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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

High-Risk Cardiac Disease in Pregnancy

Part II

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ABSTRACT

Heart disease continues to be the leading cause of nonobstetric maternal morbidity and mortality. Early diagnosis and appropriate care can lead to prevention of complications and improvement of pregnancy outcome. This paper continues the review and provides recommendations for the approach to high-risk cardiovascular conditions during gestation. (J Am Coll Cardiol 2016;68:502–16) © 2016 by the American College of Cardiology Foundation.

COMPLEX CONGENITAL HEART DISEASE

Due to the successes of congenital heart surgery, congenital heart disease (CHD) now comprises up to 80% of all pregnancies in women with heart conditions in the Western world (1,2). The maternal risk of mortality (0.5%) and morbidity is, however, relatively low and is 4 to 5 times lower than that reported in valvular heart disease or cardiomyopathy (3). Maternal morbidity (mainly arrhythmias and heart failure [HF]) is reported in 11% (4.5% to 20%) (4–8). These data are from heterogeneous populations, varying from the very simple to the most complex CHD. There are subcategories of CHD in which the risk for both mother and fetus is markedly increased. Women with CHD are often not aware that their residual lesions are associated with increased pregnancy risk. Therefore, timely counseling is important in girls and women with CHD (9). To counsel each individual woman appropriately, the risk of pregnancy needs to be assessed (**Central Illustration**). As outlined before, the most reliable system of risk estimation in CHD is the modified World Health Organization classification of maternal risk (10), and this risk estimation system is recommended by the European Society of Cardiology (ESC) (11) (see Table 2 in Part 1 of the review [12]). According to this classification, the Fontan circulation, systemic right ventricle (RV), and uncorrected cyanotic disease are high-risk congenital conditions. This part of the review will focus on these conditions.

FONTAN CIRCULATION

Patients born with a functionally univentricular heart are often palliated by creation of a modification of the Fontan circulation. In all modifications of the Fontan circulation, the single ventricle is used as a systemic ventricle and pumps highly saturated blood in the aorta, whereas deoxygenated blood flows passively from the systemic veins to the lungs. This circulation is characterized by elevated systemic venous pressures, increased venous thrombotic risk, susceptibility for atrial arrhythmias that are often poorly tolerated, and impaired ability to meet demands for increased cardiac output related to decreased preload of the ventricle. Additionally, dysfunction of the single ventricle, valvular dysfunction, and protein-losing enteropathy are not uncommon complications. Only a limited number of pregnancies in

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Fontan women have been reported. A review of 71 pregnancies and a study of 59 pregnancies both describe an increased prevalence of infertility (57% and 21%) and a high miscarriage rate (34% and 27%) (13,14). Maternal complications occur in about 10% (14). Atrial arrhythmias are the most frequent complications (13,14). Thromboembolic complications have been reported in patients both with and without anticoagulation therapy (14). Other cardiac complications are HF and deterioration of functional class. HF occurs when the often anatomically and functionally abnormal ventricle cannot accommodate the requirement for increased cardiac output, and may be aggravated by atrioventricular valve regurgitation. Additionally, the passive transpulmonary circulation depends on adequate diastolic ventricular properties and may be insufficient to transport the increased plasma volume. There is a strikingly high incidence of premature delivery (39% and 69%), often in the setting of spontaneous pre-term labor, with about one-third of premature neonates born before 33 weeks of gestation (13,14). Experts agree that Fontan patients with depressed ventricular function, cyanosis, significant atrioventricular valve regurgitation, or protein-losing enteropathy should be advised against pregnancy (11). In others, careful pre-pregnancy counseling and planning of management in an experienced tertiary center is essential. Even though there are insufficient data to prove their effects, the prothrombotic state of both the Fontan circulation and pregnancy, the potentially disastrous effect of pulmonary embolism in a passive pulmonary circulation, and reports of thromboembolic complications in several patients are reasons to offer anticoagulation therapy to all pregnant Fontan patients, in line with the recommendations in the ESC guidelines (11). Sustained atrial arrhythmias constitute an emergency and usually require prompt electrical cardioversion (15). Vaginal delivery is usually preferred. Careful fluid management is essential around delivery to avoid reduction of pre-load, as well as worsening of HF. Neuraxial anesthesia is advisable to decrease the stress of delivery. Sudden decreases in systemic arterial resistance should be avoided, and coagulation abnormalities should be ruled out. An increase in pulmonary vascular resistance should also be avoided: prostaglandin F analogs should not be used for the management of postpartum hemorrhage, and when general anesthesia is necessary, ventilation should be with low airway pressures (11,16,17). Oxytocin should only be given as a continuous infusion. When blood loss is accompanied by hypotension, judicious fluid replacement is indicated. In women with abnormal ventricular function or atrioventricular valve regurgitation, post-partum administration of furosemide should be considered.

SYSTEMIC RV

Women with a systemic RV are those who have undergone an atrial repair (Mustard or Senning correction) of complete transposition of the great arteries and those with congenitally corrected transposition of the great arteries (CCTGA). More than 200 pregnancies in women with a Mustard or Senning repair have been described. Salient outcomes are a high miscarriage rate (up to 30%) and high maternal cardiac complication rates (10% to 30%), including arrhythmias and HF. Cardiac death appears to be rare. Other complications are New York Heart Association (NYHA) functional class deterioration, RV dysfunction and worsening of tricuspid regurgitation (TR) that may be persistent after pregnancy, high rates of prematurity (25% to 50%) and small for gestational age (up to 50%), as well as fetal and neonatal death (18–24). Similar complications are described in women with CCTGA, but the complication rates are reported to be lower (25,26). Women with both a Mustard or Senning operation and CCTGA need to be counseled before pregnancy. Severe RV dysfunction or TR is a reason to advise against pregnancy (11). Management of pregnancy should be in specialized centers. Vaginal delivery is usually appropriate. Arrhythmias are primarily treated with beta-blockers, but caution is necessary because of the tendency for bradycardia due to sinus node dysfunction (Mustard/Senning) or atrioventricular block (CCTGA). Frequent surveillance of RV function, heart rhythm, and clinical symptoms is recommended during pregnancy. When deterioration of RV function is noted, early delivery is advised.

UNCORRECTED CYANOTIC HEART DISEASE WITHOUT PULMONARY HYPERTENSION

Cyanotic heart disease is usually treated surgically in childhood. Limited data are available regarding pregnancy in women with inoperable or palliated cyanotic heart disease with no pulmonary hypertension. Cardiac complications have been described in 32% (26). More than 50% of all complications are due to HF; other complications include thromboembolic events, arrhythmias, and endocarditis (27,28). Fetal outcome is associated with maternal oxygen saturation at rest; with saturation ≥90%, the live birth rate is 92%, whereas with a saturation ≤85%, the live birth rate is only 12% (26). To maintain the highest possible

ABBREVIATIONS AND ACRONYMS

BAV = bicuspid aortic valve
CHD = congenital heart disease
DCM = dilated cardiomyopathy
HF = heart failure
LV = left ventricular
LVEF = left ventricular ejection fraction
MFS = Marfan syndrome
PPCM = peripartum cardiomyopathy
RV = right ventricle/ventricular

saturation during pregnancy, which may improve fetal outcome, restriction of physical activity is advised (11). In addition, supplemental oxygen may improve oxygen saturation in some women, who may benefit from this during pregnancy (11). Women with a low saturation need to be informed that their chances of a successful pregnancy are low (26). Because both risk of thromboembolism and bleeding risk can be elevated, pros and cons of anticoagulation therapy need to be weighed, and an individualized approach is needed. When hemostasis is straightforward, thromboprophylaxis with low molecular weight heparin (LMWH) should be considered (10). Vaginal delivery is possible in uncomplicated pregnancies, but deterioration of the condition of mother or fetus can be a reason for early cesarean delivery. Management of pregnancy and delivery should always be in a specialized center (10).

PULMONARY HYPERTENSION

Pulmonary hypertension is defined as a mean pulmonary arterial pressure ≥25 mm Hg at rest. It is classified as pulmonary arterial hypertension, which can be idiopathic, heritable, drug/toxin-related, or related to connective tissue disorders or to CHD, mainly to shunt lesions (Eisenmenger syndrome); or pulmonary hypertension due to left heart disease, lung disease, thromboembolic disease, or unclear etiology (29). Pulmonary arterial hypertension carries a grave prognosis in pregnant women. The pulmonary circulation is not able to accommodate to the increased cardiac output, resulting in increased pulmonary artery pressures and RV failure. The prothrombotic state of pregnancy enhances pulmonary vascular thrombosis and pulmonary embolism, aggravating pulmonary hypertension. Women with Eisenmenger syndrome are at risk of systemic embolism and of an increase of right-to-left shunt, which leads to deoxygenation due to the fall in systemic resistance of pregnancy associated with the fixed, high pulmonary resistance (30). Pulmonary arterial hypertension is associated with high, but decreasing maternal mortality rates. During 1978 to 1996, maternal mortality was 38%; thereafter, mortality decreased to 25% ($p = 0.047$), and it is even lower (16%) in women treated with targeted antipulmonary hypertension therapies (calcium-channel blockers, nitric oxide, prostacyclin derivatives, endothelin receptor antagonists, or phosphodiesterase inhibitors) (30–32). Mortality is lower in idiopathic pulmonary arterial hypertension (17%, or 9% with specific therapies) than in Eisenmenger syndrome (28%, or 23% with specific therapies) or other classes of pulmonary hypertension (33%, or 13% with specific therapies) (29–31). The prognosis of patients with pulmonary hypertension due to left-sided heart disease (mitral stenosis or ventricular failure) is more favorable, although it is still a high-risk condition in pregnancy. Maternal mortality in pulmonary arterial hypertension has been related to late diagnosis, cesarean delivery with general anesthesia, and primiparity (31,32). Recent studies indicate that maternal prognosis may be better in patients with mild pulmonary hypertension (peak systolic pulmonary pressure <50 mm Hg or mean <40 mm Hg) or who are in a lower NYHA functional class (33,34). Early planned delivery and timely institution of targeted therapies probably contribute to a better maternal outcome (30,35,36).

Despite the improved prognosis, mortality is still high, and there is no reliable way to identify individual women who may be at lower risk. Therefore, all women with established pulmonary hypertension should be advised against pregnancy, or when pregnancy occurs, termination should be offered (11,29). When a woman chooses to continue the pregnancy she should be immediately referred to a specialized pulmonary hypertension center for management by a multidisciplinary team that includes a cardiologist experienced in the management of cardiac problems in pregnancy. Management includes restriction of physical therapy and oxygen supplementation when necessary. Anticoagulation therapy should be administered to all women who have an indication outside of pregnancy. For other women, given the prothrombotic state of pregnancy, anticoagulation should be considered on an individual basis. In women with Eisenmenger syndrome or esophageal varices, the risk of bleeding likely outweighs the benefits (11). Patients with signs of HF should be treated with diuretic agents. Specific pulmonary hypertension therapies used before pregnancy should generally be continued (11). Endothelin receptor blockers (bosentan, ambrisentan) are teratogenic in animals, and it is often advised to replace these drugs in pregnant women by sildenafil and/or prostacyclin derivatives, but an individual approach is necessary. The most frequently used calcium-channel blocker in pulmonary hypertension is nifedipine. It is probably safe, although data on its use in the first trimester are scarce and it should be noted that higher dosages are used for pulmonary hypertension than for other indications. Calcium-channel blockers are only indicated in patients with pulmonary arterial hypertension who are responders to vasoreactive testing and are contraindicated in all others. It seems that women who are responders to and stable on calcium-channel blockers have a relatively good pregnancy outcome

CENTRAL ILLUSTRATION **High-Risk Heart Disease in Pregnancy**

HIGH-RISK HEART DISEASE (HRHD) IN PREGNANCY

Pre-conception counseling and pregnancy risk stratification for all women with HRHD of childbearing age

In women considering pregnancy: Switch to safer cardiac medications and emphasize importance of close monitoring

In women avoiding pregnancy: Discuss safe and effective contraception choices or termination in early pregnancy

Valve disease	Complex congenital heart disease	Pulmonary hypertension	Aortopathy	Dilated cardiomyopathy
Pregnancy not advised in women with: • Severe mitral and aortic valve disease • Mechanical prosthetic valves if effective anticoagulation not possible	**Pregnancy not advised in women with:** • Significant ventricular dysfunction • Severe atrioventricular valve dysfunction • Failing Fontan circulation • O_2 saturation <85%	**Pregnancy not advised for:** • All women with established pulmonary arterial hypertension	**Pregnancy not advised in some women with:** • Marfan syndrome (MFS) • Bicuspid aortic valve (BAV) • Turner syndrome • Rapid growth of aortic diameter or family history of premature aortic dissection	**Pregnancy not advised in women with:** • Left ventricular ejection fraction <40% • History of peripartum cardiomyopathy
Pregnancy management: • Close follow-up • Drug therapy for heart failure or arrhythmias • Balloon valvuloplasty or surgical valve replacement in refractory cases	**Pregnancy management:** • Close follow-up	**Pregnancy management:** • Close follow-up • Early institution of pulmonary vasodilators	**Pregnancy management:** • Treat hypertension • Beta-blockers to reduce heart rate • Frequent echo assessment • Surgery during pregnancy or after C-section if large increase in aortic dimension	**Pregnancy management:** • Close follow-up • Beta-blockers • Diuretic agents for volume overload • Vasodilators for hemodynamic and symptomatic improvement
Delivery: • Vaginal delivery preferred • C-section in case of fetal or maternal instability • Early delivery for clinical and hemodynamic deterioration • Consider hemodynamic monitoring during labor and delivery	**Delivery:** • Vaginal delivery preferred • C-section in case of fetal or maternal instability • Consider hemodynamic monitoring during labor and delivery	**Delivery:** • Vaginal delivery preferred • C-section in case of fetal or maternal instability • Timing of delivery depends on clinical condition and right ventricular function • Early delivery advisable • Diuresis after delivery to prevent RV volume overload • Extended hospital stay after delivery	**Delivery:** • C-section in cases of significant aortic dilation MFS >40 mm BAV >45 mm Turner: ASI >20 mm/m^2	**Delivery:** • Vaginal delivery preferred • C-section in case of fetal or maternal instability • Consider hemodynamic monitoring during labor and delivery • Early delivery for clinical and hemodynamic deterioration

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Management strategies for women who have valve disease, complex congenital heart disease, pulmonary hypertension, aortopathy, and dilated cardiomyopathy. ASI = aortic size index; BAV = bicuspid aortic valve; echo = echocardiographic; HRHD = high-risk heart disease; MFS = Marfan syndrome; RV = right ventricular.

(36). Prostacyclin derivatives and sildenafil or tadalafil are probably beneficial for pregnant women with pulmonary arterial hypertension and seem to be associated with acceptable fetal risk. Because recent research suggests that early institution of specific therapies is associated with better outcome, we advise starting these therapies at least 3 months before delivery (30). During pregnancy, women should be carefully and frequently monitored for occurrence of symptoms, signs of HF, deterioration of RV function, and increased natriuretic peptide levels. On the basis of recent published reports, for women with moderate or severe pulmonary hypertension, an early planned delivery around 32 to 34 weeks is

usually advisable (33–35). Women who are stable with mild disease may be scheduled for a later delivery (35 to 37 weeks). The occurrence of any deterioration in symptoms, RV function, or natriuretic peptide levels can be a reason for early delivery. Expert application of epidural or spinal/epidural anesthesia, avoiding decrease of peripheral vascular resistance, is probably preferred over general anesthesia, which has been associated with worse outcome (30,32). When feasible from an obstetric point of view, vaginal delivery appears to be an equally safe option in experienced hands under epidural or spinal/epidural anesthesia. Most women benefit from (additional) diuretic therapy immediately after delivery. After delivery, we recommend an in-hospital observation period of at least 1 week. It should be remembered that increased mortality rates are not only observed before pregnancy, but also in the first months after delivery. Therefore, specific therapies should be continued for at least 3 months after pregnancy, and frequent follow-ups are recommended after discharge.

AORTOPATHY IN PREGNANCY

Aortic dissection is a rare, but often catastrophic event and occurs in patients with disorders of connective tissue, including those caused by fibrillin mutations (Marfan syndrome [MFS]), collagen mutations (Ehlers-Danlos syndrome), those caused by transforming growth factor beta receptor mutations (Loeys-Dietz syndrome), and in primary disorders of aortic wall composition, such as Turner syndrome (TS) and bicuspid aortic valve (BAV). The risk of aortic dissection associated with these conditions is markedly increased during pregnancy.

MARFAN SYNDROME. MFS is an autosomal-dominant hereditary disorder of the connective tissue caused by a mutation in the gene for MFS on chromosome 15q21 (37–39). This gene encodes the extracellular matrix protein fibrillin 1 (37,39) and leads to defects in various organ systems. The vast majority (~80%) of patients have cardiovascular involvement, which more often includes aortic dilation, aortic regurgitation, and prolapse of the mitral and tricuspid valves. The leading cause of morbidity and mortality in MFS is aortic dissection (37–39).

Diagnosis of MFS. MFS segregates as a dominant trait in ~70% of families, and the remainder of cases are caused by de novo mutations. Diagnosis is on the basis of the Ghent criteria, which were first published in 1996 and later revised to take into account the many individuals with MFS who do not have the fibrillin 1 mutation (40,41). Major criteria are found infrequently in the general population, and therefore they carry limited diagnostic sensitivity, but high specificity. Due to multisystem involvement, the evaluation of patients with possible MFS must involve a multidisciplinary approach, as well as clinical genetics. The diagnosis may be challenging, and MFS often remains undiagnosed before pregnancy and is recognized only after life-threatening complications occur in pregnancy.

RISK FOR THE MOTHER AND FETUS IN MFS AND AORTIC INVOLVEMENT. Pregnancy is associated with a substantially increased risk of aortic dissection, probably caused by a maternal increase in blood volume, heart rate, and stroke volume, and by hormonally-mediated changes in the diseased aortic wall (42). Pyeritz (43) initially described the increased risk of complications in pregnant women with MFS more than 20 years ago, reporting aortic dissection in 20 of 32 pregnant women with MFS. Later, Elkayam et al. (42) reported on 15 additional cases, of which 10 had cardiovascular complications, including aortic dissection; most developed cardiovascular complications in the second and third trimesters, although some occurred a few days after conception or during labor and after delivery, including 2 maternal deaths. Immer et al. (44) described 16 cases of pregnant women with MFS with type A dissection (with mean gestation of 31 ± 6 weeks, and mean aortic root diameter of 4.8 ± 0.8 cm). No maternal deaths were reported, but there were 3 fetal deaths. Finally, when reviewing published reports within the last decade, Goland et al. (45) reported on another 39 cases of women with MFS who experienced pregnancy-related complications, 29 of whom had an aortic dissection involving the ascending aorta (n = 19), descending aorta (n = 8), or both (n = 2). Dilation of the aorta was diagnosed before pregnancy in 19 patients, and 4 women had a history of aortic surgery. Notably, 8 of 39 women were diagnosed with MFS only after the occurrence of complications. Five patients developed acute dissection before week 20 of gestation (13 to 20 weeks), 18 patients at 24 to 40 weeks, and 6 patients after delivery. Five patients developed progressive dilation of the ascending aorta requiring surgery during pregnancy, 1 patient developed an extension of distal dissection at 1 week post-partum, and 2 patients had a chronic unchanged distal dissection. In 2 patients, intracranial hemorrhage occurred post-partum. Maternal and fetal mortality were reported in 2 patients, whereas in 2 cases, aortic dissection resulted in fetal loss despite maternal survival.

Most published reports on outcomes among pregnant women with MFS probably provide an over-representation of complications due to a bias in reporting the most severe cases. This is supported by

a number of studies demonstrating a lower rate of aortic dissection of 4% to 6%; in all cases, the aortic diameter was ≥40 mm (46–48). More recent studies reported even lower rates of aortic dissection (49–51). For instance, among 144 pregnancies, Meijboom et al. (51) reported only 1 case of aortic dissection, which involved a woman with MFS who already had a previous type A dissection and developed a type B dissection during her second pregnancy (51); they concluded that pregnancy is relatively safe in women with an aortic root diameter of <45 mm (51).

Several studies that focused on the potential growth of the aorta in pregnant women with MFS (46,49,50) reported contradictory results. Rossiter et al. (46) prospectively evaluated 45 pregnancies in 21 women with MFS and found aortic dissection in only 2, whereas the remaining women with an aortic diameter <40 mm tolerated pregnancy well, and an accelerated increase in the aortic diameter during pregnancy was not observed. Meijboom et al. (49) found no significant difference in aortic root growth during 33 pregnancies in 23 patients with MFS (aortic diameter ≤45 mm) compared with 22 matched childless women in a 6.4-year follow-up. In contrast, Donnelly et al. (50) described 98 women with MFS who experienced 199 pregnancies (50). There were no acute aortic dissections, but 2 women developed symptomatic carotid artery dissections. An increase of 3 mm in aortic diameter was observed during pregnancy, with a diameter decrease post-partum, but without complete recovery at 5-year follow-up. The prevalence of both aortic dissection and elective aortic surgery during long-term follow-up was higher in women with prior pregnancy, with larger aortic diameter and greater rate of aortic growth during pregnancy, with increased number of pregnancies, and lacking beta-blocker therapy and regular follow-up during pregnancy.

To summarize the existing information on more than 350 unselected pregnancies in patients with MFS, the expected rate of aortic dissection may reach approximately 3% on average, ranging from 1% in women with aortic diameter <40 mm to as much as 10% in high-risk patients (those with aortic root diameter >40 mm, rapid dilation, or previous dissection of the ascending aorta) (46,47). Despite the rare occurrence of aortic dissection in women with MFS and a normal-sized aorta (46,47), an event-free pregnancy cannot be guaranteed in these women (47,48). In most women, aortic dissection occurs during the third trimester or post-partum, but it may occur at any time of gestation (52,53).

It should also be noted that the development of aortic dissection in the mother carries a substantial risk to the fetus (44,46,51,53). In addition, MFS is associated with a high rate (40%) of obstetric and/or neonatal complications, such as premature delivery (15%), mainly due to premature rupture of membranes and increased neonatal mortality (7.1%) (45,51).

Pre-conception evaluation and counseling. Ideally, the management of patients with MFS should start before conception, but in reality, only 25% of women receive any evaluation or counseling (48). Women with MFS should be counseled about potential pregnancy-related complications. These include: 1) the high risk of transmission of MFS (>50%), in which severe expression of the syndrome can occur even in children of mothers who present with relatively mild MFS (48,52); 2) the risk of aortic dissection in the mother (44–46); and 3) the association of MFS with a high rate (40%) of obstetric complications and increased mortality in the offspring (17). The patient should be informed about the possibility of pre-natal diagnosis using both genetic linkage performed in early gestation and fetal echocardiography in the third trimester (53,54). It is essential that the patient undergoes a careful cardiovascular evaluation, including both a transthoracic echocardiogram (TTE) and a transesophageal echocardiogram (TEE), for the assessment of proximal and distal aortic diameter, as well as valvular and cardiac function. Evaluation of the distal aorta is especially important in patients with dilated proximal aorta and in those with a history of surgical repair of the proximal aorta, who are at increased risk of distal aortic dissection (55). Either computed tomography (56) or cardiac magnetic resonance (CMR) could be used for a precise assessment of aortic size and anatomy before pregnancy.

SURGICAL TREATMENT OF AORTIC DISEASES IN PREGNANCY.

The ESC guidelines on management of cardiovascular disease during pregnancy call for prophylactic elective surgery to prevent aortic dissection in women with MFS with aortic root dilation >45 mm who are contemplating pregnancy, adding the proviso that there is still a risk of dissection even after surgery (11). In patients with an aortic diameter of 40 to 45 mm, surgical intervention can be considered in cases with rapid growth and a family history of premature aortic dissection. Some guidelines have recommended elective surgery before pregnancy in women with an aortic root >47 mm (52). However, recently published ESC guidelines recommend aortic repair in patients with an aortic diameter ≥45 mm (11). Because the risk associated with emergency operations for aortic dissection or rupture is high (54), a progressive >5 mm dilation of

the aorta during pregnancy requires elective surgery, either after a therapeutic abortion (up to 20 weeks), during pregnancy, or after cesarean section delivery in a case of fetal maturity (11,52).

Successful surgery during gestation or shortly after delivery (42,44,45,53) has been reported in a number of women with MFS. An impressive decrease in maternal and fetal mortality over the years has been described, with maternal mortality decreasing from 30% in 1990 to 1994, to 0% in 2002 to 2004, with a corresponding decrease in fetal mortality from 50% to 10% (45). Goland et al. (45) described 8 women with type A dissection during pregnancy and reported 2 cases of fetal death: 1 before surgery and 1 after. Zeebregts et al. (57) studied the management and outcomes of 6 women presenting with acute aortic dissection in pregnancy: 2 underwent emergency cesarean section delivery immediately followed by successful aortic repair, but only 1 infant survived; 2 other women underwent cardiac surgery with in utero fetuses, with successful outcomes for both mothers and babies; and another 2 women with type B aortic dissection survived with medical therapy only, but both fetuses died from asphyxia. Because cardiac surgery continues to be associated with increased fetal loss (44,45,58), cesarean section should be performed before or concomitantly with thoracic surgery if fetal maturity can be confirmed.

Prophylactic use of beta-blockers. A number of studies have demonstrated that beta-blockers slow the growth of the aortic root and significantly reduce the rates of aortic dissection and death (50,59). However, a recently published meta-analysis of all prospective trials demonstrated that although beta-blockers were effective in aortic root growth rate reduction in patients with MFS, they had no influence on the rate of dissection and final aortic size (60).

Because of the increased risk of dissection in pregnancy, the use of selective beta-receptor blockers is recommended during pregnancy in women with MFS, with a dose titrated to reduce heart rate by at least 20 beats/min and a close follow-up to detect intrauterine growth restriction.

AORTOPATHY IN PREGNANT WOMEN WITH TS.

TS is caused by complete or partial monosomy for the X chromosome during embryonic development. This syndrome occurs in approximately 1 in 2,000 live female births, and the most common clinical features are short stature and premature ovarian failure. The prevalence of cardiovascular malformation is 25% to 50%. In addition to hypertension, BAV (~20%), dilated ascending aorta, and aortic coarctation (~12%) are the most common cardiovascular abnormalities associated with TS (61,62). Although the ascending aortic diameter is normal in absolute numbers, the smaller stature in 25% of those with TS means that these patients have dilated aortas when adjusted for body surface area. Risk factors for aortic dissection include aortic dilation, BAV, coarctation of the aorta, and pregnancy (62). Aortic dissection occurs rarely in TS, but it is 6 times more common at younger ages than in the general population (63,64), and it is always combined with aortic valve disease or coarctation (65). Although the pregnancy and live birth rates have been generally favorable, there has been a high rate of maternal death from dissection (2%). The exact incidence of aortic dissection in pregnant women with TS is unknown; however, the reported aortic dissection rate related to pregnancy is ~10% (63). The report of the International TS Aortic Dissection Registry showed that dissection occurs in young women with smaller aortic diameters, whereas cardiac malformations, including BAV, increase the risk of dissection (66). However, only 1 case of acute dissection (of 19) was associated with pregnancy (66): a woman with previously diagnosed BAV, a mildly dilated ascending aorta, and a large aneurysm of the subclavian artery, who eventually died after emergent cesarean section. In the most recent review of 122 cases of aortic dissection in TS, Wong et al. (67) reported on 14 cases of pregnancy-associated aortic dissection with a high mortality rate of 77%, possibly due to a reporting bias of the most severe cases. In this review, 5 women had BAV and 3 had coarctation of the aorta, whereas most patients had aortic root dilation or aortic size index ([ASI]; aortic diameter/body surface area) >2.5 cm.

Just as with MFS, it is essential for women with TS to receive pre-conception pregnancy counseling and careful assessment of cardiovascular involvement, especially the aortic dimensions, which must be evaluated in relation to body surface area using echocardiography (TTE and TEE) and, when needed, computed tomography or CMR. Although guidelines suggest prophylactic surgery in women with TS and an ASI >2.7 cm/m^2 (11), Matura et al. (61), in his report on 158 women with TS, described 3 cases of aortic dissections with ASIs >2.5 cm/m^2 (61). On the basis of this and 2 other recently published investigations, prophylactic aortic surgery is recommended in women contemplating pregnancy with an ASI >2.5 cm/m^2 (66) (**Table 1**). Some investigators suggest advising against pregnancy, even in women with an ASI >2.0 cm/m^2, BAV, and/or coarctation of the aorta, and uncontrolled hypertension (67). In pregnant women with TS, blood pressure control is important,

especially in women with coarctation of aorta and an increased risk of pre-eclampsia.

AORTOPATHY IN PREGNANT WOMEN WITH BAV. The incidence of aortic dissection is low, at 3.1% per 10,000 patient-years, but is 8× higher than in the general population (68). The largest study to date evaluated a community-based cohort of 88 women (216 pregnancies and 186 deliveries) with BAV and aortic dissection. Overall, 10 patients underwent aortic surgery: 3 isolated cases and 7 combined with aortic valve replacement (68). No events of aortic dissection were reported at the median follow-up of 12.3 years. A significant rate of progressive aortic dilation was observed over the years of follow-up. These results are supported by the International Registry of Aortic Dissection, which reported on more than 1,000 dissections, but only 2 were related to pregnancy in women without BAV (69). This awareness of possible aortic dissection in patients with BAV and ascending aortopathy has led to the extrapolation of clinical outcomes to those experienced with MFS and increased concern about the safety of pregnancy in this population. However, although dissection does occur in women with BAV, it occurs less frequently than in women with MFS (44). Furthermore, the significantly higher long-term rates of aortic complications after aortic valve replacement observed in patients with MFS compared with those with BAV (70) support the need for a different, less aggressive approach in the general patient population with BAV, as well as in pregnant women. All of these data have led clinicians to apply the same indications for prophylactic aortic replacement in pregnant women with BAV as for the general population (**Table 1**). Pregnancy should not be advised in women with BAV and aortic diameters ≥50 mm (11,56,71). Close follow-up of aortic size by echocardiography and, when needed, CMR without gadolinium, in addition to blood pressure control, is recommended in those with an aorta ≥4.5 cm. An individualized approach should be used in those with an aortic diameter of 4.6 to 5.0 cm (69).

Follow-up during pregnancy in women with aortopathy. Patients with aortopathy should be followed during pregnancy by their obstetrician and cardiologist in collaboration (**Table 1**). A TTE examination should be performed every 4 to 6 weeks in patients with an aortic diameter ≥40 mm, progressive dilation, or a history of aortic surgery for aortic dilation or dissection, and in each trimester in those with a normal-sized aorta. In those with suboptimal TTE results, TEE or CMR without gadolinium can be used for assessment (11).

TABLE 1 Management Strategies in Pregnant Women With Aortopathy

MFS			
	Normal-sized aorta	Follow-up each trimester	Vaginal delivery
	Dilated aorta <40 mm	Follow-up 4–6 weeks	Vaginal delivery
	Dilated aorta 40–45 mm	Follow-up monthly	Cesarean section
	Aorta >45 mm	Prophylactic surgery pre-pregnancy or during pregnancy in women with rapid growth of the aorta	
BAV			
	Dilated aorta <45 mm	Follow-up 4–6 weeks	Vaginal delivery
	Dilated aorta 45–50 mm	Follow-up monthly	Cesarean section
	Dilated aorta ≥50 mm	Prophylactic surgery pre-pregnancy or during pregnancy in women with rapid growth of the aorta	
TS			
	Aorta ASI <2.0 cm/m^2	Follow-up each trimester	Vaginal delivery
	Aorta ASI 2.0–2.4 cm/m^2 + BAV or/and CoA	Follow-up 4–6 weeks	Cesarean section
	Aorta ASI ≥2.5 cm/m^2	Prophylactic surgery pre-pregnancy or during pregnancy in women with rapid growth of the aorta	

ASI = aortic size index (aortic diameter /body surface area); BAV = bicuspid aortic valve; CoA = coarctation of the aorta; MFS = Marfan syndrome; TS = Turner syndrome.

Labor and delivery in women with aortopathy. Vaginal delivery can be performed in patients with MFS and BAV who have an aortic diameter of <40 mm and in those with BAV and aortic diameter <45 mm (11,47,53) (**Table 1**). To minimize the stress of labor, it is essential to perform an epidural anesthesia and take measures to shorten the second stage of labor. Patients with MFS and aortic dilation ≥40 mm, progressive dilation of the aorta during pregnancy, or a history of aortic repair for prior dissection are at high risk for aortic dissection and should therefore have an elective cesarean delivery. In women with BAV and aortic dilation ≥45 mm, cesarean delivery is also advisable. Because approximately 70% of patients with MFS present with lumbosacral dural ectasia, an anesthetist should be consulted before delivery to plan the appropriate form of anesthesia (37,38). Postpartum hemorrhage of the uterine vasculature after cesarean section in women with MFS has been reported (43) and should be anticipated. When progressive dilation of the aorta occurs early in pregnancy, before the fetus is viable, aortic repair with the fetus in utero should be considered. In case of an urgent need for surgery later in pregnancy, an immediate cesarean delivery followed by cardiac surgery should be considered to prevent an unfavorable fetal outcome (11,44,51).

DILATED CARDIOMYOPATHY

Dilated cardiomyopathy (DCM) is characterized by left ventricular (LV) dilation and impaired systolic

function. A variety of causative factors, such as genetic defects, infectious agents, and toxic agents, are linked to DCM; however, in approximately 50% of patients, the cause remains unknown and it is thus named idiopathic DCM (72). Peripartum cardiomyopathy (PPCM) is a unique de novo cardiomyopathy that is initiated by pregnancy in previously healthy young women, but may share many echocardiographic and clinical features and even genetic predisposition with DCM. It occurs during pregnancy or the post-partum period, and is characterized by the development of HF due to marked LV systolic dysfunction, with or without LV enlargement (73,74).

PERIPARTUM CARDIOMYOPATHY. Definition, risk factors, and diagnosis. PPCM remains an important cause of pregnancy-related maternal mortality in previously healthy young women (74–77). The clinical course of this disease is highly unpredictable and may vary from a spontaneous resolution and complete recovery in a few days to months, to a rapid progression to severe HF with persistent LV dysfunction. Recently, a revised contemporary definition of PPCM was proposed as an idiopathic cardiomyopathy presenting with HF, secondary to LV systolic dysfunction, presenting toward the end of pregnancy or in the months following delivery, where no other cause of HF is found (78). The diagnosis of PPCM is still a diagnosis of exclusion; thus, it is necessary to eliminate any other potential cardiac and noncardiac etiologies for HF. The decision to expand the definition to include women with early presentation of PPCM was made on the basis of previous data showing that a sizable minority of women with PPCM develop symptoms of HF earlier than the last gestational month, with clinical presentation, outcomes, and LV recovery similar to those with traditional PPCM (79). The incidence of PPCM varies widely, from between 1 in 100 and 1 in 300 live births in Africa and Haiti to 1 in 3,000 live births in the United States and 1 in 6,000 live births in Japan (74–77). Recently, a trend for an increased incidence of PPCM in the United States, from 8.5 to 11.8 per 10,000 live births, has been reported (80). Later age of gestation, increased incidence of multifetal pregnancies, awareness, and improved diagnostic capabilities are probably the main reasons for the growing incidence of PPCM.

Although its etiology is still unknown, there are multiple risk factors associated with PPCM, including African-American (AA) descent, older maternal age, multifetal gestations, and hypertensive disorders during pregnancy (74,75,78). Recent studies have shown that PPCM may occur in the context of familial or genetically determined DCM, suggesting that, in some patients, PPCM may have a genetic cause (81,82). Multiple studies from the United States have reported a higher frequency of PPCM, more severe disease, and worse outcomes in those with AA heritage, suggesting racial disparities that may be related to genetic predisposition and environmental differences (77,83,84).

Etiology. Although the etiology of PPCM remains unclear, a number of mechanisms have been proposed, including a low selenium level, viral infections, stress-activated cytokines, inflammation, and autoimmune reactions, in addition to genetic factors (74,75). Recent data from animal models suggest that PPCM may be a vascular disease triggered by the hormonal changes of late pregnancy (85). Unbalanced oxidative stress during pregnancy leads to proteolytic cleavage of the nursing hormone prolactin into a vasotoxic, proapoptotic, proinflammatory 16-kDa prolactin fragment, leading to up-regulation of microribonucleic acid-146a, and causing impairment of both endothelial function and cardiomyocyte metabolism (86). In addition, sFLT-1, another antiangiogenic factor released from the placenta during later stages of pregnancy, leads to prominent inhibition of proangiogenic factors (87). These studies, therefore, suggest that PPCM may be caused by integration of oxidative stress, angiogenic imbalance, and impaired cardiomyocyte protection. A significantly elevated serum level of sFLT-1 has been associated with pre-eclampsia and is also seen in women with PPCM (85). However, although pre-eclampsia may cause cardiac dysfunction and HF, it usually affects diastolic LV function. Recently, a significantly higher prevalence of pre-eclampsia in PPCM (22%), compared with that in the general population (5%), was described and, in conjunction with the experimental data, strongly suggests the concept of a shared pathogenesis of the 2 diseases (88,89).

Clinical presentation. Normal pregnancy is often associated with signs and symptoms that can overlap with those of HF. Therefore, the diagnosis of PPCM can be easily missed in the absence of awareness of this disease and unfortunately is often delayed. In a retrospective review and analysis of 182 patients with PPCM, diagnosis delayed by >1 week was found in 48% of patients who later experienced severe, possibly preventable complications and death (83). Physical examination usually reveals the typical findings of HF, whereas an electrocardiogram may show nonspecific ST-segment and T-wave changes, and a chest radiograph commonly demonstrates pulmonary congestion/edema and, in some cases, pleural effusion. TTE demonstrating LV systolic

dysfunction (left ventricular ejection fraction [LVEF] <45%) in the presence of a dilated or normal-sized LV confirms the diagnosis. The role of CMR is still not well established, but scattered reports showed that it might provide additional information on cardiac structure and remodeling. Levels of the commercially available biomarker N-terminal pro-B-type natriuretic peptide are normal in healthy pregnant women, but have been shown to be significantly elevated in symptomatic patients with PPCM, similar to those with HF from any cause (90). Troponin T, a marker for cardiac injury, is less sensitive and may be only slightly elevated in acute PPCM, but has been shown to predict persistent LV dysfunction (91,92).

Prognosis. Although the prognosis is more favorable in PPCM than in other types of cardiomyopathies, PPCM may be associated with mortality or severe and lasting morbidity, including pulmonary edema, cardiogenic shock, fatal arrhythmias, and thromboembolic events (83). Retrospective reports in the United States have suggested a mortality rate ranging from 0% to 19%, compared with the considerably higher mortality in South Africa and Haiti of up to 30% (74-77). The risk of death is associated with older age, multiparity, severe impairment of LV function, AA ethnicity, and delayed diagnosis (73,93,94). In a recent prospective IPAC (Investigation in Pregnancy Associated Cardiomyopathy) study of 100 patients, the reported 1-year mortality was only 4% (94).

In a large cohort of patients, life-threatening complications were reported in 25% of patients and were associated with a low LVEF (≤25%) at diagnosis, AA descent, and delay in diagnosis (≥1 week). In addition, one-third of the surviving women experienced anoxic brain damage (83). Therefore, timely diagnosis and treatment can significantly improve outcomes in young and previously healthy women. In the first, recently published IPAC study, 100 women with PPCM were followed after their index presentation (94). By 1 year, 13% of women had experienced major events (death 4, transplantation 1, or left ventricular assist device [LVAD] implantation 4) or had persistent severe LV dysfunction with LVEF <35%. The event-free survival (without LVAD implantation and heart transplantation) was 93%, and it was similar for AAs and non-AAs. Significantly worse event-free survival has been found among women with LVEF <30% compared with those with LVEF ≥30% (82% vs. 99%; $p = 0.004$).

LV function recovery. The rates and time of LV recovery differ among studies. On the basis of earlier reports, recovery of LV function (LVEF ≥50%) occurs in ~50% of cases in the United States, whereas an even higher rate was reported by the recent IPAC prospective study (72%) (94). A single study of 40 indigent patients in the United States, most AA women, reported a significantly lower rate of LV recovery (35%), similar to those reported in South Africa, Haiti, and Turkey (74,95). In contrast to this and other retrospective studies, a recent large prospective study in the United States (IPAC) found that ~60% of AA women with PPCM achieved complete LV recovery and had similar event-free survival as non-AA women, emphasizing the importance of prospective designs to define the outcome and prognosis of PPCM (94). Most studies suggest that improvement of LVEF occurs within 6 months of diagnosis (74,96,97), but delayed recovery of LV function may occur (98,99). Goland et al. (96), in the largest retrospective study to date, showed that LV recovery in patients with PPCM is significantly related to the degree of myocardial insult at the time of diagnosis. Lower LVEF and larger left ventricular end-diastolic diameter (LVEDD) at diagnosis appear to be significant adverse predictors for recovery, in addition to AA descent (96). These results were recently supported by the IPAC study, which showed that baseline severe LV systolic dysfunction and larger LVEDD were associated with less recovery: no women with LVEDD ≥60 mm and LVEF ≤30% had recovered fully at 1 year of follow-up. In addition, AA race and late PPCM presentation (>6 weeks postpartum) were also associated with persistent LV dysfunction (94). In the IPAC study, AA women had lower LVEF at presentation, and lower magnitude of LV function improvement at the 6-month and 1-year follow-ups.

Subsequent pregnancies. This topic was extensively discussed by Elkayam (100) in a recent State-of-the-Art review in the *Journal*. In a retrospective U.S. study from 2001, Elkayam et al. (101) reported a decrease in the LVEF >20% during subsequent pregnancy (SSP) in 21% of women with PPCM with LV recovery (LVEF ≥0.50), compared with 44% of non-recovered women (101). There were no deaths with SSPs in the recovered group, but mortality of 13% was reported in those without LVEF recovery. In a prospective U.S. study of post-PPCM pregnancy patients identified through an internet support group, Fett et al. (102) reported relapse in 67% of women with LVEF <45% and in 33% of those with LVEF 50% to 54%, but also in 17% of women with LVEF 55% (102). Combined, these 2 largest studies from the United States demonstrated relapse with worsening of symptoms and deterioration of LV function in almost one-third of cases (101,102). Women with persistent LV dysfunction are at significantly higher risk (~50%)

for clinical deterioration than patients with LV function recovery before SSP, and the likelihood of recovery after pregnancy is low. Normalization of LV function after PPCM does not guarantee an uncomplicated SSP; approximately 20% of such patients are still at risk of significant deterioration of LV function, which persists after delivery in 20% to 50% of patients (74,100,101).

Treatment. Standard treatment consists of guideline-recommended optimal therapy for HF, with attention to preventing side effects in the fetus. Sodium restriction is recommended for all patients, whereas loop diuretic agents are indicated for the symptomatic relief of significant peripheral edema or pulmonary congestion. Medications such as angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) are contraindicated in pregnant women or those who might become pregnant due to their toxic fetal effects; the combination of nitrates and hydralazine can be a safe alternative for LV pre-load and afterload reduction. Beta-blockers are indicated for HF treatment in women with PPCM. Women taking beta-blockers should continue these medications during pregnancy. Nonselective beta-blockade could facilitate uterine activity; the use of beta-1-selective beta-blockers is generally preferred, particularly metoprolol tartrate because it is often used in pregnancy for the management of other conditions, including hypertension, arrhythmias, mitral stenosis, and myocardial ischemia. Digoxin can be used during pregnancy for the relief of HF symptoms, in addition to optimized doses of beta-blockers and vasodilator treatment. Generally, the use of spironolactone is not recommended during pregnancy because of limited safety data and antiandrogen effects, which have resulted in feminization in male animals and endocrine dysfunction in both sexes. Anticoagulation seems to be of particular importance in patients with PPCM and LVEF <40% because of an increased incidence of TE complications, and is recommended during pregnancy and for at least the first 8 weeks post-partum because of the hypercoagulable state (103). Although mortality is mostly due to HF, sudden arrhythmic death is not uncommon. Recently, 4 events of ventricular fibrillation with appropriate shock were reported in 3 of 7 women who received a wearable cardioverter-defibrillator. Therefore, use of this device should be considered during the first 6 months in women with PPCM with severely reduced LV function as a bridge to improvement of LVEF "beyond the device threshold," or to implantable cardioverter-defibrillator implantation in women with persistent LV dysfunction (104). Mechanical support, such as an LVAD used as a bridge to recovery or to heart transplantation, should be considered in critically ill women with refractory HF.

With regard to women who are diagnosed antepartum and remain in stable condition on appropriate therapy, close monitoring and continuation of pregnancy is possible with attention to appropriate timing and mode of delivery. In those with worsening LV function and symptoms of HF despite use of optimal treatment, termination of pregnancy or early delivery is indicated, with possible clinical improvement in many cases.

There is a paucity of data concerning breastfeeding in women with PPCM. An internet-based study reported breastfeeding in 67% of women who were diagnosed with PPCM and found better outcomes in these women compared with those who did not breastfeed (105). Similarly, in the recent prospective IPAC study, breastfeeding was not associated with lower rates of LV recovery (94). The safety of HF medication used during pregnancy and lactation has been discussed in detail elsewhere (103). Generally, the concentration of metoprolol tartrate, enalapril, and captopril in the breast milk is very low and most likely is insignificant for the infant. In addition, the concentration of canrenone, the active metabolite of spironolactone, is found in milk at clinically insignificant doses. Given the importance of breastfeeding for infant health and the lack of data on adverse effects to the mother with PPCM, women in clinically stable condition with PPCM should not be advised against breastfeeding.

Long-term follow-up in women with PPCM who have experienced LV function recovery is recommended due to a number of reported cases of spontaneous LV function deterioration (83). There is no clear answer as to when to stop the ACEIs and beta-blockers in recovered patients. Gradual discontinuation with frequent monitoring of LV function is reasonable in patients with complete recovery of LV systolic function (LVEF >55%) and normal LV size. Because of evidence for subclinical dysfunction in women with recovered LV function, assessment of contractile function by stress echocardiogram may be advisable before discontinuation of medications.

Specific therapeutic concepts in PPCM treatment. A small open-design study of the use of intravenous immune globulin in PPCM, compared with historical control subjects on standard therapy, reported a beneficial effect, but results were not evaluated further in a controlled trial (106). Sliwa et al. (107) reported a significant improvement in the combined endpoint of death, persistent LV dysfunction, or NYHA functional class III to IV in a group of

women with PPCM from South Africa treated with pentoxifylline, as an anti-tumor necrosis factor alpha treatment, in addition to conventional HF therapy. No further studies have been done to confirm these results. A recent open-label study compared standard HF management to levosimendan in 24 patients with acute PPCM. This study was not able to show any differences in the resolution of HF, LV function improvement, or all-cause mortality (108).

On the basis of the recent experimental observation of preventing PPCM in mice by prolactin inhibition with bromocriptine, early experience of its use in patients with PPCM in South Africa and Germany has been reported with promising results. A small, randomized open-label study performed in South Africa demonstrated significantly greater improvement in LVEF in patients with PPCM compared with those receiving standard care only (109). However, the validity of these results has been questioned, given the small sample size, the higher than expected incidence of persistent LV dysfunction and mortality rate in the standard care group, and possible differences in PPCM characteristics in patients in Africa and other countries. The recent registry from Germany found that the greatest improvement occurred in PPCM patients receiving bromocriptine in addition to standard therapy (90). However, the percentage of patients showing full recovery of LV function was similar in the 2 groups, and the rate of LV recovery in the German cohort was very similar to that reported by North American IPAC investigators, where bromocriptine had not been used. In addition, patients with low LVEF failed to improve, suggesting that treatment with bromocriptine was not effective in sicker patients with PPCM. More information from a well-controlled, large-scale study is needed to further evaluate a potential role of bromocriptine in the treatment of PPCM. Until such data becomes available, because of the potential complications, the use of bromocriptine for this indication should be considered experimental and may only be used on an individual basis.

Pre-existing DCM. The prevalence of DCM among young women of childbearing age is low. As mentioned earlier, there is an overlap in the clinical and echocardiographic features, as well as in the clinical course and complications of PPCM and DCM. Nonetheless, in addition to having higher LV recovery rates, the general prognosis in women with PPCM seems to be better (110,111). When women with pre-existing DCM become pregnant, they are at risk of maternal and fetal complications due to the hemodynamic, arrhythmogenic, and thrombotic burdens of pregnancy. A very recent study of more than 2,000 women with the diagnosis of cardiomyopathy in the United States looked at outcomes at the time of delivery. Women with pre-existing DCM had a high rate of major adverse cardiovascular events, mainly HF (39%), but this rate was lower than in PPCM patients (46%). There was also a very low (<1%) mortality rate in all women at the time of delivery (112).

Only a few studies on the outcomes of pregnant women with pre-existing DCM were published, reporting cardiac complication rates of 25% to 42% (113,114). The outcomes of 36 pregnancies in 32 Canadian women with pre-existing DCM were recently described. In that series, 39% of the pregnancies were complicated by at least 1 cardiac adverse event, but all complications were successfully treated and no maternal death occurred (115). Moderate to severe LV dysfunction and/or NYHA functional class III to IV were found to be strong predictors of adverse maternal cardiac events. An increased rate of fetal complications was related to the presence of either maternal or fetal factors. When compared with nonpregnant women with DCM, a higher rate of adverse events was seen among pregnant women (115). This can be explained by both the hemodynamic changes of pregnancy and the inability to use important HF medications, such as ACEIs/ARBs, which are contraindicated in pregnancy. Optimally, women with pre-existing DCM should be evaluated before conception to discuss the potential risk of pregnancy for themselves and their fetuses. Functional capacity should be evaluated by history and stress testing. LV function and size, the degree of mitral regurgitation, and pulmonary hypertension need to be assessed by echocardiography, and CMR may be helpful in selected patients to evaluate LV morphology. Cardiac status and treatment should be optimized before conception. Appropriate changes to medical therapy would include changing ACEIs/ARBs to nitrates and hydralazine. On the basis of the available data, it is important that women with pre-existing DCM, especially those with moderate/severe LV dysfunction and/or NYHA functional class III to IV, should be informed about the potential risks of pregnancy (11). The therapeutic approach in pregnant women with DCM is similar to PPCM and was discussed earlier. Anticoagulation (LMWH or warfarin, depending on gestational age) is recommended in those with atrial fibrillation and may be advisable in women with LVEF <40% due to the hypercoagulability state of pregnancy. A multidisciplinary team, including a cardiologist, obstetrician, and anesthesiologist, should plan the management and follow-up during pregnancy and the mode and timing of

delivery. The frequency of follow-up visits with clinical and echocardiographic assessment depends on the cardiac and functional status of the patient. In stable patients, vaginal delivery is preferable. Cesarean delivery is recommended for patients with advanced HF or hemodynamic instability (11), but should also be considered in those with deterioration of LV function; nevertheless, the decision should be individualized. Early termination of pregnancy should be considered in women with symptomatic HF and significant LV dysfunction to prevent severe maternal and fetal complications (11).

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