tetralogy of Fallot, pulmonary stenosis (PS), congenitally corrected transposition of the great arteries, and anatomically corrected malposition of the great arteries. The indication for TPVR was PS in 2 patients, PR in 2 patients, and mixed PS and PR in the remaining 3. **Table 2** presents the procedural data for each woman at the time of TPVR implant. The procedures were uncomplicated, and none of them experienced valve reintervention, endocarditis, or symptomatic iliac venous obstruction between implant and pregnancy.

TABLE 1 Baseline Clinical Characteristics

Patient #	Age (yrs)	Diagnosis	Number of Prior Surgeries	Type of Repair	Time Post-TPVR (yrs)	Anticoagulation/ Antiplatelet During Pregnancy	Cardiac Comorbidities
1	34.7	TOF/PA	4	Homograft	9.4	No	N/A
2	34.4	TOF/PA	3	Homograft	7.0	No	N/A
3.1	34.4	Dextrocardia/ ccTGA	2	Mustard/Rastelli	2.2	ASA	N/A
3.2	37.8	Dextrocardia/ ccTGA	2	Mustard/Rastelli	5.7	No	N/A
4	32.4	ACMGA	2	Homograft	2.8	ASA	Remote history of endocarditis
5.1	25.9	TOF/PA	2	Homograft	1.0	ASA	HTN
5.2	30.0	TOF/PA	2	Homograft	5.2	No	HTN
6	30.5	TOF/PS	2	RVOT patch Carpentier Edwards Bioprosthesis	1.6	No	Prior stroke, prior congestive heart failure, HTN
7	28.9	PS	2	Valvectomy/Mitroflow bioprosthesis	4.5	No	N/A

ACMGA = anatomically corrected malposition of the great arteries; ASA = aspirin; ccTGA = congenitally corrected transposition of the great arteries; HTN = hypertension; N/A = not applicable; PS = pulmonary stenosis; TOF/PA = tetralogy of Fallot/pulmonary atresia; TOF/PS = tetralogy of Fallot/pulmonary stenosis; TPVR = transcatheter pulmonary valve replacement.

Figure 1 demonstrates the pulmonary valve peak gradient at 3 timepoints: pre-pregnancy, third trimester, and postpartum. Notably, no increase in PR was observed in any of the patients. The peak gradient increased during the third trimester in most patients, but returned to baseline postpartum in all but 1 patient. That patient was 37 years of age with dextrocardia and congenitally corrected transposition of the great arteries, ventricular septal defect, and PS, who had undergone a Rastelli procedure with atrial switch early in life, and had her first pregnancy 2.2 years following TPVR placement without any significant change in gradient at that time. The subsequent pregnancy occurred 5.7 years following TPVR, and the discrepancy in the gradients may reflect a lower pre-pregnancy gradient for the second pregnancy (21 mm Hg vs. 30 mm Hg for the first pregnancy). Importantly, the postpartum gradients were nearly identical (31 and 33 mm Hg) despite the passage of 3.5 years between pregnancies.

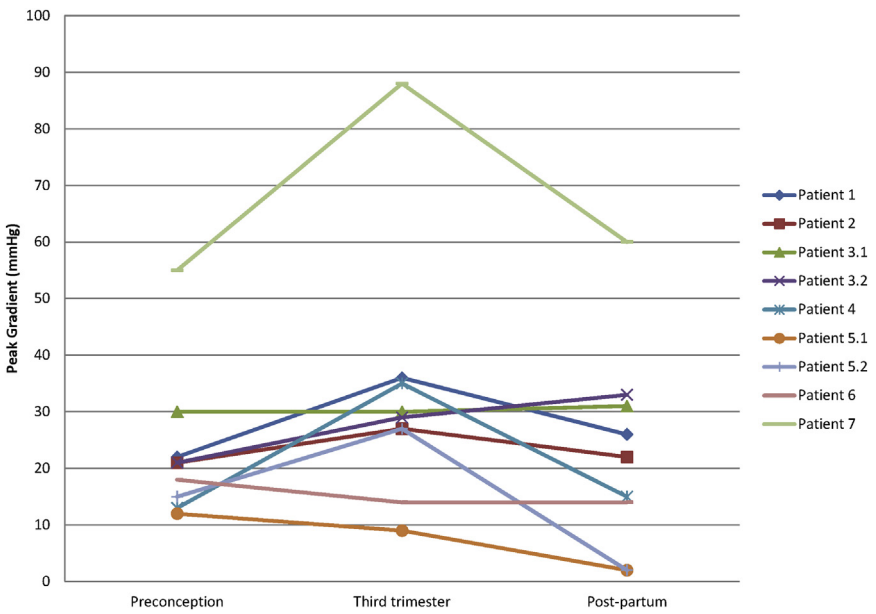
Additionally, 1 woman had a significantly elevated peak gradient of 55 mm Hg prior to pregnancy, prompting a right-heart catheterization. That study revealed an invasive peak-to-peak gradient of 25 mm Hg, suggesting that the echocardiogram had considerably overestimated the gradient. This discrepancy was taken into account when interpreting the increased gradient across the TPVR in the third trimester. Therefore, no change was made to the delivery plan, and she underwent a vaginal delivery

TABLE 2 Procedural Data at the Time of TPVR Implantation

Patient #	Indication for TPVR	Nominal TPVR Implant Diameter (mm)	Invasive Peak-to-Peak Gradient Across the TPVR Post-Implantation (mm Hg)	Peak Gradient on Post-Procedure Echocardiogram (mm Hg)
1	PS/PR	18	30	36
2	PS	22	10	27
3.1	PR	18	25	30
3.2	PR	18	25	30
4	PS	18	15	27
5.1	PR	20	11	<10
5.2	PR	20	11	<10
6	PS	22	20	23
7	PS/PR	22	10	15

PR = pulmonary regurgitation; PS = pulmonary stenosis; TPVR = transcatheter pulmonary valve replacement.

FIGURE 1 Peak Gradient Across the Transcatheter Pulmonary Valve During Pregnancy



Median peak gradient pre-conception: 21 (interquartile range [IQR]: 15 to 22), median peak gradient third trimester: 29 (IQR: 27 to 35), median peak gradient postpartum: 22 (IQR: 14 to 31). Subjects are labeled as numbers, and subjects 3 and 5 each had 2 pregnancies included (3.1, 3.2, 5.1, 5.2). Echocardiogram measurements of peak pulmonary valve gradient at 3 timepoints: before pregnancy, in the third trimester of pregnancy, and postpartum. Patient 3.2, who delivered prematurely at 29 weeks gestational age, has a second trimester echocardiogram in place of the third trimester echocardiogram. The pulmonary valve prosthesis gradients increased during pregnancy, but returned to baseline postpartum.

TABLE 3 Maternal Cardiac, Obstetric, and Fetal Outcomes

Patient #	Cardiac	GA at Delivery (weeks)	Obstetric	Mode of Delivery	Baseline Hemoglobin (g/dl)	Third Trimester Hemoglobin (g/dl)	Fetal CHD
1	No	36	Pre-term labor, pre-term delivery	NSVD	N/A	12.1	T21-TOF-AVC
2	No	39.14	Postpartum hemorrhage	NSVD	13.9	13.3	No
3.1	No	35.57	Pre-term delivery, chorioamnionitis/endometritis	NSVD	12.7	12.7	No
3.2	No	29.86	Pre-term labor, pre-term delivery, placental abruption, subchorionic hematoma, incompetent cervix	NSVD	14	12.8	No
4	No	39.57	No	NSVD	14.3	11.4	No
5.1	No	39	No	NSVD	12.1	13.1	No
5.2	No	38.86	No	Cesarean delivery: breech with failed version	12.8	11.9	No
6	No	36.71	Pre-term delivery	Unplanned Cesarean delivery: failure of progression of labor	10.6	10.9	No
7	No	35.57	Pre-term labor, pre-term delivery, placental abruption	NSVD	11.8	11.2	No

CHD = congenital heart disease; GA = gestational age; N/A = not applicable; NSVD = normal spontaneous vaginal delivery; T21-TOF-AVC = Trisomy 21, tetralogy of Fallot, atrioventricular canal.

at 35 weeks gestation secondary to placental abruption.

Maternal cardiac and obstetric data are included in Table 3. The mode of delivery was spontaneous vaginal in 7 cases, and by Cesarean in 2. Indications for Cesarean delivery were breech presentation and failure of progression of labor. The rate of pre-term birth was high, 5 of 9 pregnancies, 3 of which were associated with pre-term labor. The mean gestational age was 36 weeks 5 days. All of the women underwent a fetal echocardiogram between 18 and 20 weeks gestation, identifying 1 fetus with tetralogy of Fallot with atrioventricular canal defect (this newborn had Trisomy 21 and was delivered at a gestational age of 36 weeks).

DISCUSSION

This cohort describes the outcomes of 9 pregnancies in 7 women with various forms of CHD who had undergone TPVR prior to pregnancy. Importantly, no major adverse cardiac events or mortality occurred in these women. From an obstetric standpoint, it is worth noting that pre-term birth occurred frequently in these pregnancies (5 of 9). As pregnancy progressed with increased maternal plasma volume, we observed an increase in the peak gradient across the TPVR; however, as expected, these gradients returned to baseline in the postpartum period, except in 1 woman. In that specific case, it was the second pregnancy following TPVR and the pre-pregnancy echocardiogram peak gradient may have been underestimated, resulting in this discrepancy.

Additionally, in an illustrative case, echocardiography markedly overestimated the TPVR gradient prompting hemodynamic catheterization prior to conception (echocardiography peak gradient 55 mm Hg vs. peak-to-peak gradient 25 mm Hg by catheterization). This woman had an echocardiographic peak gradient of 88 mm Hg in the third trimester; however, no change in delivery plan was made due to the reassuring pre-pregnancy invasive data. She did not have maternal cardiac complications despite the gradient; however, she delivered at 35 weeks in the setting of placental abruption.

There are currently no guidelines pertaining to frequency of imaging for women with TPVR during pregnancy. This case series reveals that the postpartum TPVR function did not change significantly from the pre-pregnancy function, and right ventricular function was stable. Pregnant women who had undergone TPVR did not experience heart failure, clinically significant arrhythmia, or endocarditis during pregnancy. There were no maternal or fetal deaths. This data suggests that increased valve gradients are most likely due to physiologically increased cardiac output and plasma volume during pregnancy in the absence of structural changes in the valve. This case series highlights the importance of placing the cardiac diagnostic information obtained during pregnancy in context with the physiological changes based on timing of acquisition. At this time, there is no data to suggest that women with TPVR will fare any differently following pregnancy than those with surgical PVR.

ACKNOWLEDGMENTS The authors thank members of the STORCC team which include Laith Alshawabkeh, MD, Gabriele Egidy-Assenza, MD, Yoni Buber, MD, Nancy Barker, MS, PA-C, Jean Marie Carabuena, MD, Matthew R. Carazo, MD, Emily Dollar,

BS, Sheila Drakeley, BS, Sarah Rae Easter, MD, Kimberlee Gauvreau, ScD, Michelle Gurvitz, MD, Daniel Halpern, MD, Amy Harmon, PsyD, Kelsey Hickey, BA, Jenna Hynes, MD, Caitlyn Joyce, PA-C, Michael J. Landzberg, MD, Roisin B. Morgan, MD, Mary P. Mullen, MD, Patrick O'Gara, MD, Alexander Opotowsky, MD, Sarah Partington, MD, Dorothy Pearson, PA-C, Saraubh Rajpal, MD, Carrie Rouse, MD, Zöe J. Schefter, BA, Keri Shafer, MD, Michael N. Singh, MD, Shailendra Upadhyay, MD, and Fred Wu, MD.

ADDRESS FOR CORRESPONDENCE: Dr. Anne Marie Valente, Department of Cardiology, Boston Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115. E-mail: anne.valente@cardio.chboston.org. Twitter: @AnneValente1.

REFERENCES

1. Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. J Am Coll Cardiol 2018;71:2419–30.

2. Therrien J, Siu SC, McLaughlin PR, Liu PP, Williams WG, Webb GD. Pulmonary valve replacement in adults late after repair of tetralogy of Fallot: are we operating too late? J Am Coll Cardiol 2000;36:1670–5.

3. Sabate Rotes A, Eidem BW, Connolly HM, et al. Long-term follow-up after pulmonary valve replacement in repaired tetralogy of Fallot. Am J Cardiol 2014;114:901–8.

4. Cheatham JP, Hellenbrand WE, Zahn EM, et al. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. Circulation 2015;131:1960–70.

5. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. Lancet 2000;356:1403–5.

6. Egbe AC, El-Harasis M, Miranda WR, et al. Outcomes of pregnancy in patients with prior right ventricular outflow interventions. J Am Heart Assoc 2019;8:e011730.

7. Kozicka U, Weronski K, Ruzyllo W, et al. Pregnancy After Transcatheter Pulmonary Valve Implantation. Can J Cardiol 2017;33:1737.e5–7.

8. Valente AM, Landzberg MJ, Gauvreau K, et al. Standardized outcomes in reproductive cardiovascular care: the STORCC initiative. Am Heart J 2019;217:112–20.

KEY WORDS congenital heart defect, pregnancy, pulmonic valve, tetralogy of Fallot, valve replacement