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Management of high risk cardiac conditions in pregnancy: Anticoagulation, severe stenotic valvular disease and cardiomyopathy☆

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ABSTRACT

Cardiovascular disease contributes to approximately one third of all maternal mortality and remains a significant source of peri– and postpartum morbidity. As more women at risk for and with cardiovascular disease are desiring pregnancy, it is imperative that general cardiologists and obstetricians participate collaboratively in preconception counseling and are more facile with management of these lesions during peri– and postpartum periods. This review aims to address this growing need and highlights the management strategies for some of the major high risk cardiac conditions encountered during pregnancy including anticoagulation, cardiomyopathies as well as severe mitral and aortic stenosis; aortopathy, pulmonary hypertension, and severe congenital heart lesions will not be addressed.

Introduction

Once the most feared cause of death in young women, maternal mortality has declined dramatically in the 20th century from 50 per 100,000 live births in 1950 to 10 per 100,000 live births in 1984 [1]. Unfortunately, since 1987, we have seen a rise in pregnancy-related mortality up to a present rate of 17 per 100,000 live births (Fig. 1). Cardiovascular disease (CVD) contributes to approximately 1/3 of all maternal mortality [2]. Among cardiac conditions in pregnancy, an analysis of pregnancy-related mortality in the United States from 1987–2010 found that rates of cardiomyopathy and general cardiovascular conditions were rising, while hypertensive diseases were declining. As women are increasingly delaying childbearing or utilizing assisted reproductive technologies, the rates of cardiovascular complications during pregnancy are unsurprisingly rising [3]. Finally, with the improvement in the care of congenital heart disease (CHD) and childhood cancers, more women with CHD or women who have undergone treatment for cancer are surviving into adulthood and desiring pregnancy, introducing further complexity to the care of pregnant women today [4]. As more women with CVD are desiring pregnancy, it is imperative that general cardiologists and obstetricians become more expert in the management of high risk lesions during pregnancy. This review aims to address this growing need and highlights the management strategies for some of the major high risk cardiac conditions encountered during pregnancy; aortopathy and pulmonary hypertension will not be addressed.

Hemodynamics of normal pregnancy (Fig. 2)

During pregnancy

Pregnancy is a vulnerable time for women with preexisting cardiac disease and may unmask undiagnosed conditions. Cardiac output increases by 30–50%, marked by a 40% increase in plasma volume initially followed by an increase in heart rate by up to 15–20% by the third trimester. Late third trimester, cardiac output begins to fall largely due to uterine compression of the IVC and aorta (reducing preload and afterload), but does not return to baseline values until 2–4 weeks postpartum. Systemic vascular resistance (SVR) and mean arterial pressure decrease early in pregnancy by 30–50% due in large part to effects of the development of the low resistance placental circulation and endogenous vasodilators. Finally, there is an increase in circulating plasma volume relative to erythrocyte mass resulting in a physiologic anemia, reducing blood viscosity and promoting placental arterial perfusion [5].

During labor

Cardiac output increases steadily during labor (15–20% early, 50% during active labor, and up to 80% postpartum). Pain, blood

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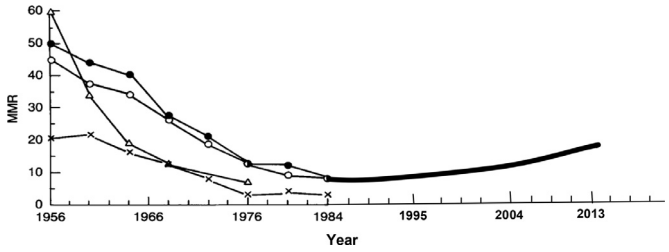

Fig. 1. Maternal Mortality Trend from 1956 to 2013. Composite of Maternal Mortality Rates (MMR, number per 100,000 live births) from 1956 to 1984 (NEJM 1987; 316(11): 667–72) modified to include contemporary MMR from Trends in Pregnancy Related Mortality in the U.S. from 1987–2013 (CDC). Open circles: rate reported by NCHS for the US (death within 42 days postpartum); triangles: Swedish rate; closed circles: maternal mortality in Massachusetts reported by the Maternal Mortality Committee (death within 90 days postpartum); X's: maternal mortality in Massachusetts reported by the National Center for Health Statistics (death within 42 days postpartum).

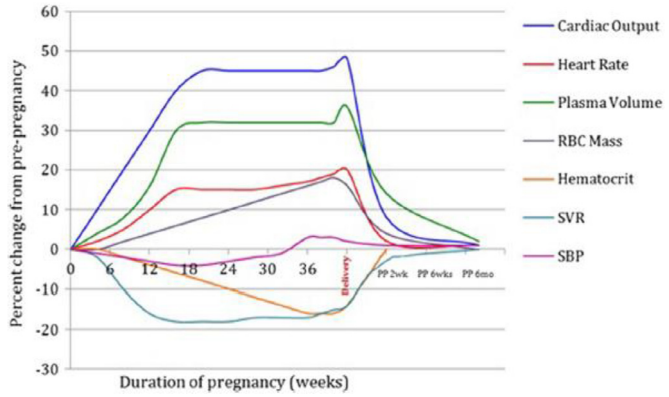

Fig. 2. Physiologic adaptations in normal pregnancy. An increase in plasma volume and heart rate leads to a 30–50% increase in cardiac output. There is physiological anemia due to a larger rise in plasma volume than the red blood cell mass. Systolic blood pressure remains mostly unchanged due to a decrease in systemic vascular resistance. All major changes occur in the early second trimester and begin to normalize within 24–48 h and mostly return to baseline within 2 weeks post-delivery. *RBC* – red blood cell, *SBP* – systolic blood pressure, *SVR* – systemic vascular resistance, *PP* – postpartum. *Reprinted with permission from Evin Yucel. (Yucel E, DeFaria Yeh D. Curr Treat Options CV Med. 2017;19(9):73).*

loss, uterine contractions, and Valsalva contribute to the hemodynamic shifts during the labor process. Uterine contractions and pain can effectively increase the central venous pressure by approximately 15 mmHg, the pulmonary capillary wedge pressure by approximately 11 mmHg, arterial blood pressure up to 20 mmHg, and stroke volume by 300–500 mL per contraction, while a combination of blood loss and Valsalva transiently reduce preload at the time of labor [6,7].

Delivery & postpartum period

The transient reduction in preload during labor is immediately offset by an acute rise in preload following delivery due to autotransfusion of the placenta, relief of IVC compression, and a relatively steep increase in SVR. Most of the hemodynamic changes including increase in cardiac output, stroke volume, heart rate, and SVR will resolve by 2 weeks after delivery, but the cardiovascular system does not return to pre-pregnancy baseline until 6 months postpartum [8,9].

Anticoagulation in pregnancy

Pregnancy is a period of marked hypercoagulability resulting from the combination of increase in coagulation factors, decrease in natural anticoagulant mechanisms, and inhibition of fibrinolysis. The highest thrombotic risk occurs postpartum, and the risk does not return to baseline levels until 12 weeks postpartum. Populations at risk for thrombosis during pregnancy include women with prosthetic heart valves, venous thromboembolism, and thrombophilias. We will limit our discussion to the management of prosthetic heart valves.

Prosthetic valves & valve thrombosis: vitamin K antagonism

Pregnant women with prosthetic heart valves experience higher rates of thrombosis and thromboembolism, threatening the safety of both mother and fetus [10]. Selection of anticoagulation during pregnancy is challenging, and data are limited to guide our management strategies. Insights have come largely from systematic reviews and meta-analyses given the challenges of conducting randomized trials in the pregnant population. In 2016, Xu et al. meta-analyzed 51 studies comprising 2113 pregnancies in 1538 women with mechanical heart valves [11]. The authors looked at 4 anticoagulant strategies: (1) vitamin K antagonist (VKA) throughout pregnancy, (2) low molecular weight heparin (LMWH) throughout pregnancy, (3) LMWH or unfractionated heparin (UFH) during the first trimester followed by VKA (H/VKA), and (4) UFH throughout pregnancy. The VKA only regimen demonstrated the best maternal outcomes (maternal thromboembolic event: 2.79% in VKA only; 7.42% in H/VKA regimen, 4.42% in LMWH only, and 29.9% in UFH only) but also demonstrated the highest risk of fetal adverse events (2.13% warfarin vs. 0.74% in H/VKA and 0% in both LMWH and UFH heparin groups). In a subgroup analysis of high dose VKA versus low dose VKA (<5 mg/day), the risk of warfarin embryopathy was significantly higher in the high dose VKA group but there was no difference in maternal outcomes. Furthermore, when comparing low dose VKA to alternative strategies, there was no difference in adverse fetal outcomes between low dose VKA and LMWH or UFH only strategies and was favorable to the H/VKA regimen. These findings have been confirmed in contemporary analyses [12,13].

Overall, maternal risk appears to be lowest with VKA monotherapy and fetal risk is best mitigated with LMWH. Strategies that reserve VKA after embryogenesis did not appear to significantly mitigate fetal risk and did increase maternal risk as compared to VKA monotherapy. Low dose VKA has emerged as a potential therapeutic option for pregnant women requiring anticoagulation but data still demonstrates residual risk of adverse fetal events even on warfarin doses < 5 mg/day [14]. Owing to these data, the 2014 AHA/ACC) guidelines now recommend warfarin at doses ≤ 5 mg/day throughout pregnancy for women with mechanical heart valves, even considered reasonable during the first trimester. However, many expert centers recommend LMWH with peak and trough testing as the anticoagulant of choice given the nonzero rates of fetal adverse events with low dose VKA [15].

Low molecular weight heparin (LMWH)

Monitored LMWH has now emerged as the anticoagulant of choice for some high-risk pregnancy centers despite AHA/ACC guidelines advocating the use of low dose warfarin. LMWH does not cross the placenta, and is therefore safe for the fetus in pregnancy. Because there is a dramatic increase in GFR, particularly in the second trimester through the postpartum period, careful dose adjustment must be routinely checked to ensure therapeutic anticoagulation. Historically, only peak anti-Xa peak levels were monitored (recommended to be checked 4–6 h after dose administration), but a study of 30 pregnant women receiving LMWH found that while peak anti-Xa levels were mostly in the therapeutic range (1.0−1.2 U/mL), trough levels were subtherapeutic (< 0.6 U/mL) in more than half of the measurements [16]. As such,

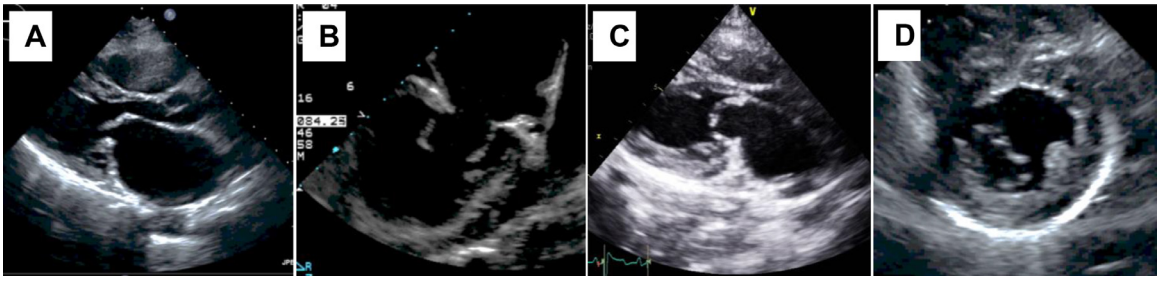

Fig. 3. Mitral stenosis in pregnancy. A: Rheumatic mitral stenosis with classic hockey stick deformity, B: Supravalvular mitral ring with restriction at the leaflet base and then wide opening at the leaflet tips, C, D: Long and short axis views of parachute mitral valve with convergence of subchordal apparatus to a single papillary muscle. Mitral valvuloplasty can be performed in rheumatic mitral stenosis, but is not feasible for patients with supravalvular mitral ring or parachute mitral valve.

we recommend that both peak and trough anti-Xa levels are monitored for pregnant women.

Alternative anticoagulants

At the time of delivery, women taking LMWH should be transitioned to UFH to bridge through the intrapartum and postpartum period to maximize the opportunity for neuroaxial anesthesia. The American College of Obstetricians and Gynecologists recommends waiting 24 h prior to neuroaxial blockade for women taking therapeutic LMWH, 12 h for UFH with doses > 10,000 IU/day, and 4–6 h for prophylactic doses of UFH with doses < 5000 IU/day. Despite the advantages of UFH in the partum period, LMWH is otherwise preferred to UFH given risk of heparin induced thrombocytopenia, osteopenia, and less reliable absorption. Its long half-life is attractive but it must be discontinued by the late third trimester to maximize the opportunity for neuroaxial anesthesia peri–delivery.

Direct oral anticoagulants (DOACs), rivaroxaban, dabigatran, and apixaban, are widely available in routine practice, but the experience in pregnancy is extremely limited. DOACs are known to cross the placenta, but effects on maternal and fetal outcomes are uncertain. In a German registry of 37 pregnancies with exposure to rivaroxaban, there were 62.2% live births, 21.6% elective terminations, and 16.2% spontaneous abortions [17]. Rivaroxaban was discontinued in all but one woman in the first trimester. A 2016 systematic review of DOAC use in 233 pregnancies found 48.9% live births, 22.6% miscarriages, and 28.5% elective terminations. Among live births, birth abnormalities occurred in 5.1% of cases but only 3 cases (2%) could be interpreted as embryopathy [18]. Of note, the overall prevalence of all major birth defects in the US is 3% [19]. While meaningful conclusions cannot be extrapolated from these limited data, DOACs are presently not recommended for use in pregnancy.

Mitral stenosis

Mitral stenosis (MS) is an important source of maternal morbidity and mortality worldwide. Rheumatic disease is responsible for most cases, although congenital MS occurs as well (Fig. 3). Indeed, 67% of women with severe MS develop a maternal cardiac event during their pregnancy. The most common maternal complications include pulmonary edema, atrial tachyarrhythmias, thromboembolism, and even, death [20]. If unrecognized, MS in pregnancy can be destabilizing and even fatal. In a study of 1000 pregnant women followed from 1989 to 1999, 88 women had MS, and among them, 8 died of cardiac complications [21]. A small study of 46 pregnant women with MS found maternal mortality rates up to 34%. Fortunately, more contemporary studies demonstrate more favorable mortality rates. In the ROPAC registry of 1321 pregnant women worldwide between 2007 and 2011, there were 13 maternal deaths; 4 were attributed to MS [22]. Contemporary registries of pregnant women with MS in North America and Europe have no documented maternal deaths related to MS [23].

Cardiac complications of MS in pregnancy are still common, particularly with increasing severity of stenosis. In a contemporary North American registry of 46 pregnancies with MS, risk of maternal and fetal complications rose with increasing severity of MS [23]. Compared to mild MS, women with severe MS had markedly increased risk of heart failure (HF) (78% in severe vs. 11% in mild), arrhythmias (33% vs. 0%), and hospitalizations (78% vs. 11%). Risk of adverse fetal outcomes were also stratified by severity of MS. Preterm delivery (44% vs. 5%), fetal growth restriction (33% vs. 16%), and stillbirth (11% vs. 0%) rates were all increased in severe MS.

Women with MS contemplating pregnancy should always be referred to a tertiary care center with expertise in cardio-obstetrics. Patients with moderate MS should be advised that pregnancy is high risk and will require careful monitoring throughout pregnancy. Given the high risk of maternal and fetal outcomes, women with severe MS should be advised against pregnancy until their condition has been optimized by appropriate surgery such as percutaneous balloon mitral valvuloplasty (PBMV) if rheumatic MS with favorable anatomy or mitral valve replacement if congenital MS or unfavorable rheumatic anatomy. For patients with severe asymptomatic MS prior to pregnancy, expert consensus recommends PBMV if favorable anatomy [15].

During pregnancy, the medical management of MS largely involves careful diuresis, rhythm and rate control if atrial arrhythmias develop, and anticoagulation. Beta-blockers are the pharmacologic agent of choice for heart rate control in pregnant women with MS, however dose escalation is often required during pregnancy due to accelerated metabolism. Some investigators have published data suggesting that the use of beta-blockers in pregnancy contributes to fetal growth restriction, but in the absence of randomized controlled trials, this remains controversial [24,25]. Restricted activity is also recommended for pregnant women with severe MS but supporting evidence is limited. In cases of severe symptomatic MS refractory to medical therapy, intrapartum valve intervention is necessary. Valvuloplasty via PMBV is the favored intervention for pregnant women with severe MS and favorable anatomy. The success rate of PBMV is near 100% and on average, improved the MVA from 0.7–1.2 cm^2 to 1.7–2.2 cm^2 [26]. Complications are rare but include tamponade, hemorrhage, worsened mitral regurgitation (MR), atrial fibrillation (AF), and systemic embolization, as well as fetal compromise due to radiation exposure. Surgical valve replacement is reserved for the most severe cases that are unsuitable for PBMV. In a series of 45 women with severe MS, fetal mortality in the PBMV group was 4.8% as compared to 38% in the surgical group, and there was 1 maternal death in the PBMV group in contrast to 8 deaths in

the open surgical group [27]. In a series of 161 pregnant women, mitral valve surgery during pregnancy was associated with 9% maternal mortality and 29% fetal or neonatal mortality [28].

Aortic stenosis

Unlike MS, isolated aortic stenosis (MS) in pregnancy is generally better tolerated, but still associated with a high rate of adverse outcomes [29]. Most cases of AS in pregnancy are a result of congenital bicuspid aortic valve but rheumatic disease is also common outside the US. Complications include HF, tachyarrhythmias, and pulmonary edema. A 2016 analysis of 96 women with moderate to severe AS from the ROPAC registry found that 20.8% were admitted to the hospital for cardiac reasons [30]. Women with severe AS were significantly more likely to be hospitalized during their pregnancy (35.3% in severe AS vs. 12.9% in moderate AS, $p = 0.02$); indeed, severe symptomatic AS had the highest rates of cardiac hospitalization (42.1%). Most cases of cardiac admissions were related to worsening HF or arrhythmias. Only 2 patients required intervention beyond medical therapy: one patient with previously undiagnosed critical AS (peak and mean gradients 156 mmHg and 71 mmHg) underwent aortic valvuloplasty and the second patient underwent mechanical aortic valve replacement due to aortic valve endocarditis. Importantly, there were no cases of maternal death in this series at 7 day post partum follow up. Fetal and obstetric outcomes were also impacted. When compared to moderate AS, severe AS was associated with shorter median pregnancy durations and higher rates of Cesarean section (75.0% vs. 48.3%, $p = 0.008$). Preterm birth and low birth weight were more common in women with severe AS compared to moderate AS. In a multivariable analysis, severity of AS and peak aortic gradient were identified as independent predictors of maternal hospitalization, low birth weight, and small for gestational age neonates. While AS in pregnancy is not generally a fatal condition, it is associated with significant morbidity. Of note, 50% of women already had a diagnosis of symptomatic AS, an indication for AVR, prior to pregnancy, underscoring the need for improved preconception counseling in women with underlying structural heart disease.

While fatality rates for AS in pregnancy are exceedingly low, there have been rare case reports of sudden death occurring in pregnant women with AS [31]. When examining these maternal deaths, most of the women have a concomitant diagnosis in addition to severe AS, such as pulmonary hypertension; maternal death in isolated severe AS is extremely rare.

The management of AS in pregnant is predicated on beta blockade, diuresis, and restriction of activity to maintain normal intracardiac filling pressures. For intractable HF, percutaneous valvuloplasty can be considered [32]. In very rare cases, surgical AVR can be considered, but the rate of fetal mortality due to cardiopulmonary bypass is high (30–40%). Following pregnancy, it has been observed that rates of valve intervention are higher among multiparous women as compared to nulliparous women for unclear reasons [33]. It has been proposed that pregnancy may accelerate native heart valve disease but supporting evidence remains limited.

Cardiomyopathy

Cardiomyopathy (CMP) is an increasingly important source of maternal morbidity and mortality. From a 2006–2010 analysis of the Healthcare Cost and Utilization Project's National Inpatient Sample, the estimated incidence of CMP was 46.8/100,000 [34]. Among hospitalized pregnant women with CMP, 50.0% were peripartum (23.4/100,000), 2.5% were hypertrophic (1.2/100,000), and 47.5% were classified as other (largely dilated) (22.2/1000,000). The authors of this analysis examined maternal outcomes and found that 42.1% of women with CMP experienced a major cardiovascular event (33% HF, 7% arrhythmia, 0.5% stroke, 1.2% myocardial infarction, or death) as compared to 0.4% in women without CMP.

Dilated cardiomyopathy

Dilated CMP in pregnancy is a growing challenge for modern cardiologists and obstetricians. Maternal cardiac deaths in the Confidential Enquiries into Maternal Death in the United Kingdom were frequently related to ventricular dysfunction [35]. A 2010 sub-study of the Longitudinal Canadian Pregnancy and Heart Disease program examined outcomes of 36 pregnancies in 32 women with dilated cardiomyopathy from 1994 to 2008 [36]. Thirty nine percent of pregnancies were complicated by at least 1 maternal cardiac event (HF, atrial and ventricular arrhythmias, and transient ischemic attack). Previous studies had recognized NYHA functional class as an independent risk factor for adverse maternal outcomes; [37,38] this study further identified moderate or severe LV dysfunction (LVEF < 40%) and/or NYHA functional class III or IV as determinants of adverse maternal outcomes.

The authors further analyzed maternal outcomes in pregnant women with dilated CMP and LV dysfunction and compared them to nonpregnant age-matched controls. The 16-month event-free survival was significantly worse among pregnant women with severe LV dysfunction and dilated CMP (28%) than their nonpregnant counterparts (83%, $p = 0.02$). This observation highlights the notion that the hemodynamic load of pregnancy can precipitate cardiac decompensation. However, the non-pregnant cohort was more likely to receive guideline-based HF therapy that introduces a source of confounding.

Fetal and obstetric outcomes were also less favorable. In 36 pregnancies, there were a total of 5 adverse obstetric outcomes including preeclampsia and postpartum hemorrhage. Adverse neonatal outcomes were described in 20% (low birth weight and preterm delivery). In comparison, the rate of neonatal adverse outcomes in the healthy population is approximately 7% [39].

The medical management of dilated CMP in pregnancy is similar to the management in non-pregnant patients [40]. Chronic HF therapy should be continued if possible, with ACE inhibitors and aldosterone antagonists being notable exceptions due to teratogenicity. Vasodilator therapy with hydralazine or amlodipine can substitute for ACE inhibitors. Beta-blockers should be continued and digoxin can be used for symptom relief after beta-blockers and vasodilators have been optimized. In an acute decompensation, IV diuretics and/or vasodilator therapy with nitroglycerin can also be employed safely. Beyond medical therapy, rare instances of left ventricular assist device (LVAD) and transplant have been documented in the pregnant population.

Labor and delivery is a crucial time for women with dilated CMP. A multidisciplinary team including cardiologists, obstetricians, and obstetrical anesthesiologists should be immediately available for consult throughout labor, delivery, and the early postpartum period. Invasive hemodynamic monitoring is not required in all patients with systolic dysfunction, but right heart catheterization and arterial line placement can be utilized in pregnant women with decompensated HF. In general, vaginal delivery at term is the recommended mode of delivery for women with CMP, but early delivery should be considered in patients with HF refractory to medical therapy. Anesthesia and pain control are paramount in these cases because they blunt the increased hemodynamic stressors that accompany labor and delivery. Once in labor, women should be advised to lie in a left lateral decubitus position to avoid uterine compression of the IVC. Second stage of labor can be assisted with forceps or vacuum extraction to hasten delivery if needed. Outside of refractory HF necessitating urgent delivery, Caesarean section is generally performed only for obstetrical indications.

The postpartum period is also a vulnerable time. Cardiac complications including worsening HF, arrhythmias, and cerebrovascular accidents were most common in late pregnancy and in the first 16 months post-partum [36]. SVR and volume can increase dramatically immediately postpartum due to the delivery and autotransfusion of the placenta. As a result, women can often decompensate quickly in this immediate postpartum time. It is important to remain vigilant during this period and continue hemodynamic and ECG monitoring for the first several days after delivery at a minimum.

Peripartum cardiomyopathy (PPCM)

Peripartum CMP (PPCM) is an entity unique to pregnancy. By definition, PPCM is the development of HF in late pregnancy or within several months following delivery, in the absence of a determinable etiology for HF or demonstrable heart disease before the last month of pregnancy [41]. The incidence is rising. In the early 1900s, the incidence over time was 1 in 4350 and has steadily increased to most recent estimates of 1 in 1149 live births in the U.S. [42]. Most patients present late in pregnancy, during the third trimester, or postpartum. In fact, in a series of 123 patients with PPCM, 75 were diagnosed 1 month postpartum [43]. Risk factors for the development of PPCM include older maternal age, teenage pregnancy, multiparity, multifetal pregnancy, African/Haitian descent, hypertension, diabetes, prior toxin exposure, preeclampsia, and smoking.

Maternal outcomes in PPCM are guarded. Most patients present with typical symptoms of HF, including dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Death due to PPCM is usually caused by progressive pump failure, sudden death or thromboembolic events. LV size and function predicts outcome. A study of 100 women with PPCM followed through 1 year postpartum found that severe LV dysfunction (LVEF < 30%) was predictive of adverse cardiovascular events (death, transplant, or LVAD implantation) [44]. Other studies have identified depression of LVEF at 12 months, LV end diastolic dimension > 56 mm, LV thrombus, troponin T elevation, black race, and multiparity as independent predictors of maternal adverse outcomes [45,46]. Fortunately, when examining overall outcomes amongst all cardiomyopathies in pregnancy, PPCM had the most favorable survival rates (adjusted HR for death 0.31, 95% CI 0.09–0.98) [47]. Better survival in PPCM may be related to the possibility of LV recovery. In the study of 100 women with PPCM, transthoracic echocardiograms were performed at baseline, 2, 6, and 12 months postpartum [44]. LV recovery to an LVEF ≥ 50% was evident in 66% of women. However, if LV recovery is stratified by baseline LVEF, 86% of women with a baseline LVEF ≥ 30% showed LV recovery whereas only 37% of women with a baseline LVEF <30% had LV recovery. Predictors of persistent LV dysfunction were similar to predictors of adverse maternal outcomes including LVEF < 30%, LV end diastolic dimension >60 mm, elevated troponin T, and reduced RV function. There has been some interest in better understanding the relationship of RV function to LV function in PPCM. A prospective 30-center study of 100 PPCM patients showed that baseline RV fractional area change was independently associated with subsequent LV recovery and clinical outcome [48].

While LV recovery and prognosis are generally more favorable in PPCM, all women should be counseled about the risks associated with subsequent pregnancies. Women who recovered their LV function fare better, but they are still not free of maternal events. Indeed, in a series of women with LV recovery, 21% developed HF, 21% had >20% fall in LVEF, and 14% developed persistent LV dysfunction following their subsequent pregnancy [43]. Rates were even worse in women who sustained residual LV impairment following their initial pregnancy (44% HF, 25% with >20% fall in LVEF, 31% with persistent dysfunction, and 19% with maternal mortality). In a survey study of 60 subsequent pregnancies in 44 women with a history of PPCM, all women had worsening outcomes including a drop in LVEF, HF symptoms, and persistent LV dysfunction [49]. Again, outcomes were worse among women who had persistent LV dysfunction prior to their subsequent pregnancy. Subsequent studies have confirmed the same themes in women with PPCM: (1) LVEF generally improves postpartum, (2) LVEF drops in subsequent pregnancies, and (3) LVEF predicts outcomes after both the index pregnancy and subsequent pregnancies are better [50–52].

The medical management of PPCM is similar to dilated CMP in pregnancy. Continuation of chronic HF therapy including beta-blockers and vasodilators (hydralazine and nitrates) are important. Careful volume management is also key, particularly in the first 2–7 days following delivery, and it is important that women are not discharged prematurely. Again, vaginal delivery is preferred and breastfeeding is encouraged. In light of the gravity of subsequent pregnancies in PPCM, a contraception plan should be discussed prior to discharge. In very serious cases refractory to medical therapy, mechanical assist devices such as LVAD and even cardiac transplantation have been necessary. In 2 small case series of 130 patients with PPCM, 4 women died, 4 underwent LVAD implantation, and 4 underwent cardiac transplantation [44,53].

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is rare in pregnancy, accounting for only 2.5% of pregnant women with CMP, an already small group. The primary risks of HCM during pregnancy include hemodynamic decompensation, arrhythmias, or sudden death. Most women with HCM tolerate pregnancy very well and are often asymptomatic. The increased blood volume and stroke volume normally seen in pregnancy increases the LV cavity size, which can lower the outflow tract gradient. However, women with significant LV outflow tract (LVOT) obstruction are at high risk for hemodynamic deterioration during pregnancy or sudden cardiac death [40]. Risk factors for maternal adverse events include previous arrest or documented sustained ventricular tachycardia (VT) or strong family history of HCM with sudden death. Few data are available to guide management of pregnant women with HCM. Generally, continuation of beta-blocker or calcium-channel blocker therapy is recommended but this is not universally accepted. Labor and delivery should be performed at a high-risk center with a multidisciplinary team of experts. Contrary to delivery for dilated CMP or PPCM patients, epidural anesthesia should be avoided in HCM due to potential for hypotension. Similarly, the use of prostaglandins for labor induction is not recommended due to the vasodilatory effects. Although reported caesarian section rates are high, vaginal delivery is considered safe in these women [54].

Mode of delivery

Historically, planned C-section was perceived to be safer than vaginal delivery in women with high-risk pregnancies. Indeed, in a 2017 retrospective study of inpatient admissions in the Healthcare Cost and Utilization Project's California State Inpatient Database, women with CHD were significantly more likely to undergo cesarean delivery as compared to women without CHD (39.3% vs. 32.0%, $p < 0.001$), although overall rates for both groups were staggeringly high. Increasingly, studies have demonstrated that outcomes with planned vaginal delivery are superior to those with C-section [55]. In this retrospective cohort study of all women in Canada who delivered from 1991 to 2005, rates of severe morbidity (27.3/1000 deliveries in C-section vs 9.0/1000 deliveries for vaginal delivery) were significantly higher with planned C-section versus planned vaginal delivery. The planned cesarean group had an increased risk of postpartum cardiac arrest (OR 5.1, 95% CI 4.1–6.3),

wound hematoma (OR 5.1, 95% CI 4.6–5.5), hysterectomy (OR 3.2, 95% CI 1.2–3.8), anesthetic complication (OR 2.3, 95% CI 2.0–2.6), hemorrhage (OR 2.1, 95% CI 1.2–3.8), infection (OR 3.0, 95% CI 2.7–3.4) and venous thromboembolism (OR 2.2, 95% CI 1.5–3.2). In a more contemporary registry of pregnancies in women with structural heart disease from 2007 to 2011, propensity matched analysis of performed vaginal delivery versus performed cesarean section found no difference in maternal mortality (0.9% vs. 0.9%, $p = 1.00$), postpartum hemorrhage (4.0% vs. 4.9%, $p = 0.63$), or neonatal mortality (0.7% vs. 0.7%, $p = 1.00$) [56]. Importantly, there was less postpartum HF in the vaginal delivery group (4.3% vs. 7.8%, $p = 0.023$). These data demonstrate that even in women with high-risk cardiac disease, vaginal delivery should be recommended over cesarean delivery. Consistent with this observation, the current guidelines recommend vaginal delivery for women with heart disease except for women who require urgent delivery due to decompensated HF refractory to medical therapy, MFS and dilated aorta ≥ 4.0–4.5 cm, acute or chronic aortic dissection, or therapeutically anticoagulated and in labor [57].

Conclusions

The advancement of cardiovascular care has made pregnancy possible for many women with complex CVD. While a tremendous opportunity for our patients, pregnancy in women with high risk CVD is associated with significant risk for adverse maternal and neonatal outcomes, even death. A multidisciplinary approach and awareness of the potential complications and management strategies for pregnant women with CVD are vitally important to the health and long-term outcomes of women with complex heart disease and their offspring.

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