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STATE-OF-THE-ART REVIEW

CARDIO-OBSTETRICS

Catheter-Based Interventions for the Management of Valvular Heart Disease During Pregnancy

Uri Elkayam, MD,[a,b] Priya Bansal, MD,[a] Anil Mehra, MD[a]

ABSTRACT

Pregnancy is associated with a significant increase in hemodynamic burden. These changes can lead to maternal morbidity and mortality as well as unfavorable fetal outcomes in patients with valvular heart disease and limited cardiac reserve. Mechanical interventions may be needed for the management of severe hemodynamic deterioration not responding to medical therapy. Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy. The purpose of this article is to review indications, potential advantages, and limitations of catheter-based interventions for the management of women with valvular heart disease in pregnancy. (JACC Adv 2022;1:100022)

The presence of valvular heart disease (VHD) due to both congenital and acquired etiologies in pregnant patients continues to pose a challenge to clinicians and their patients. Because of the marked hemodynamic changes including an increase in blood volume, heart rate, and stroke volume, there is often clinical deterioration that can lead to maternal and fetal morbidity and even mortality.[1] When medical therapy is ineffective, invasive interventions are needed to save the mother and, if possible, the fetus. Because surgery is associated with a high rate of fetal loss,[2,3] catheter-based percutaneous interventions have emerged as an alternative therapy. The purpose of this article is to provide an update on indications, potential benefits, and limitations of available percutaneous interventions for the treatment of various valvular conditions during pregnancy.

TEAM APPROACH TO CATHETER-BASED INTERVENTIONS FOR VALVULAR DISEASE IN PREGNANCY

The management of severe VHD prior to and during pregnancy is associated with diagnostic and therapeutic challenges that require collaboration between multiple disciplines. The cardio-obstetrics valve team (**Central Illustration**) should consist of high-risk maternal fetal medicine, cardiology with expertise in cardio-obstetrics, VHD, advanced echocardiography, and cardiac radiology, structural cardiology, cardiovascular surgery, obstetrical and cardiac anes-

From the [a]Division of Cardiology, Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA; and the [b]Department of Obstetrics and Gynecology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.
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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

CHD = congenital heart disease

PBPV = percutaneous balloon pulmonic valvuloplasty

PHT = pulmonary hypertension

PMBC = percutaneous mitral balloon commissurotomy

RHD = rheumatic heart disease

RVPAC = right ventricle to pulmonary artery conduit

TAVR = transcatheter aortic valve replacement

TPVR = transcatheter pulmonic valve replacement

VHD = valvular heart disease

thesia, neonatology, nursing, social work, and any other medical specialty needed. The comprehensive cardio-obstetrics model of care provides the necessary skill and knowledge to manage women with VHD during preconception, pregnancy, labor and delivery, and the post-partum period.

RISK OF RADIATION

Risk of radiation is a main concern for fetal safety in transcatheter interventions. All fluoroscopically and computed tomography-guided interventions should be optimized to achieve the clinical purpose with no more radiation exposure than necessary.[4] The risk to the fetus depends on the radiation dose and the gestational age with the highest radiosensitivity occurring during organogenesis (weeks 2-8) and the neuronal stem cell proliferation phase (weeks 8-14). If possible, the procedure should be performed after this period, and a consultation with a qualified medical physicist is encouraged to estimate potential conceptus dosing.[5] In general, the radiation dose to the fetus should be kept as low as possible (<50 mGy). Although the use of shielding between the patient's abdomen and pelvis and the beam has been suggested,[6,7] such shielding may be of only limited effectiveness and may even result in an increase in fetal radiation exposure due to inability for internal scatter to exit the abdomen.[8] For procedures outside of the abdomen or pelvic region, most of the conceptus dose is attributable to internal scatter from the thorax of the mother.[9] In the catheterization laboratory, collimation of windows, avoiding angulated views, optimal table height, decreasing the fluoroscopy frame rates, and utilizing "fluoroscopy-save" features instead of cineangiography can all reduce the extent of radiation to the patient and fetus.

AORTIC STENOSIS

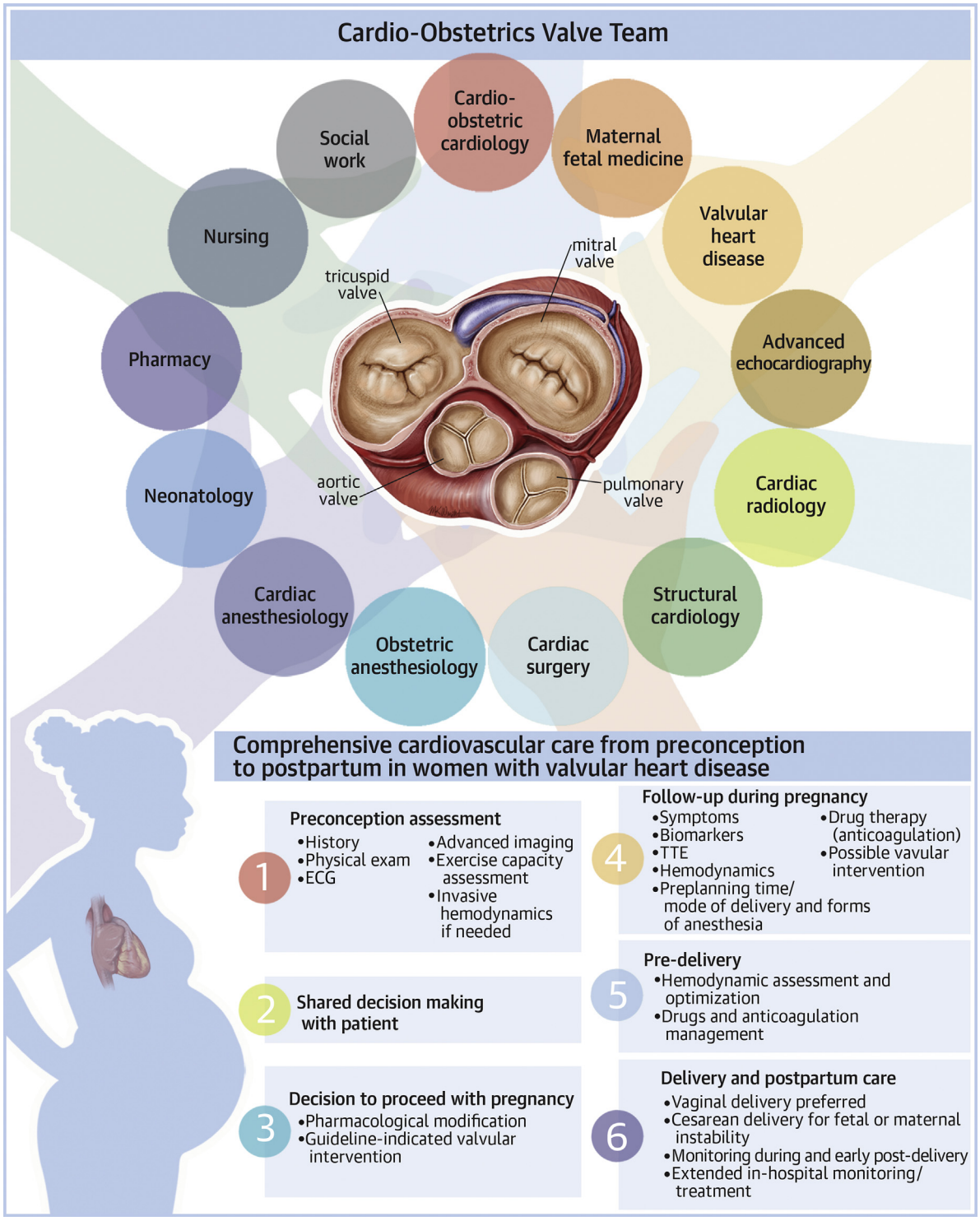
Valvular aortic stenosis (AS) in the childbearing age is mostly due to congenital etiology (**Figure 1**).[1,10] Rheumatic AS is more common in developing countries and occurs in conjunction with mitral valve (MV) disease in approximately 5% of pregnant women with rheumatic heart disease (RHD).[11] In congenital AS, the valve is most commonly bicuspid (95%) with a single fused commissure and uncommonly, dome-shaped unicuspid or tricuspid with 3 unseparated cusps. Bioprosthetic valve deterioration as well as cases with subvalvular and supravalvular AS has also been described in pregnancy.[12,13]

HIGHLIGHTS

- Invasive interventions may be needed for the management of severe hemodynamic deterioration in pregnant women with valvular disease.
- Cardiac surgery during pregnancy is associated with high fetal loss and prosthetic valves with risk of complications and early deterioration.
- Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy.
- Discussions regarding decision-making and performance of catheter-based interventions should be undertaken by an experienced multidisciplinary cardio-obstetrics valve team.

PRE-CONCEPTION EVALUATION. Given the risk of surgical aortic valve replacement (SAVR) and the potential complications related to the aortic prosthesis during and after pregnancy, indication for intervention prior to pregnancy should be determined based on comprehensive and multimodality evaluation. In general, the severity of AS along with related symptoms and cardiac events such as heart failure (HF) or arrhythmias prior to pregnancy are important predictors of complications during pregnancy.[14,15] Pre-conception evaluation, therefore, should include a history with emphasis on past cardiac events and assessment of AS severity including physical examination and 12-lead electrocardiogram (**Central Illustration**). Transthoracic echocardiography (TTE) is the gold standard for the diagnosis and assessment of the severity of AS and can provide information on the presence of pulmonary hypertension (PHT).[16] There are, however, limitations to TTE including technical challenges, variability, and discordances between severity grading criteria and symptoms.[17] Therefore, exercise stress testing should be performed for an objective assessment of functional capacity in "asymptomatic" patients. Invasive hemodynamic evaluation should also be considered in patients with discordant echocardiographic variables[18] and performed by an experience operator in tertiary centers. Criteria for the abnormal exercise test include symptoms (angina, syncope, severe dyspnea at low-level exercise), reduced workload <5 METS, fall of systolic blood pressure >20 mmHg during exercise, and complex ventricular arrhythmias.[17] A >20 mmHg increase in the mean aortic

CENTRAL ILLUSTRATION **Multidisciplinary Cardio-Obstetrics Valve Team**



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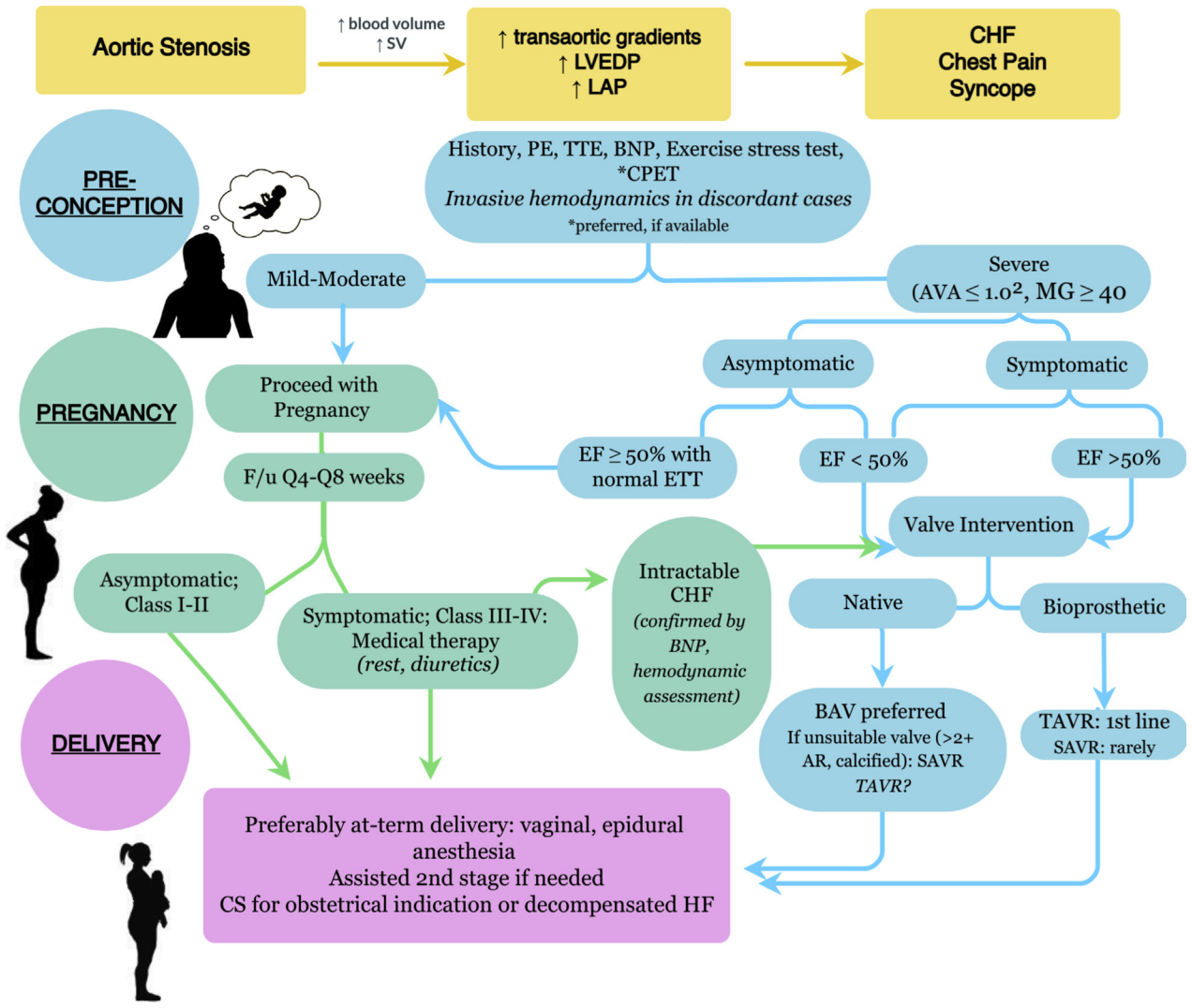
ECG = electrocardiogram; TTE = transthoracic echocardiogram.

FIGURE 1 **Evaluation and Management of Aortic Stenosis From Preconception to Postpartum**



AR = aortic regurgitation; AVA = aortic valve area; BAV = balloon aortic valvuloplasty; BNP = brain natriuretic peptide; CHF = congestive heart failure; CPET = cardiopulmonary exercise test; CS = cesarean section; EF = ejection fraction; ETT = exercise tolerance test; LAP = left atrial pressure; LVEDP = left ventricular end-diastolic pressure; MG = mean gradient; PE = physical exam; q = quaque (every); SAVR = surgical aortic valve replacement; SV = stroke volume; TAVR = transcatheter aortic valve replacement; TTE = transthoracic echocardiography.

valve (AV) gradient measured by exercise echo and an increase in pulmonary artery (PA) systolic pressure to >60 mmHg during exercise have been reported to provide incremental prognostic information.[19] It should be noted, however, that an increase in the gradient during exercise may not be a sign of severity but represents a physiologic adaptation to exercise-induced increase in cardiac output. An inherent limitation of exercise testing alone in the assessment of exercise capacity in sedentary women with AS is that results may be due to deconditioning rather than severity of the disease. For this reason, cardiopulmonary exercise testing (CPET) is preferred in women with decreased exercise performance. Predictors of risk provided by CPET are reduced maximum oxygen uptake (VO_2 max) to 16 ml/min/kg or less (Class C).[20] A markedly elevated plasma brain natriuretic peptide (BNP) concentration level (>3 × age-corrected normal ranges) is a complementary tool for risk stratifying patients with asymptomatic AS.[21] If needed, an invasive hemodynamic evaluation may further provide information regarding severity

of AS and correlation among left ventricular (LV) end-diastolic pressure, PA pressure, exercise performance, and BNP level.

INTERVENTIONS BEFORE PREGNANCY. Indications. Most recent European Society of Cardiology guidelines for valvular disease suggest that pregnancy should be discouraged and intervention should be considered before pregnancy in symptomatic patients due to severe AS or asymptomatic patients with severe AS and impaired LV function (LV ejection fraction [EF] <50%) or an abnormal exercise test. Further considerations for interventions are suggested even in asymptomatic patients with an LVEF >50% and normal exercise test if the procedural risk is low with poor prognostic indicators, such as transvalvular mean gradient ≥60 mmHg, peak velocity ≥5 m/s, or markedly elevated BNP levels.[22] The 2020 American College of Cardiology and American Heart Association guidelines also recommend pre-pregnancy interventions in women with severe AS (peak velocity ≥4.0 m/s or mean gradient ≥40 mmHg) even in those who are asymptomatic due to concern for progressive or sudden hemodynamic deterioration that may occur during pregnancy and delivery.[23] Available published information has shown, however, that majority of asymptomatic patients with moderate and severe AS can tolerate pregnancy well. In 60 such patients included in the Registry of Pregnancy and Cardiac Disease (ROPAC), the most common complication was HF, which was limited to 8% of the patients and could be managed medically.[14] The fetal outcome was also favorable with a 10% incidence of low birth weight—which is lower than the reported worldwide incidence of 14%.[24] Similar data were reported by Silversides et al[12] in 49 pregnancies with AS that was severe in one-half of them. There was no pregnancy-related mortality; cardiac complications (pulmonary edema and atrial arrhythmias) occurred in 10% of patients with severe AS and were managed medically in all patients except one with critical AS (AV area [AVA]: 0.5 cm^2 and peak gradient: 112 mmHg) who required urgent percutaneous balloon aortic valvuloplasty (PBAV) at 12 weeks' gestation.

In summary, pre-conceptual intervention should be considered in women with AS who desire to become pregnant and meet recommended criteria for intervention. However, considering inherent variabilities in individual diagnostic and prognostic predictors of complications during pregnancy, as well as the disadvantages of premature SAVR with either mechanical or bioprosthetic valve including the Ross procedure, intervention prior to pregnancy in a woman with asymptomatic severe AS and a normal LVEF needs to be determined based on extensive, multimodality evaluation. Prophylactic interventions prior to pregnancy in women who do not meet recommended criteria are not advisable. Our experience is that asymptomatic women with severe AS, with normal LV function, and with normal exercise tolerance can proceed with pregnancy with close follow-up by an experienced multidisciplinary cardio-obstetrics team with expected good outcomes.

Interventions. In women with symptomatic severe AS who meet criteria for an intervention, SAVR may be considered. However, because of the risk of mechanical prosthetic valve complications during pregnancy[15,25] and the risk of early bioprosthetic valve deterioration,[26] PBAV, if feasible, should be preferred. This procedure, if successful, allows the patient to proceed with pregnancy and can serve as a bridge for SAVR after the delivery if needed.[27] Most native AVs in young individuals (bicuspid or rheumatic) are associated with pliable, rather than heavily calcified leaflets with commissural fusion which can result in successful balloon dilation and significant gradient reduction. The most common complication is aortic regurgitation (AR) which is mostly mild to moderate.[28] Pillai et al[29] reported 92 young patients (mean age: 12.7 years) with congenital bicuspid AS who underwent successful PBAV with >50% reduction in the gradient in 86% and partially successful results in 9%. The mean AV gradient decreased from 41 to 17 mmHg and was sustained at 1 and 5 years. AR was noted in 35% of the cases after the procedure but was severe in only 2%. The same group of investigators also reported similar results in 92 young patients (average age: 21.7 years) with rheumatic AS.[30] Reintervention with PBAV or SAVR also remained low (13%) over 14-year follow-up.[31]

INTERVENTIONS DURING PREGNANCY. PBAV during pregnancy. Indication during pregnancy should be based on severity of stenosis, degree of LV function, aortic root size, and the severity of symptoms. American College of Cardiology and American Heart Association guidelines suggest PBAV or SAVR in pregnant patients with severe AS only if there is hemodynamic deterioration despite medical therapy or persistence of New York Heart Association (NYHA) class III to IV HF symptoms.[23] Reliance on symptoms during pregnancy, however, is problematic and can lead to unnecessary interventions. Decreased exercise tolerance, orthopnea, and even syncope are commonly reported by healthy pregnant women and can mimic the presentation of HF.[1] Change in the BNP level and echocardiographic PA pressures can help to

TABLE 1 Published Cases of PBAV During Pregnancy

First Author, Year	Age (y)	GA (weeks)	Etiology of Aortic Disease	Gradient Preprocedure (mmHg)	Gradient Postprocedure (mmHg)	Fluoroscopy Time (min)	Post-Procedure AR	Maternal Complications	Fetal Complications
Angel, 1988[35]	17	19	Congenital	150 (peak)	68 (peak)	20.1	NA	None	None
McIvor, 1991[36]	19	14	Congenital	64 (peak)	32 (peak)	29	NA	None	None
Savas, 1991[37]	22	22	Rheumatic	45 (peak)	22 (peak)	46[a]	NA	None	None
Banning, 1993[38]	26	14	Congenital	128 (peak)	50 (peak)	NA	Moderate	None	None
Banning, 1993[38]	19	16	Congenital	123 (peak)	60 (peak)	NA	NA	None	None
Lao, 1993[39]	26	16	Congenital	70 (mean)	30 (mean)	NA	NA	Transient seizure following 48 s of hypotension during the second inflation	None
Perloff, 1994[40]	26	36	Congenital	100 (peak)	30 (peak)	NA	NA	None	None
Bhargava, 1998[41]	27	26	Rheumatic	132 (peak)	41 (peak)	4.1	Trivial	None	None
Tumelero, 2004[42]	16	27	Congenital	105 (peak)	20 (peak)	NA	Mild-moderate	None	Emergency CS secondary to oligohydramnios and placental insufficiency
Radford, 2004[43]	36	13	Congenital	40 (mean)	11 (mean)	53	Moderate	Pulmonary edema post-delivery	CS at 39 wks due to fetal heart rate decelerations
Yap, 2006[44]	25	16	Rheumatic	65 (mean)	28 (mean)	N/A	Moderate	None	None
Dawson, 2012[45]	43	28	Rheumatic	40 (mean)	18 (mean)	N/A	Moderate	None	None
Dawson, 2012[45]	32	26	Congenital	70 (mean)	25 (mean)	N/A	N/A	N/A	N/A
Vinotha, 2012[46]	27	19	Congenital; endocarditis	118 (peak)	N/A	N/A	Mild	Sinus tachycardia (120 s) after PBAV, managed medically	Emergency CS at 32 wks secondary to fetal compromise with IUGR

[a]Fluoroscopy time includes triple valve intervention.

AR = aortic regurgitation; CS = cesarean section; GA = gestational age; IUGR = intrauterine growth restriction; mmHg = millimeters of mercury; N/A = information not available; PBAV = percutaneous balloon aortic valvuloplasty.

differentiate between symptoms related to hemodynamic deterioration and those associated with physiological changes of normal pregnancy. However, PA pressures may be overestimated by echocardiogram during pregnancy[32,33]; therefore, invasive hemodynamic evaluation should be considered prior to any catheter-based intervention. An increased pressure gradient across the AV alone is expected due to increased stroke volume during pregnancy, and is not an indication for intervention in the asymptomatic patient.[34]

Because of the higher maternal risk and fetal loss associated with SAVR, PBAV is considered a first-line option in pregnancy if suitable valve morphology is present. There are no large series of PBAV in pregnancy, but multiple isolated reports show favorable results (Table 1).[35-46] Gestational age at the time of these procedures ranged between 14 and 36 weeks, and the AVA prior to the procedure ranged between 0.50 and 0.67 cm^2. The transvalvular peak gradient ranged between 45 and 150 mmHg and was reduced by >50% after the procedure in all patients. Maternal complications were limited to development of mild-to-moderate AR and transient seizure following the second inflation in one patient. There were no significant fetal complications intraprocedurally or post-procedurally, with most patients having successful induction of delivery at term.

Complications reported in older, nonpregnant populations have included vascular complications, aortic annular rupture, conduction abnormalities, tamponade from wire perforation or annular disruption, MV chordal rupture, brady or tachyarrhythmias, severe LV dysfunction after rapid pacing especially in patients with LV dysfunction, and severe AR.[47,48] An approach to PBAV can be retrograde via the femoral artery or antegrade via the femoral vein and transseptal puncture. Bhargava et al[41] published the only case of PBAV during pregnancy via an antegrade approach using a single Inoue balloon to reduce radiation dose, balloon slippage, and serial balloon size increases. The standard retrograde technique involves accessing the femoral artery using a micropuncture needle under ultrasound guidance, and the most common sheath size is 12-F. Percutaneous preclosure devices should be used to reduce bleeding complications. We recommend using a long 12-F sheath (55 or 70 cm) positioned below the left subclavian artery for rapid catheter exchange without fluoroscopy of the abdomen. Alternatively, a radial

TABLE 2 Published Cases of TAVR During Pregnancy

First author	Hodson et al[53]	Gandhi et al[54]	Maluenda et al[55]	Berry et al[56]	Chengode et al[a 57]	Herbert et al[58]	Zhong et al[59]
Patient age (y)	22	29	39	33	34	30	29
GA at procedure (wk)	22	14	23	22	22	19	12
Type of the valve	Native BAV	23-mm CE Perimount Magna	21-mm Freestyle Medtronic	21-mm CE Magna	21-mm CE Perimount Magna (M-27 mm)	19-mm Magna Ease	27-mm Freestyle Medtronic
Age of prior intervention (y)	9 (PBAV)	24	23	N/A	26	25	16
Symptoms	Dizziness, DOE, chest pain	NYHA class III HF, CCS class 3	NYHA class III HF	Progressive DOE	NYHA class III HF	NYHA class III HF	NYHA class III HF
Peak/mean aortic gradient before TAVR	110/56	149/98	98/51	102/61	148/66	153/92	104/65
AVA before procedure (cm^2)	1	0.8	N/A	0.66	0.7	0.8	0.63
Degree of AR	Moderate	Mild	Severe	Moderate	Mild-to-moderate	None	None
PA pressure (mmHg)	N/A	Normal	NA	N/A	72	52	N/A
LV function	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Imagining modality	IVUS, 3D-TEE, Fluoro	TEE, Fluoro	CTA, Cine	CTA	TEE, Fluoro	TEE, Fluoro, Cine	FA US, CT chest, TEE, Fluoro
Type of valve	Core Valve	Sapien XT	Sapien XT	Sapien 3	Sapien XT	Sapien 3	Core Valve
Size of TAVR valve (mm)	26	23	23	20	23	20	26
Fluoroscopy time (min) + radiation dose (mGy)	10.03 (AK 101 mGy)	16.03 (AK 298 mGY)	NA	N/A	3:06 (AK 16 mGy)	18	30 mGy (fetal radiation dose estimate for all procedures)
Peak/mean aortic gradient post-TAVR (mmHg)	N/A	47/23	NA	61/23	68/24	52/27	24/14
AVA post-procedure (cm^2)	N/A	N/A	NA	1.1	N/A	N/A	N/A
Procedural complications	LBBB/mild PVL	No PVL	No PVL	Trace PVL	No PVL	No PVL	Trace PVL
Meds post-procedure	ASA 81 mg every day	Dalteparin 12,500 units SQ/d × 1 mo; ASA 81 mg/d indefinitely	Clopidogrel 75 mg every day (ASA allergy)	N/A	ASA 81 mg/d; LMWH 80 mg SQ/d until admission for delivery	N/A	LMWH during pregnancy. ASA post-delivery
Delivery mode	Vaginal	Vaginal	NA	CS	Vaginal	Vaginal	Planned vaginal converted to CS
GA at delivery (wk)	38	39	NA	37	Full term	33	36
Maternal complications	Persistent LBBB	None	None	None	None	None	Premature rupture of the membrane
Fetal complications	None	None	None	None	None	None	None

[a]Transcatheter aortic and mitral double valve-in-valve implantation through left ventricular apical approach.

3D = 3-dimensional; AK = air kerma; AR = aortic regurgitation; ASA = aspirin; AVA = aortic valve area; BAV = bicuspid aortic valve; CCS = Canadian Cardiovascular Society; cine = cineangiography; CS = Cesarean section; CTA = computed tomography angiography; DOE = dyspnea on exertion; FA = femoral artery; Fluoro = Fluoroscopy; GA = gestational age; IVUS = intravascular ultrasound; LBBB = left bundle branch block; LMWH = low-molecular-weight heparin; LV = left ventricle; meds = medications; NA = information not available; NYHA = New York Heart Association; PA = pulmonary artery; PBAV = percutaneous balloon aortic valvuloplasty; PVL = paravalvular leak; SQ = subcutaneous; TEE = transesophageal echocardiography; US = ultrasound.

approach using smaller sheath size may be considered.[49]

A recent report by Li et al[50] described retrograde PBAV under TTE guidance without fluoroscopy with excellent short-term results in 30 patients (one pregnant). Similarly, Mizutani et al[51] used 3-dimensional transesophageal echocardiography (TEE) to guide antegrade multiple-inflation PBAV. These techniques can reduce radiation exposure while still appropriately sizing the balloon and monitor immediate results to avoid over-dilatation and detect complications early. Hemodynamic changes during pacing can be avoided by use of newer valvuloplasty balloons. Aortic balloon sizing is usually predetermined by TTE, while aortic annulus can be measured on TEE. In pregnancy, the PBAV goal is to carry the pregnancy to term without maternal complications; therefore, the conservative approach is recommended. Symptom control can mostly be achieved with reduction in the gradient by 50%, while avoiding acute severe AR, which could require emergency rescue SAVR. The use of balloons larger than the sinotubular junction and AV annular diameters should therefore be avoided. We recommend starting with balloon sizes 2 to 3 mm smaller than the maximal size selected and abort the procedure if new 1 to 2+ AR is detected.

TRANSCATHETER AORTIC VALVE REPLACEMENT DURING PREGNANCY. Transcatheter aortic valve replacement (TAVR) is now an established treatment

for severe symptomatic AS in older patients, and its use has increased rapidly.[52] This procedure offers a theoretical advantage over SAVR in pregnant patients not suitable for PBAV (>2+ AR or severe AV calcification), patients with degenerative bioprosthesis including the Ross procedure with severe AS/AR, and those who develop severe acute AR post-PBAV. Reported experience with TAVR in pregnancy is limited; however, it is anticipated to be increasingly considered by clinicians as a first-line therapy over SAVR in the future. It is therefore essential to understand the potential advantages and limitations of this technology when performed during pregnancy. There are currently 7 reported cases of TAVR during pregnancy (**Table 2**),[53–59] 1 in a native bicuspid AV (BAV) and 6 in deteriorated bioprosthetic valves. The only case of TAVR in a native valve was reported by Hodson et al[53] in a 22-year-old female with the BAV, presenting at 15 weeks' gestation with dizziness and dyspnea on exertion. The transvalvular mean gradient was 38 mmHg, with calculated AVA of 1.0 cm^2, normal LVEF, and moderate AR. Stress TTE revealed an exercise capacity of 8 to 9 METS with an increase of the mean gradient during exercise from 56 mmHg to 76 mmHg. A TAVR with 26-mm CoreValve was performed successfully. The patient developed a new left bundle branch block, which remained stable, and had a planned vaginal delivery at 38 weeks to a healthy baby. Although the case demonstrates feasibility, there are several challenges along with short- and long-term potential consequences of TAVR of a native AV in young pregnant patients which must be considered and discussed with the patient (**Table 3**).[60–74]

VALVE-IN-VALVE TAVR. Early deterioration of a bioprosthetic valve is common in women in the childbearing age.[14] In patients presenting with severe hemodynamic compromise before 32 weeks' gestation, redo SAVR was previously the only solution, but it is associated with a high incidence of fetal loss. PBAV may yield inconsistent and limited relief of stenosis with a higher risk of significant AR and acute cardiovascular collapse. Valve-in-valve (VIV) TAVR in such cases has become a nonsurgical option during pregnancy (**Table 2**). Reported patients presented with NYHA functional class III HF during pregnancy due to severe AS and mild-to-moderate AR secondary to bioprosthetic valve deterioration between 5 and 13 years after SAVR. VIV TAVR was performed between 12 and 22 weeks' gestation using a balloon-expandable valve in 5 patients and self-expandable in one. The transvalvular mean pressure gradient was reduced from 51-98 mmHg to 14-27 mmHg with zero to trace paravalvular leak and no maternal or fetal complications. Patients were treated with various antiplatelets and anticoagulation regimens. We recommend anticoagulation regimens similar to nonpregnant patients during PBAV and TAVR, with unfractionated heparin 70 to 100 U/kg to maintain activated coagulation time between 250 and 300 seconds and protamine post-procedure to reverse the anticoagulation. In patients undergoing TAVR without an indication for anticoagulation, aspirin alone at a dose of 80 to 160 mg (which is safe during pregnancy) significantly reduces bleeding without increasing thromboembolic events, compared with dual antiplatelet therapy.[75,76]

In summary, need for cardiac interventions in patients with severe AS in pregnancy is rare and should be considered only in severely symptomatic patients due to hemodynamic deterioration refractory to medical therapy. In women with severe AS, PBAV should be considered as first-line therapy as a bridge for SAVR or repeat PBAV if needed, after the delivery. TAVR is emerging as a viable option, but it is limited in patients with the BAV by technical challenges, likelihood of suboptimal results, high incidence of a permanent pacemaker, limited durability of the prosthetic valve, and the complexity of SAVR after TAVR (**Table 3**). This procedure should, therefore, be considered only in selected patients with severe hemodynamic deterioration who are unsuitable candidates for PBAV and when early delivery is undesirable due to extreme prematurity. Limited information on VIV TAVR suggests short-term efficacy and safety in the treatment of deteriorated bioprosthetic valves. More experience, however, will be needed to determine the long-term durability of the valve and the outcome of the inevitable repeat SAVR in the future.

SUBAORTIC STENOSIS

Women with subaortic stenosis (subAS) who meet criteria for surgery include a maximum gradient ≥50 mmHg with subAS-related symptoms and <50 mmHg gradient with symptoms of HF, ischemia, or LV dysfunction.[77] SubAS is found in 6% of adults with congenital heart disease.[78] It was reported in 23% of 96 patients with AS included in the ROPAC registry and was described as severe in 50% and asymptomatic in two-thirds of the patients.[14] No information was provided on the outcome of these patients in comparison to the patients with other forms of AS. There was no mortality for the entire group. The leading complication was new or worsening HF (11%), with a higher incidence in those with a history of HF prior to the pregnancy. All patients

TABLE 3 Challenges and Consequences of TAVR During Pregnancy in Women With BAVs

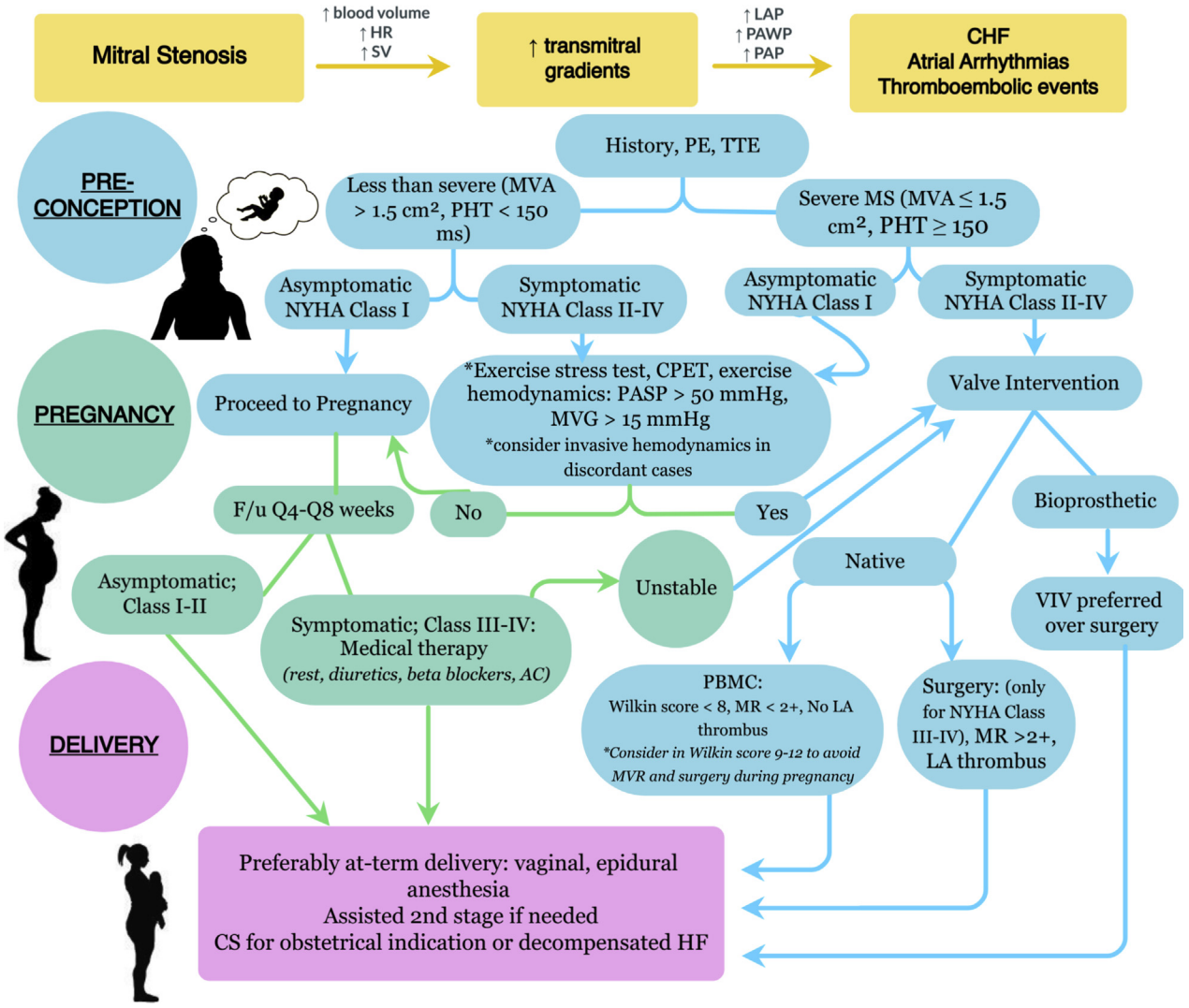
Variable anatomy of BAVs	• Larger annular dimensions compared to tricuspid valves, which may be outside of the range covered by currently available THVs[60] • AV outflow shapes result in a variable site of maximal narrowing (supra-annular vs annular) which introduces difficulty in correct sizing of the THV • A higher ellipticity index (maximum diameter/minimum diameter) and number of raphe result in eccentric, less circular deployment and uneven forces on surrounding structure increasing risk of PVL or wall injury
Limited use of TEE compared to CT	• TEE is less accurate than CT[61] in assessing coronary heights and exact site of AV complex maximal narrowing and understanding of AV complex shape which is important for sizing • It is recommended to undersize when intercommissural distance is smaller than mean annular diameter[62]; however, undersizing can increase risk of embolization, malposition, and PVL[63] • Oversizing may lead to risk of annular rupture, new LBBB, or need for PPM • Self-expanding valves rather than balloon-expandable valves may be preferred to avoid radiation from CT but can lead to a higher rate of post-procedural PPM, aortic wall injury, and compromised coronary access issues in the future
Reduced tissue holding	• Selection of size and type of THV and the deployment technique are challenging because reduced tissue holding forces increase risk of embolization, PVL, and early need for AV reintervention[64] ○ In the absence of annular calcification, there is a higher risk of embolization with the balloon-expanded valves ○ Consideration can be given to slightly oversize the valve or choose a more ventricular implant to circumvent the absence of calcification,[65] but ventricular implantation may increase PPM need
Risk of coronary occlusion	• Coronary anomalies are more frequent in the BAV than those in the TAV[64] • One or both coronary ostia may lie near the commissure with a larger fused coronary cusp that may increase the risk of coronary obstruction
More common horizontal orientation of the aorta in the BAV	• Defined as <30° between the plane perpendicular to the aortic annulus and a horizontal reference line, CT may need to be used to define it more accurately • If present, it complicates positioning of the valve and increases risk of device embolization and need for a second valve implantation, especially if using a self-expanding valve[65] • Balloon-expanding valves may be preferred in this setting
Associated vascular changes and aortopathy	• Because of the hormone-mediated changes in the aortic wall, the incidence of ascending and descending thoracic aorta dissection and perforation caused by stiff wire or catheter-related injury to the aortic wall associated with TAVR may be higher during pregnancy[66,67]
Need for PPM and long-term consequences	• If self-expanding valves are preferred due to variable anatomy and to reduce radiation risk, the incidence of PPM remains high despite newer-generation valves and advances in deployment techniques[68] • Possible commitment to a lifelong dependency on ventricular pacing in a young woman may be associated with device-related complications, TV injury, increased risk of HF hospitalizations, and mortality[69]
Long-term durability and risk of future SAVR after TAVR	• Pregnancy has been shown to accelerate deterioration of bioprosthetic valves and may have a similar effect on THVs[70] • In case of deterioration of the TAVR valve in young patients, SAVR after TAVR is a complex surgery owing to adhesion of the TAVR valve to the surrounding aortic tissue (self-expanding valves) and sometimes the anterior leaflet of the MV • TAVR valve explant may disrupt the aortic root and often requires aortic root replacement with coronary reim plantation and sometimes MV repair/replacement[71,72] with worse than expected outcomes as compared to SAVR as the initial form of valve replacement[73]

AV = aortic valve; BAV = bicuspid aortic valve; CT = computed tomography; HF = heart failure; LBBB = left bundle branch block; MV = mitral valve; PPM = permanent pacemaker; PVL = paravalvular leak; SAVR = surgical aortic valve replacement; TAV = tricuspid aortic valve; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography; THV = transcatheter heart valve; TV = tricuspid valve.

were managed medically, and none required a mechanical intervention. Pre-pregnancy evaluation of women with subAS should be like valvular AS. The severity of the subvalvular obstruction is determined by TTE, but Doppler-derived gradients may overestimate the obstruction.[79]

Women planning for pregnancy who meet guideline-recommended criteria should undergo surgery prior to pregnancy.[79] The most common type of subAS (75%-85%) is a fibrous crescent or ring just below the AV.[79] In patients with discrete subAS,[80] percutaneous transluminal balloon tearing (TBT) of the membrane has been performed with excellent long-term results in a select group of patients with a thin membrane and no AR. In 76 nonpregnant patients with the mean age of 19 ± 16 years and thin (<3 mm) subaortic membrane,[81] the subvalvular gradient decreased from 70 ± 27 to 18 ± 12 mmHg ($P > 0.001$) without significant AR. Complications included one mortality due to wall perforation, mild mitral regurgitation (MR) through a small cleft-like tearing of the anterior mitral leaflet in one, nodal rhythm in one, and transient left bundle branch block in 16 patients. After a mean follow-up of 16 ± 6 years, 80% were free of subvalvular renarrowing. Singh et al[82] published a case of successful TBT in a 22-year-old pregnant patient presenting with Class III symptoms at 26 weeks' gestation. Cardiac catheterization showed elevated left heart filling pressure and a peak and mean gradient of 224 and 124 mmHg, respectively. TBT was performed with a 23-mm balloon under fluoroscopic and cineangiographic guidance and rapid pacing. The immediate post-procedural peak-to-peak gradient was reduced to 19 mmHg. There were no complications with full-term delivery at 38 weeks.

FIGURE 2 Evaluation and Management of Mitral Stenosis From Preconception to Postpartum



AC = anticoagulation; BNP = brain natriuretic peptide; CHF = congestive heart failure; CPET = cardiopulmonary exercise test; CS = cesarean section; HR = heart rate; LA = left atrium; LAP = left atrial pressure; MR = mitral regurgitation; MVA = mitral valve area; MVG = mean valve gradient; NYHA = New York Heart Association; PAP = pulmonary artery pressure; PASP = pulmonary artery systolic pressure; PAWP = pulmonary artery wedge pressure; PE = physical exam; PHT = pressure half time; q = quaque (every); SV = stroke volume; TTE = transthoracic echocardiography; VIV = valve-in-valve.

In summary, TBT may be used as an alternative to surgery during pregnancy in the rare cases of significant hemodynamic deterioration not responding to rest and medical therapy. Because of the limitation of available information, individual decision must be considered after extensive discussion by the cardio-obstetrics valve team. Outside of pregnancy, surgical resection remains the optimal therapy.

AORTIC REGURGITATION

The most common etiologies of chronic AR encountered during pregnancy are BAV, RHD, and bioprosthetic valve degeneration.[83] Indications for interventions in patients with AR before pregnancy include severe symptomatic AR or asymptomatic AR with an EF <55% and an LV end-systolic diameter >50 mm or >25 mm/m².[23] Because of the

physiologic decrease in systemic vascular resistance during pregnancy, AR is well-tolerated and the incidence of complications is low. In nonpregnant patients at a high risk of surgery, TAVR for treatment of severe AR has been reported[84,85]; however, current commercially available devices in the United States for AR are considered off-label. Because of technical difficulties and lack of transfemoral-dedicated devices, the results are less favorable compared to AS with a higher risk of device embolization, second valve implantation, and significant residual paravalvular leak.[64,86,87] There have been no reports of TAVR in pregnant women with primarily regurgitant AV disease.

MITRAL STENOSIS

Mitral stenosis (MS) in women in childbearing age is almost exclusively due to rheumatic etiology (**Figure 2**). Other reasons are bioprosthetic valve degeneration, prosthetic valve mismatch, or prosthetic valve thrombosis.[88,89] Although RHD has been nearly eliminated in high-income countries, worldwide rheumatic MS is still a common cause of cardiac maternal morbidity and mortality. In a recent publication from a single center in India, 57% of 681 pregnant women with RHD had MS,[11] and in the ROPAC registry, two-thirds of the 390 women with VHD had MS.[89] The physiologic increase in stroke volume and shortening of diastolic filling period due to increased heart rate in pregnancy result in a rise in left atrial (LA) and pulmonary pressures and often lead to clinical deterioration (**Figure 2**).[90] In the ROPAC registry, 49% of women with severe MS and 32% with moderate MS were hospitalized during pregnancy or early post-partum for HF. The risk of maternal events was higher if women were symptomatic prior to pregnancy; however, maternal mortality was low (0.5%). Severity of MS was also associated with worse fetal outcomes. Cardiac interventions, primarily percutaneous mitral balloon commissurotomy (PMBC), were performed in only 6% of patients with isolated MS.

Asymptomatic patients contemplating pregnancy with mild MS (MV area [MVA] $\geq$1.5 cm^2) usually have favorable pregnancy outcomes,[88] and valve intervention is not indicated. In general, PMBC is preferred over open or closed surgical mitral commissurotomy in the appropriate patients with isolated MS. The patient selection for an intervention prior to pregnancy should follow the guidelines' recommendations and include moderate-to-severe symptoms (NYHA functional class II-IV) due to severe MS (MVA $<$1.5 cm^2) and favorable valve morphology with less than moderate (2+) MR and absence of LA thrombus.[23] Recent guidelines suggest PMBC even in asymptomatic women with severe rheumatic MS if valve morphology is suitable.[23] Other indications for PMBC in asymptomatic severe MS include high thromboembolic risk (history of systemic embolism, dense spontaneous LA contrast, new onset paroxysmal atrial fibrillation [AF]) and increased PA pressure at rest or exercise. Because of the variability between different noninvasive methods of measuring the MVA,[91] when noninvasive estimations of the valve gradient and MVA are inconsistent with one another or with symptoms, exercise testing and invasive hemodynamic assessment should be performed to verify the severity of MS. To prevent MV replacement (MVR) prior to pregnancy, PMBC may also be considered in patients with severe symptomatic MS and with suboptimal valve anatomy (Wilkin's score: 9-12).[92,93] Patients with MS and with concomitant mild-to-moderate AR, AF, or restenosis post-PMBC remain good candidates for PMBC. The management of patients with severe MS prior to pregnancy will minimize or even prevent potential clinical deterioration and reduce pharmacologic or interventional therapy during pregnancy.[94]

Optimal medical management during pregnancy should aim to reduce LA and pulmonary pressures by restricting physical activity and administering β-adrenergic receptor blockers, which are relatively safe and, in general, well tolerated by both the mother and fetus.[95,96] Diuretics can be added, if needed. Because of increased sympathetic activity during gestation, the use of higher beta-blocker doses is usually needed to achieve optimal heart rate control compared with the nonpregnant patients.[97] In patients with AF, digoxin may also be useful and safe during pregnancy for control of ventricular rate.[95] Diuretics should be added if needed.

Women with valvular AF, prior embolic stroke, or LA thrombus should be treated with therapeutic anticoagulation during pregnancy. Because of the risk of embryopathy and fetal loss related to warfarin, the use of low-molecular-weight heparin is preferred during the first trimester. Given the prothrombotic effect of pregnancy and the reported thromboembolic complications in women with MS in sinus rhythm,[98] it is our practice to provide anticoagulation to pregnant women in sinus rhythm with an enlarged left atrium (diameter $>$50 mm or volume $>$60 mL/m^2).

Most patients with moderate-to-severe MS present with increasing symptoms during the late second

trimester or early third trimester.[99] There are no specific recommendations for the timing of PMBC during pregnancy, though performing the procedure after 20 weeks of gestation to reduce risk of radiation injury to the fetus during fetal development is preferred. Moreover, to avoid the risk of extreme prematurity in the case of need for early delivery due to procedural complications, it should be performed preferably during 26 to 30 weeks of pregnancy. PMBC during the third trimester can be technically more challenging, and may increase the risk of maternal complications due to inferior vena caval compression from the large gravid uterus hindering catheter manipulations.

Raoui et al[100] have recently reported PMBC in 246 pregnant women (mean age: 28 ± 5 years) with severe symptomatic MS performed at mean gestational age of 28 ± 4 weeks. The procedural complication rate was 1.8%. One patient developed severe MR, with subsequent cesarean delivery, and underwent MVR post-partum. Two patients died of stroke, and one developed cardiac tamponade. Successful PMBC was associated with improvement in the NYHA functional class to I to II in all patients. Pregnancy reached full term in 95% of the cases with a low fetal morbidity or mortality; spontaneous labor began at 38 ± 1 weeks, and 85% of the women underwent vaginal deliveries with an average birth weight of 2,800 ± 250 g. The results of the procedure during pregnancy were maintained long term and were similar to those of nonpregnant patients. Earlier meta-analysis by Hameed et al[101] also showed comparable results in 515 published cases of PMBC during pregnancy. The mean age was 26 ± 6 years; the gestational age was 25 ± 6 weeks; the baseline MVA was 0.9 ± 0.3 cm^2 and increased to 2.0 ± 0.4 cm^2 after the procedure. The MV gradient was reduced from 23 ± 9 mmHg to 6 ± 4 mmHg, and the systolic PA pressure was reduced from 61 ± 23 mmHg to 40 ± 16 mmHg. The reported rate of complications was low but included cardiac tamponade, excessive blood loss, transient AF, worsening MR, systemic embolization, initiation of uterine contractions, and precipitous labor. The rate of maternal mortality was 0.2%, and fetal loss was 2%. The fluoroscopy time ranged between 3.6 ± 3.2 minutes and 21 minutes with an average of 8.5 ± 7.3 minutes.

Recent publications have reported normal growth and development of children born to women who underwent PMBC during pregnancy.[100] Gulraze et al[102] reported on a mean follow-up of 10 ± 5 years in 23 children of women who underwent PMBC during the second trimester; all exhibited normal growth and development. Similarly, Raoui et al[100] reported follow-up of up to 4 years in over 240 children born after PMBV during pregnancy who showed growth and intellectual development comparable to children of the same age. Seventeen-year retrospective follow-up also showed no radiation-related developmental or other injuries.

In summary, extensive experience with PMBC suggests that this procedure can be performed effectively and safely during pregnancy with excellent short- and long-term results. The main concern is fetal exposure to radiation that can be minimized with the use of echocardiography.

In women with degenerative bioprosthetic valves presenting as symptomatic severe MS in pregnancy, there are case reports of transcatheter MV implantation (**Table 4**).[57,103,104] All cases presented between 20 and 22 gestational weeks with symptomatic severe MS secondary to the deteriorated bioprosthetic valve. One of these patients had an additional severely stenotic aortic bioprosthetic valve, who underwent successful concomitant, transcatheter double balloon-expandable VIV implantations through the left ventricular apical route with significant reduction of both transmittal and transaortic pressures (**Table 4**). The total duration of fluoroscopy was just 3 minutes and 6 seconds. The other 2 patients had a successful transfemoral, transseptal valve implantation of a balloon-expandable valve within the MV prosthesis without complications. Postprocedurally, patients were treated with low-molecular-weight heparin through the remaining pregnancy. This limited experience is encouraging and suggests that transcatheter MV implantation can be a promising alternative to surgery during pregnancy in severely symptomatic patients with failed mitral bioprosthesis.

In summary, PMBC when performed prior to pregnancy in patients with severe MS can prevent hemodynamic and symptomatic deterioration during pregnancy and need for premature deliveries. This procedure can be performed effectively with a low risk of complications during pregnancy but should be reserved for patients with hemodynamic deterioration despite medical care.

MITRAL REGURGITATION. Most common etiologies of chronic MR in young women are RHD, myxomatous degeneration, and bioprosthetic valve degeneration.[83] Women with MR who contemplate pregnancy should undergo surgical intervention prior to conception if they meet guideline Class I recommendations with symptoms related to severe MR or LV systolic dysfunction (LVEF <60%, LV end-systolic diameter >40 mm) in asymptomatic patients.[23] To

TABLE 4 Mitral Valve-in-Valve Procedures During Pregnancy

First author	Ribeyrolles et al[103]	Chengode et al[a 57]	Johnson et al[104]
Patient age (y)	28	34	32
GA at procedure (wk)	20	22	N/A
Type of the bioprosthetic valve	29 mm Pericarbon Sorin	27 mm CE Perimount MAGNA	29 mm CE Perimount Magna
Age of prior intervention (y)	23	26	23
Reasons for intervention	Acute pulmonary edema	NYHA class III HF	DOE, palpitations
Mean gradient before procedure by TTE (mmHg)	26	15	18 (invasive: 20)
MVA before procedure (cm^2) by TTE	0.67	0.8	N/A
Degree of MR	N/A	N/A	None
PASP (mmHg)	N/A	N/A	68
LV/RV function	Normal	Normal	RV systolic dysfunction
Imaging modality	TEE, CT, Fluoro	TEE, Fluoro	CT, Fluoro, 3D-TEE
Type of valve	N/A	29-mm Sapien XT	29-mm Sapien 3
Fluoroscopy time (min)/fetal exposure (mGy)	20 mGy	3.06 min	60 min
Mean gradient post-procedure (mmHg)	6	5	1.5
MVA post-procedure (cm^2)	N/A	N/A	N/A
Procedural complications	None	Dehiscence of the old mitral valve leaflet	None
Meds post-procedure	LMWH during pregnancy; warfarin post-delivery	ASA 81 mg/d; LMWH 80 mg SQ/d until time of admission for delivery	N/A
Delivery mode	Planned CS	Vaginal	Vaginal
GA at delivery (wk)	Full term	Full term	30
Maternal complications	None	None	None
Fetal complications	None	None	SGA (1,290 g)

[a]Transcatheter aortic and mitral double valve-in-valve implantation through left ventricular apical approach.

3D = 3-dimensional; ASA = aspirin; CS = cesarean section; CT = computed tomography; DOE = dyspnea on exertion; Fluoro = fluoroscopy; GA = gestational age; HF = heart failure; LMWH = low-molecular-weight heparin; LV = left ventricle; MR = mitral regurgitation; MVA = mitral valve area; NA = information not available; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RV = right ventricle; SGA = small for gestational age; SQ = subcutaneous; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

prevent premature valve replacement, CPET for functional capacity assessment and hemodynamic exercise testing using Doppler echocardiography are recommended in patients with symptoms that may be attributable to MR. Although noninvasive imaging is adequate for evaluation of MR in most cases, invasive hemodynamic evaluation may be necessary in some, especially when there is a discrepancy between symptoms and noninvasive testing.[17]

Because of physiological decrease in systemic vascular resistance during pregnancy, the volume overload of pregnancy is well-tolerated in patients with chronic MR and normal LV function.[94] Recent reports from the ROPAC registry and the Cardiac Disease in Pregnancy database have provided pregnancy outcome information in high-risk patients with MR.[15,89] In the ROPAC registry, 65 patients had isolated moderate-to-severe rheumatic MR. A substantial number of these patients had indications for interventions prior to pregnancy, including history of HF in 20% and PHT in 32%. Mortality due to cardiogenic shock at 39 weeks was reported in one patient with severe MR with normal LV function pre-pregnancy, and one patient required MVR at 10 weeks of gestation. HF occurred in 17% of women with MR compared to 32% of women with MS. Multivariate analysis showed right ventricular (RV) systolic pressure >30 mmHg and severity of MR to be predictive of adverse cardiac events. Despite the high incidence of complications, all patients were treated medically without interventions; the median pregnancy duration was normal at 39 weeks, and the fetal outcome was not affected. Pfaller et al[83] also reported outcomes of pregnancy in 145 women with MR of various etiologies. There was one cardiac death and one cardiac arrest, 11% developed HF, and 3% (n = 4) required interventions. The highest risk of HF was in women with multivalvular lesions, LV dysfunction, and PHT.

In summary, women with MR and normal LV function without PHT and history of cardiac events prior to pregnancy are at a low risk of cardiac complications during pregnancy. Women with severe chronic MR who have high-risk features are at an increased risk of cardiac events, primarily HF. Most of these patients, however, can be treated medically, and emergent surgical valve intervention is rare. The intra-aortic balloon pump has been used successfully in conjunction with medical therapy to stabilize patients with severe HF in pregnancy and can be used in the uncommon patients with MR and severe hemodynamic deterioration to achieve hemodynamic

TABLE 5 Reports of PBPV During Pregnancy

First author	Oylumlu et al[112]	Johny et al[113]	Sener et al[114]
Patient age (y)	32	34	23
GA at procedure (wk)	28	31	34
Type of valve	Congenital	Congenital	Congenital
Age at prior intervention (y)	None	PBPV at the age of 26 y during the first pregnancy (second trimester)	None
Reason for intervention	Exertional chest pain, mild dyspnea	NYHA class III HF	NYHA class II HF
Peak gradient before valvuloplasty (mmHg)	126 (TTE)	192 (invasive)	122 (TTE)
Degree of regurgitation	None	N/A	None
RV function	Normal	Normal	RV dilatation, RV hypertrophy
Imagining modality	Fluoroscopy	Fluoroscopy	Fluoroscopy
Fluoroscopy time (min)	N/A	N/A	N/A
Peak gradient post valvuloplasty (mmHg)	37 (peak instantaneous)	120 (peak-to-peak)	48 (peak instantaneous)
Procedure complications	None	Mild hypotension with uterine contractions for 30 mins	None
Delivery mode	N/A	CS	CS
GA at delivery (wk)	N/A	36	Full term
Maternal complications	None	None	None
Fetal complications	None	None	None

CS = cesarean section; GA = gestational age; HF = heart failure; min = minute; N/A = information not available; NYHA = New York heart association; PBPV = percutaneous balloon pulmonary valvuloplasty; RV = right ventricle; TTE = transthoracic echocardiography.

stabilization and delay time of delivery to allow fetal maturity.[105,106]

Several catheter-based therapies have been introduced recently targeting patients with severe MR, particularly the transcatheter edge-to-edge MV repair.[107] There have been, however, no reported cases describing the use of this technique during pregnancy. In addition, transcatheter MV replacement has emerged as a nonsurgical approach for the treatment of MR, and several devices are under clinical investigation.[108] These devices may present a less invasive approach and an alternative to surgery during pregnancy in the future for women with severe MR and HF not responding to medical therapy.

PULMONIC STENOSIS

Pulmonic stenosis (PS) during pregnancy is usually due to congenital valve stenosis. Other causes are stenosis of the pulmonary homograft as part of Ross procedure or RV to PA conduit (RVPAC) stenosis.

PERCUTANEOUS BALLOON PULMONIC VALVULOPLASTY. Women who meet criteria for intervention (symptomatic moderate or severe stenosis, peak instantaneous gradient >36 mmHg) should have percutaneous balloon pulmonic valvuloplasty (PBPV) before conception.[77] Surgical repair should be reserved to severely symptomatic patients when the valve is not amenable to PBPV. Similarly, in symptomatic patients with severe pulmonary regurgitation with RV dilation or RV dysfunction, pulmonary valve replacement is recommended before conception.[77]

Patients with PS and normal RV, including those with severe stenosis, usually tolerate the hemodynamic changes of pregnancy well.[109-111] For this reason and because the performance of PBPV during pregnancy may impact unfavorably on fetal well-being secondary to radiation exposure and potential intraprocedural hemodynamic instability, intervention can usually be postponed to after the delivery. There have been a number of reports of PBPV during pregnancy mostly in women with very severe PS. Presbitero et al[111] briefly described successful PBPV during pregnancy in 2 women with supra-systemic RV pressures and one who had combined PMBC and PBPV. Detailed information on 3 additional cases is shown in **Table 5**.[112-114] Chest pain and HF were the main indications for PBPV in these cases which was performed in the third trimester. The transpulmonary peak pressure prior to procedure was 122 to 192 mmHg and was markedly reduced in 2 patients. A high residual gradient was reported in one patient which was theorized to be due to infundibular hypertrophy caused by long-standing pulmonic valve stenosis. The same patient developed mild hypotension during the procedure with uterine contractions for 30 minutes.[112-114]

PERCUTANEOUS PULMONIC VALVE IMPLANTATION. Unlike isolated valvular PS with normal RV function, pulmonary conduit or homograft stenosis and RV dysfunction in women with complex congenital heart disease and prior Ross procedure can have detrimental effects on both maternal and fetal outcomes. In severely symptomatic patients or in cases where

TABLE 6 Pulmonic Valve Implantation During Pregnancy

First author	Detzner et al[115]	Ormerod et al[116]
Patient age (y)	20	21
GA at procedure (wk)	13	23
Type of conduit	22-mm Contegra conduit RV-PA	19-mm homograft conduit RV-PA
Age at prior intervention	12	3
Reason for intervention	NYHA class II HF, with concern for worsening symptoms during pregnancy	Asymptomatic but fetal IUGR
Peak gradient before procedure (mmHg)	42	23
Valve area before procedure (cm^2)	N/A	N/A
Degree of PR	Moderate	Severe
RV pressure (mmHg)	70/18	72/15
RV function	Normal	Normal
Imagining modality	Low frame rate fluoro	MRI, Fluoro, Cine
Type of valve	22-mm Melody	22-mm Melody
Fluoroscopy time (min)	N/A	N/A
RV pressure/PV gradient post-procedure (mmHg)	RV 44/13; PV 7	RV 76/12; PV 27 (trivial PR)
VA post-procedure (cm^2)	N/A	N/A
Procedural complications	None	None
Meds post-procedure	N/A	N/A
Delivery mode	N/A	CS
GA at delivery (wk)	30 + 6	32
Maternal complications	None	Pre-eclampsia
Fetal complications	Dichorionic twins	SGA (1,500 gm)

Cine = cineangiography; CS = cesarean section; Fluoro = fluoroscopy; GA = gestational age; HF = heart failure; IUGR = intrauterine growth restriction; meds = medications; MRI = magnetic resonance imaging; N/A = information not available; NYHA = New York Heart Association; PA = pulmonary artery; PR = pulmonic regurgitation; PV = pulmonary valve; RV = right ventricle; SGA = small for gestational age; VA = valve area.

fetal health may be affected, percutaneous pulmonic valve implantation (PPVI) may be considered. Published information is limited to 2 cases (Table 6), the first by Detzner et al[115] who reported a successful PPVI at 13 weeks of twin pregnancy in a mildly symptomatic 20-year-old patient with RVPAC obstruction and regurgitation. PPVI was performed to prevent possible worsening HF as pregnancy progressed. The

TABLE 7 Percutaneous Tricuspid Valvuloplasty During Pregnancy

	Gamra et al[118]	Bahl et al[119]	Malpani et al[120]	Savas et al[37]
Patient age (y)	27	22	24	22
GA at procedure (wk)	19	23	22	22
Type of valve	Rheumatic	Rheumatic	Rheumatic	Rheumatic
Other interventions (y)	PBMC at the age of 25 y	Simultaneous PBMC	Simultaneous PBMC	N/A
Reasons for intervention	Threatened third miscarriage (with a history of repeated miscarriages)	NYHA class III	NYHA class IV	Progressive dyspnea, fatigue
Mean TV gradient pre-valvuloplasty (mmHg)	8	12	6	8
TVA before procedure (cm^2)	0.8 (TTE)	N/A	1.0 (TTE)	0.9 (invasive)
Degree of TR	Trivial	N/A	Moderate	None
RV function	Normal	N/A	Normal RV	Normal
Imagining modality	Fluoroscopy, TTE	Fluoroscopy, TTE	Fluoroscopy, TTE	Fluoroscopy. TTE
Type of balloon	Double balloon	Inoue Balloon	Inoue	Double balloon
Fluoroscopy time (min)	10	0.3	N/A	N/A
Mean gradient post-valvuloplasty (mmHg)	4	3	N/A; RAP 5	5 (invasive)
TVA post-procedure (cm^2) by TTE	2.2	N/A	2.1	1.0
Procedure complications	None	None	None	None
Delivery mode	Vaginal	Vaginal	N/A	N/A
GA at delivery (wk)	Full term	Full term	Full term	N/A
Maternal complications	None	None	None	None
Fetal complications	None	SGA (2000 g)	None	None

GA = gestational age; N/A = information not available; NYHA = New York Heart Association; PBMC = percutaneous balloon mitral commissurotomy; RAP = right atrial pressure; RV = right ventricle; SGA = small for gestational age; TR = tricuspid regurgitation; TTE = transthoracic echocardiography; TV = tricuspid valve; TVA = tricuspid valve area.

TABLE 8 Tricuspid Valve-in-Valve During Pregnancy

First author	Adejumo et al[121]
Patient age (y)	36
GA at procedure (wk)	23
Type of valve	29 CE Perimount 6900
Age of prior intervention	21
Symptoms	NYHA class III-IV
Mean gradient pre-procedure (mmHg)	15
Valve area pre-procedure (cm^2)	N/A
Degree of TR	Moderate
Right ventricular function	RV dysfunction
Imagining modality	Fluoroscopy, TEE
Type of valve	29-mm Sapien 3
Fluoroscopy time (min)	N/A
Mean gradient post-procedure (mmHg)	2
Procedural complications	None
Delivery mode	Vaginal
GA at delivery (wk)	37
Maternal complications	None
Fetal complications	SGA (2,000 g)

GA = gestational age; N/A = information not available; NYHA = New York Heart Association; RV = right ventricle; SGA = small for gestational age; TEE = transesophageal echocardiography; TR = tricuspid regurgitation.

procedure resulted in a significant reduction in the gradient across the RVPAC; however, the pregnancy course was complicated by intrauterine fetal demise of one of the twins at 23 weeks and preterm delivery at 31 weeks. The second patient was a 21-year-old woman with a history of pulmonary atresia and a 19-mm valved homograft RVPAC which was found during pregnancy to be degenerated with PS and severe regurgitation.[116] She underwent successful Melody valve implantation at 23 weeks' gestation. Although the patient was asymptomatic, the procedure was performed for possible deterioration later in her pregnancy and the theory that the fetus who had growth retardation could benefit from increase in cardiac output. The procedure did not result in a decrease in the RV outflow gradient but was followed by improvement in RV size and function and increase in systemic blood pressure. Despite these changes, preterm delivery at 32 weeks ensued with a very low birth weight of 1.5 kg.

In contrast to pulmonary conduit or homograft stenosis, RV outflow failure with predominantly regurgitation is usually well tolerated and is rarely an indication for PPVI during pregnancy.

In summary, valvular PS with normal RV function is usually well tolerated in pregnancy, and PBPV is not required and can be delayed and be performed after the delivery. More information is needed to determine the indications and maternal and fetal effect of PPVI in women with RVPAC obstruction.

TRICUSPID STENOSIS

Tricuspid stenosis (TS) is rare and found in <1% of patients with RHD combined with MS, with or without concomitant AS, or in patients with prosthetic valve degeneration.[117,118] The information on catheter-based interventions in patients with rheumatic TS in pregnancy is anecdotal, and criteria for the indications for this procedure have not been well established. Percutaneous tricuspid valvuloplasty has been reported in 4 patients, one combined with PMBC, performed in the second trimester in all patients (**Table 7**).[37,118–120] The reason for the procedure was symptomatic deterioration in 3 patients and an attempt to prevent a threatened miscarriage in one. The transvalvular mean gradient prior to the procedure ranged between 8 and 12 mmHg. All procedures were uncomplicated, and full-term deliveries were reported in 3 patients.

A recent report by Adejumo et al (**Table 8**)[121] described a 36-year-old woman with 2 miscarriages and one prior termination who presented at 18 weeks' gestation with symptoms of progressive NYHA functional class III to IV HF and severe bioprosthetic TS and moderate tricuspid regurgitation. The patient had a prior tricuspid valve replacement with the 29-mm Carpentier-Edwards 6900 Perimount Plus pericardial valve (Edwards Life Science, Irvine, California) due to endocarditis. At 23 weeks, the patient underwent fluoroscopy and TEE-guided VIV placement of a 29-mm Edwards Sapien 3 valve, resulting in a reduction of the transvalvular gradient from 15 to 2 mmHg without tricuspid regurgitation and an increase in CO from 3.3 to 5.3 L/min.

Based on this limited information, this approach may be considered in the rare pregnant patient with prosthetic tricuspid degeneration unresponsive to medical therapy and when fetal health is in jeopardy.

SUMMARY AND CONCLUSIONS

Mechanical interventions may be needed in pregnant patients with severe VHD to prevent or treat hemodynamic deterioration which can lead to maternal morbidity and even mortality as well as fetal prematurity and complications. Valve replacement with a mechanical prosthesis prior to pregnancy is associated with increased thrombotic and bleeding complications during pregnancy as well as a risk for

warfarin-related fetal embryopathy and fetal loss. Bioprosthetic valves in young women are associated with early deterioration and possibly require multiple future interventions. Cardiac surgery during pregnancy is associated with high rates of nonpreventable fetal loss. Catheter-based percutaneous interventions can provide an alternative therapy to surgery prior to and during pregnancy. These techniques, however, are associated with the risk of ionizing radiation to the fetus and mother, mechanical complications, suboptimal results, and short- as well as long-term consequences. In addition, there are still uncertainties about absolute indications for interventions and a need for standardization of approach and more data accrual. For these reasons, transcatheter interventions should be considered only in severely symptomatic patients refractory to medical therapy when symptoms are clearly related to hemodynamic deterioration. Decisions should be made by a multidisciplinary cardio-obstetrics valve team with cardiologists experienced in cardio-obstetrics, VHD, advanced imaging, and structural cardiology along with high-risk maternal fetal medicine, anesthesiology, cardiac surgery, and neonatology, with support by nursing and social work at a comprehensive care center.

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ADDRESS FOR CORRESPONDENCE: Dr Uri Elkayam, Division of Cardiovascular Medicine, USC School of Medicine, 2020 Zonal Avenue, Room 331, Los Angeles, California 90033-1034, USA. E-mail: elkayam@usc.edu. Twitter: @uelkayam.

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