



Cardiac interventions and cardiac surgery and pregnancy

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ABSTRACT

Both cardiac surgery and cardiac interventions are rare in pregnancy but are generally more common in the developing world. Women with known cardiac disease should receive contemporaneous preconception counselling to assess all risks associated with pregnancy including whether surgery or cardiac interventions may need to be considered prior to pregnancy. Some women may need to undergo emergency surgery or procedures during pregnancy and decisions regarding this should be multidisciplinary including cardiologists, cardiac surgeons, anaesthetists, obstetricians and neonatologists. In this review we discuss both conditions where surgery or percutaneous interventions may need to be considered and both the outcomes for the mother and her baby.

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1. Introduction

Cardiac disease complicates approximately 1–2% of pregnancies, but it accounts for up to 15% of maternal deaths, with the overall number of deaths not showing any decline even in the developed world [1,2]. Nevertheless the number of women who require cardiac interventions during pregnancy remains small; a Swedish review of 720,000 pregnant women demonstrated that only 40 women (0.006%) underwent cardio-pulmonary interventions during pregnancy [3]. In the developing world, the need for cardiac intervention during pregnancy appears more common. In a review of 1000 women with known heart disease, who were followed up during pregnancy, a total of 47 (5%) underwent an intervention during pregnancy (over half were for percutaneous mitral valvuloplasties for underlying rheumatic heart disease) [4]. These procedures are not without risk particularly to the fetus and so both surgical and percutaneous interventions in pregnancy are usually only undertaken when other therapies have failed or are inappropriate. Furthermore, because they are so rare, surgical interventions during pregnancy should be undertaken by specialists practicing as part of a multidisciplinary team of cardiac surgeons, cardiac anaesthetists, obstetricians, haematologists, neonatologists and cardiologists.

2. Indications for percutaneous and surgical interventions

2.1. Valvular disease-mitral valve disease

Globally, rheumatic mitral stenosis is the most common cardiac valvular lesion encountered in pregnancy, particularly so in developing

countries [5]. During pregnancy, the maternal cardiovascular system undergoes remarkable adaptive changes to accommodate the 40% increase in blood volume and cardiac output. With a combined rise in maternal heart rate there is reduced diastolic filling, meaning that women with stenosed mitral valves encounter great problems. Recent data from the Registry on Cardiac Disease and Pregnancy (ROPAC) showed that, in women with severe mitral stenosis, the overall mortality was 1.9% and that 50% had heart failure during pregnancy [6]. The degree of maternal complications was directly proportional to the severity of mitral stenosis and ranged from 26% with mild mitral stenosis (mitral valve area >1.5 cms) to 67% with severe MS (valve area <1.0 cms). Mitral stenosis management in pregnancy typically relies on medical therapy but if treatment is refractory to this then a percutaneous approach would be considered as the next option. Indeed with increasing expertise in minimal invasive techniques, percutaneous mitral balloon valvuloplasty (PMBV) using the Inoue technique has almost replaced surgical commissurotomy. However, this is not technically feasible for all women and potential success depends upon the degree of calcification and abnormalities of the mitral valve [7]. Mitral regurgitation is commonly encountered in pregnancy particularly in the context of mitral valve prolapse. Chronic mitral regurgitation, in the presence of normal systolic ventricular function, is well tolerated even if severe. Indeed, the decreased systemic vascular resistance and systolic blood pressure are haemodynamically favourable for patients with mitral regurgitation. In cases where women present with acute mitral regurgitation in pregnancy, due to a ruptured chordae, typically require urgent surgery. Cases such as these are vanishingly rare [8] (Table 1).

2.2. Aortic valve-aortic stenosis

Obstructive heart lesions such as aortic stenosis are aggravated by the increased stroke volume in pregnancy. Aortic stenosis is a relatively

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Table 1
Cardiac complications in pregnancy.

Lesion	Cardiac complications	Management
Mitral stenosis		
Mild	Usually well tolerated	Diuretics and betablockers
Moderate or severe	Arrhythmia, heart failure, and pulmonary hypertension	As above, may require percutaneous intervention in more severe cases
Mitral regurgitation		
Mild	No significant effect	Typically no treatment required
Moderate or Severe	Pulmonary oedema and heart failure in severe cases	Diuretics
Aortic stenosis		
Mild	Well tolerated	If symptomatic may required betablockers and diuretics only if overloaded
Moderate/severe	In severe cases risk of heart failure	Admission if necessary for bed rest, and medical therapy as above
Aortic regurgitation		
Mild	Well tolerated low risk of complication	Usually no treatment needed
Moderate/severe	In severe cases may develop pulmonary oedema	Diuretics.

uncommon lesion in women of child bearing age, but maternal complications such as heart failure are seen in over 6% of women who are symptomatic prior to pregnancy [9]. Typically women may be admitted for bedrest and medical therapy such as diuretics [9] Aortic balloon dilatation is employed during pregnancy for women only with severe symptomatic stenosis that is unresponsive to conservative measures [10]. Outside of pregnancy, the technique was developed for children and young adults and also for those considered were too frail for surgery [11]; it has also been used as a staged procedure prior to valve replacement at a later date. The number of described cases of aortic balloon dilatation in pregnancy remains small, but potential maternal complications include bleeding and severe acute aortic incompetence requiring urgent surgery. In the longer-term restenosis may develop.

Aortic Regurgitation as with mitral regurgitation is well tolerated in pregnancy because of the reduction in afterload. In the presence of left ventricular dysfunction, the volume load of pregnancy may induce symptoms of pulmonary congestion, necessitating restriction of activities, dietary interventions aimed at lowering sodium intake, and medical therapy for heart failure including diuretics, beta-blockers, and/or vasodilators. In cases such as severe infective endocarditis which result in marked aortic incompetence it maybe necessary to replace the damaged aortic valve although cases such as these are very sporadic [12]

2.3. Transcatheter aortic valve replacement

trans-Catheter aortic valve replacement is an approved procedure for symptomatic patients with severe aortic stenosis, who are too frail to have surgery. At present, there are only a handful of successful reports describing the use of TAVR in pregnancy [13,14]. In cases of aortic valve stenosis in pregnancy where balloon dilatation may result in severe valvular incompetence, TAVR provides a promising alternative, although longterm results are not known yet. Furthermore, the use of TAVR avoids the complications that are related to on-pump cardiac surgery, including placental hypoperfusion caused by cardiopulmonary bypass.

2.4. Aorta-aortic dissection

The aorta undergoes a marked alteration in structure with disruption of elastic lamellae, reduced proteoglycans and hypertrophy and hyperplasia of vascular smooth muscle [15]. Such changes are most marked in the third trimester and in the early postpartum period. Those with hypertension, pre-eclampsia and underlying aortopathies experience the greatest change in aortic structure [16,17]. Aberrant medial remodelling may contribute to the pathogenesis of aortic dissection, the incidence of which is substantially increased in pregnancy [18] A North American cross over cohort study of almost five million women comparing the period of pregnancy total control period of one year later showed pregnancy significantly increased the risk of dissection Odds Ratio 4 [18]. Indeed, according to the Confidential Enquiry into

Maternal Death in the United Kingdom, which has shown that cardiac disease is the leading cause of indirect maternal death, aortic dissection is the single largest underlying cardiac cause [2]. Aortic dissection in pregnancy in those without cardiac disease is rare. The risk of aortic dissection is greater in inherited aortopathies than the general obstetric population. A recent literature review of women with Marfan syndrome, a described 39 cases of dissection out of a total of 1271 pregnancies in women with Marfan syndrome of which 72% were Stanford Type A dissections [19]. Cardiac surgery is warranted in women with known aortic disease prior to pregnancy who have evidence of aortic dilatation, although dissection has been described in pregnancy even after previous root replacement [20]. For women with Marfan syndrome contemplating pregnancy with an aortic root reaching 45 mm then surgery prior to pregnancy should be considered; if there is a strong family history of sudden death or dissection then a lower threshold maybe considered. Furthermore, for women with bicuspid aortic valves, those with a root of >50 mm maybe best advised to consider aortic surgery prior to pregnancy [1]. In those with a dilated aortic root who become pregnant, imaging should be undertaken at bi-monthly intervals to assess for progression in aortic dilatation. This can either be done using echocardiography and MRI scanning particularly to image the distal part of the ascending aorta. Recent advice from the American College of Obstetrics and Gynaecology suggest that gadolinium scanning can be undertaken in pregnancy should it be necessary [21].

Women with acute Type A dissection will require immediate surgical management. In cases of Type B aortic dissection, this is best managed medically with strict blood pressure control, unless there is evidence of organ malperfusion when an endovascular approach may be considered.

2.5. Mechanical valve thrombosis

Thrombotic events are more common in pregnancy, probably related to the pro-thrombotic shift resulting from the increase in clotting factors and the reduction in thrombolytic activity [22]. The incidence of a valve thrombosis during pregnancy in women with a mechanical valve varies, but a prospective UK cohort study involving all UK maternity units, which was conducted over a 3 year period and included 58 women, gave a rate of (3.7 per 100,000 maternities [23], with two maternal deaths that were attributable to valve thrombosis. In the ROPAC study the rate of valve thrombus in their study 4.7% (10 women), with two maternal deaths, they reported 4 fetal deaths in this cohort [24]. In addition, a systematic review, which evaluated various anticoagulation regimens in pregnant women with a mechanical heart valve, found that the rate of valve thrombosis varied from 2.7%–8.7% [25].

Valve thrombosis can either be managed medically with thrombolysis or surgically, with valve repair or replacement. In pregnancy, there are little data to base the optimal management of a thrombosed metallic valve, which is often dictated by local expertise and available resources. In cases of a large thrombus for instance, thrombolysis is less likely to

have a favourable outcomes with higher risks of embolization in the systemic circulation and so surgery maybe the first treatment modality. On the other hand surgical treatment can be employed when thrombolysis has failed or when cardiac function is acutely compromised or in those with a large obstructive thrombosis necessitating urgent treatment.

2.6. Coronary disease

With increasing rates of obesity in the pregnant population and the trend to delay motherhood to later life when medical co-morbidities are more common, ischaemic heart disease is increasingly encountered during pregnancy [26]. About 10% of all episodes of myocardial infarction occur in women under 40 years of age [27]. Data from a UK prospective study estimated the incidence of ischaemic heart disease in pregnancy and up to one week postpartum to be 0.7 per 100,000 maternities, with age, smoking, hypertension and pre-eclampsia identified as independent risk factors [28]. In addition to ischaemic heart disease the incidence of coronary dissection, and coronary thrombosis all appear to be higher during pregnancy compared with outside pregnancy [26]. Hormonal changes in pregnancy cause a hypercoagulable state, whilst progesterone influences collagen in the vessel wall, enhancing the risk of coronary dissection [29].

3. Maternal and fetal risks of cardiac surgery during pregnancy

A recent systemic review and meta-analysis involving ten studies of cardiac surgery in pregnancy showed an overall maternal mortality of just over 11% [30]. Inevitably studies have shown emergency surgery was associated with a poorer maternal outcome and higher rate of death [31]. The need for reoperation and higher NYHA class have also been shown to correlate with increased maternal mortality [31]. In the study by Jha et al., the overall pooled rate of maternal complications stood at 15%, with the greatest single complication being maternal heart failure (5.8%), followed by arrhythmia (2.1%) and post-operative bleeding (2.1%) [30]. Arnoni et al. showed that the fetal mortality rate (overall 18.6%) was positively correlated with the need for reoperation (Odds Ratio 7.4) and emergency surgery (Odds Ratio 4.7) [31]. Fetal outcomes for women undergoing emergency surgery without prior delivery are unfavourable, with a fetal loss rate of over 30%. In their study, Avila et al. showed that of the 27 livebirths, 10% had evidence of serious neurological compromise (typically due to cerebral hypoxia). In a Brazilian review of almost 40 cases of cardiac surgery in pregnancy, the combined maternal complication and fetal complication rate was greater at 59%. They demonstrated higher rates of heart failure, but in their study the re-operation rate was 37% [32]. The majority of cases of surgery occurred in the second trimester. The overall pregnancy loss rate was 29% with 34% of women being delivered by caesarean section; after excluding cases of caesarean section performed prior to bypass surgery, this figure fell to 22.8% [49].

3.1. Mitral Valve disease treatment during pregnancy

Recent data from the ROPAC registry shows the risk of maternal death with mitral stenosis was almost 2% and that 23% of women with severe disease developed heart failure [6]. In their study 16/273 women required an intervention during pregnancy (14 percutaneous balloon treatment and two had open surgical repair. [33]. Several reports describe the benefits of intervening, both with an immediate improvement in maternal cardiac function and on the outcome of pregnancy [34,35].

A single centre study from India, performed over 13 years, included 96 patients who had undergone percutaneous valvuloplasty for mitral stenosis; the mean gestational age at intervention was 24 weeks [36]. It was successful in 72 women (80%), but 5 (6%) of women developed severe mitral regurgitation. In the group of women who had a successful cardiac outcome, 98% had favourable obstetric outcomes, with only one

documented case of intrauterine demise and the majority of women delivering at term. Mean follow up after delivery was 5 years in which time seven (9%) of women required repeat intervention for restenosis. Further report of percutaneous valvuloplasty have also shown very favourable maternal and fetal outcomes, with high rates of vaginal deliveries at term [37].

3.2. Aortic disease treatment during pregnancy

Maternal outcomes for women with aortic stenosis in pregnancy have improved significantly over the last few decades [9]. The ROPAC authors reported on 96 women with aortic stenosis in pregnancy (34 women had severe aortic stenosis); only one women required valvotomy during pregnancy [9]. In all other cases heart failure secondary to aortic stenosis could be managed medically. The rate of heart failure in their study was 11.5% consistent with other studies [38].

Type A dissection presents itself as a surgical emergency with immediate treatment for the mother. In a review of 75 women with dissection, of which 48 were Type A, over 75% occurred in the third trimester and the majority underwent Caesarean section followed by immediate repair. If surgery for type A dissection is required and if circulatory arrest is needed, then survival of the fetus is unfavourable, forcing a decision regarding the delivery of the fetus even at the extreme of viability.

In their cohort cross-over analysis Kamel et al. demonstrated that the risk of maternal death with Type A dissection in pregnancy was 28%. There were 36 cases of dissection identified, almost a third of which were managed surgically. They did not however report any fetal outcomes. Nevertheless a recent single centre UK series reported eleven cases of aortic surgery where the eight fetuses that survived surgery were all born at term [39], a better result than reported by Arnoni et al., who reported a fetal mortality rate of 18.6% [31]. Shu et al. described a small series of 4 women undergoing endovascular stenting due to Type B dissection (two occurred postpartum and two occurred in late third trimester at 38 weeks, with both babies delivered prior to percutaneous intervention [40].

3.3. Valve Thrombosis treatment during pregnancy

In their systematic review D'Souza et al. examined 66 cases of valve thrombosis where thrombolysis was used, there were seven cases of major bleeding reported, two maternal deaths (due to cardiogenic shock) and one fetal death due to a cerebral bleed [25]. A small prospective study (n = 29) evaluated the use of a low dose infusion of tissue plasminogen activator with favourable maternal and neonatal outcomes [41]. A systematic review comparing the management of thrombosed valves outside of pregnancy suggested that complications rates, such as thrombus reformation for patients managed with thrombolysis as opposed to surgical intervention were higher [42]. Thrombolytic agents are large molecules and are protein bound so do not appear to cross the placenta. Streptokinase and tissue plasminogen activator are the most widely used agents for mechanical valve thrombosis in pregnancy. Nevertheless, these treatments are associated with higher risk of maternal bleeding.

4. Management of coronary artery disease

The primary treatment modality for acute coronary syndrome in the general population is percutaneous intervention with stenting which should remain as the first choice in pregnant women also [1].

Coronary angiography can be undertaken in pregnancy with appropriate modification, to reduce fetal (and maternal exposure) to radiation. This includes a radial approach, high dose acquisition and reduced screening time as well as utilisation of echocardiographic guidance. UK data from the Royal College of Radiologists would suggest that the additional risk of childhood cancer attributable to angiography

is approximately 1 in 8000, where the background risk of childhood cancer is 1 in 500. Coronary artery assessment can also be done using CT angiography, but radiation doses here maybe just as great or greater.

In cases where coronary stenting is required both bare metal stents (BMS) and drug-eluting stents (DES) can be considered. BMS require a shorter duration of antiplatelet therapy (typically 1 month as opposed to 12 months for DES). However, long-term rates of repeat revascularisation are lower in women who have undergone DES as compared to BMS [43]. Therefore, the risk of re-stenosis should be balanced against that of bleeding. Clopidogrel has been successfully used without any reports of fetal concerns [44], but there is a concern for an increased risk of maternal bleeding [45]. It is prudent to stop Clopidogrel approximately 7 days prior to anticipated delivery to reduce the risk of bleeding, although there is a paucity of data to reaffirm this. There is no safety data to confirm the use of ticagrelor in pregnancy and at present it is contraindicated. As myocardial ischaemia can be caused by thrombus formation, treatment with heparins is considered the optimal management in pregnancy. They do not cross the placental and so have no fetal effect.

Open-heart surgery maybe performed in pregnancy which confers the same risk to the mother as outside of pregnancy with a high incidence of fetal death (20–33%). It appears that data for outcomes following coronary artery bypass surgery is similar to that of valve replacement [29].

5. Strategies to optimise outcomes

Ideally women with known valvular or aortic disease should be evaluated prior to pregnancy as part of preconception counselling (PCC) to consider if pre-pregnancy treatment is indicated or pregnancy contraindicated. In many circumstances women are not referred for PCC which may adversely impact on pregnancy outcomes [23]. Ideally women should be referred to a combined clinic where they have access to meet both a cardiologist, obstetrician and/or an obstetric physician. However, if pregnancy is unplanned or if women present without known disease and require surgery, then most clinicians generally believe that the second trimester is the safest period to operate for the fetus and potentially the mother also. This is a period when fetal organogenesis is largely complete, but the haemodynamic burden of pregnancy is not at its greatest [39,46]. Should semi-elective surgery be undertaken in the third trimester there is a greater perceived risk of preterm labour. Indeed it may be preferable to deliver by caesarean section prior to surgery with, consideration towards treatments that reduce the risks of morbidity associated with prematurity. This should include the administration of steroids to promote fetal lung maturation, magnesium sulphate infusion for fetal neuroprotection, and close liaison with the neonatal team, to ensure their presence at delivery.

Emergency surgery should be undertaken at any point during pregnancy if necessary, as generally the health of the mother outweighs any risk to the fetus and the outcome of the fetus highly depends on the status of the mother. In cases where the fetus is viable, it is largely preferable to deliver, typically by caesarean section, prior to cardiac surgery; this should always be in close co-ordination with the obstetric team [47]. In peri-viable cases, where there is a desire to continue the pregnancy to maximise the chances of fetal survival, then detailed multidisciplinary planning must be undertaken considering factors such as the exact gestational age and fetal birthweight. Recent guidance from the American College of Obstetricians and Gynaecologists suggests that in cases of non-obstetric surgery, where the fetus is viable, the fetal heart should be monitored before, during and after surgery.

6. Management of cardiopulmonary bypass during pregnancy

Cardiopulmonary bypass has multiple potentially adverse effects on pregnancy outcome as a result of changes in blood pressure, flow, and temperature [48]. Fetal death is most commonly noted during the

cooling and rewarming phases of bypass, which can be avoided with near normothermic bypass. Hypothermic circulatory arrest almost invariably results in fetal death and therefore should be avoided [49,50]. Further, pulsatile as opposed to non-pulsatile perfusion during bypass and high flow provide better uteroplacental perfusion reducing hypoxia, as has been shown in experimental models [51]. This increase in blood flow is thought to be partly due to release of nitric oxide [52]. Monitoring of the fetus using Doppler ultrasonography to assess blood flow in the umbilical and middle cerebral arteries can be considered to ensure adequate fetal brain oxygenation. Vasoconstrictor drugs should be avoided since they can precipitate reduced placental perfusion and fetal hypoxia. Serial fetal assessment by way of obstetric ultrasound following cardiac bypass should be considered to assess for fetal growth and signs of placental insufficiency [52,53].

7. Conclusion

Cardiac surgery remains rarely necessary in pregnancy, particularly in the developed world and due to the high risks should be used only when other alternatives are not valid. However, should cardiac surgery in pregnancy become necessary, then it is imperative that a team of clinicians with the appropriate expertise plans and carries out the surgery and that there is access to high-level neonatal care.

Conflict of interest

None.

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