Interventional cardiology in pregnancy

Introduction

Pregnancy is associated with significant haemodynamic changes in the maternal cardiovascular system, which increase the work load of the heart[11]. The patient with cardiovascular disease who is well in the non-pregnant state may have cardiac failure as the demand on the cardiorespiratory system increases during pregnancy. Over the last 15 years, interventional cardiology has emerged as a new therapeutic tool and as an effective alternative to surgical therapy in several cardiac diseases, but although interventional cardiology has been performed in the pregnant patient, there have been no large scale studies. However, some preliminary considerations can be made on the basis of existing literature, personal experience, and results obtained in non-pregnant women.

Mitral valve stenosis

Mitral valve stenosis is the most common and the most important cardiac valvular problem during pregnancy. With severe disease, pregnancy-related mortality is 5%. Labour, delivery, and the immediate puerperium appear to be the periods most at risk[2]. The symptoms may occur for the first time during pregnancy, usually in the middle trimester. The pressure gradient across the narrowed mitral valve may increase greatly during pregnancy because of the physiological increase in heart rate (decreasing the left ventricular diastolic filling time) and cardiac output of about 50%.

Labour and delivery are an additional burden on the maternal cardiovascular system. Increased left atrial pressure may result in atrial flutter or fibrillation, increasing the risk of the development of pulmonary oedema[3,4]. Treatment modalities include bed rest, reduction of the heart rate with beta-blockade, restriction of sodium intake, and appropriate diuretic therapy. However, in patients with significant mitral stenosis and class III New York Heart Association early in pregnancy, consideration should be given to either surgical intervention or percutaneous balloon mitral valvuloplasty. Surgical commissurotomy, open or closed, has been performed in recent decades during pregnancy with good results. Open mitral commissurotomy and valve replacement carry a greater risk of fetal demise than closed commissurotomy because of the necessity of cardiopulmonary bypass.

Closed mitral commissurotomy in pregnancy was first reported in 1952 when Brock[5], Cooley and Chapman[6], Logan and Turner[7], and Mason[8], performed a total of 11 closed mitral commissurotomies with one maternal death and one premature delivery. Since then several reports on closed mitral com-
grade of mitral regurgitation is predicted by the presence of regurgitation and the severity of stenosis before the procedure. In patients with pliable valves, the development of mitral regurgitation is less frequent. Creation of a significant atrial septal defect secondary to septal dilatation has been reported to vary from 5 to 20%[22,26,44] and is haemodynamically insignificant in all patients. The long-term effect of these shunts is unknown, but it seems that most atrial septal defects close within 24 h[22].

Since 1988, there have been 141 reports of percutaneous balloon mitral valvuloplasty in pregnant women with severe mitral stenosis[35-71]. Immediate clinical and haemodynamic results are well documented for 115 patients and are shown in Table 1. The mean gradient across the stenotic mitral valve declines from a mean value of 21 to 5 mmHg, with the mitral valve area increasing from a mean value of 0·9 to 2·1 cm². There have been no reports of serious maternal complications and only one fetal death[71]. The reported incidence of mitral regurgitation is low, and in most cases it was only trivial or mild.

Table 1 Results of percutaneous balloon mitral valvuloplasty in pregnancy in the series reported in the literature

<table>
<thead>
<tr>
<th>Study authors</th>
<th>Number of patients</th>
<th>Age (years)</th>
<th>Gestation period (weeks)</th>
<th>Gradient (mmHg)</th>
<th>Valve area (cm²)</th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>Mangione[47]</td>
<td>5</td>
<td>27</td>
<td>27</td>
<td>24</td>
<td>7</td>
<td>1·1</td>
</tr>
<tr>
<td>Smith[48]</td>
<td>1</td>
<td>29</td>
<td>23</td>
<td>14</td>
<td>6</td>
<td>0·9</td>
</tr>
<tr>
<td>Esteves[49]</td>
<td>13</td>
<td>26</td>
<td>25</td>
<td>20</td>
<td>4</td>
<td>0·9</td>
</tr>
<tr>
<td>Drobnik[50]</td>
<td>1</td>
<td>27</td>
<td>19</td>
<td>16</td>
<td>2</td>
<td>1·1</td>
</tr>
<tr>
<td>Tugeman[51]</td>
<td>1</td>
<td>26</td>
<td>20</td>
<td>24</td>
<td>7</td>
<td>0·8</td>
</tr>
<tr>
<td>Zimaring[52]</td>
<td>1</td>
<td>26</td>
<td>23</td>
<td>13</td>
<td>5</td>
<td>0·9</td>
</tr>
<tr>
<td>Ribiero[53]</td>
<td>7</td>
<td>32</td>
<td>24</td>
<td>—</td>
<td>—</td>
<td>0·8</td>
</tr>
<tr>
<td>Lee[57]</td>
<td>1</td>
<td>28</td>
<td>26</td>
<td>32</td>
<td>8</td>
<td>0·9</td>
</tr>
<tr>
<td>Glante[62]</td>
<td>1</td>
<td>27</td>
<td>29</td>
<td>19</td>
<td>2</td>
<td>0·6</td>
</tr>
<tr>
<td>Patel[63]</td>
<td>19</td>
<td>30</td>
<td>29</td>
<td>18</td>
<td>6</td>
<td>0·8</td>
</tr>
<tr>
<td>Kokov[64]</td>
<td>13</td>
<td>19-32</td>
<td>—</td>
<td>25-40</td>
<td>2-8</td>
<td>0·9-1·7</td>
</tr>
<tr>
<td>Cardoso[65]</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>21</td>
<td>10</td>
<td>0·7</td>
</tr>
<tr>
<td>Ledesma-Velasco[67]</td>
<td>2</td>
<td>—</td>
<td>33</td>
<td>15</td>
<td>2</td>
<td>0·7</td>
</tr>
<tr>
<td>Rachor[69]</td>
<td>1</td>
<td>26</td>
<td>17</td>
<td>—</td>
<td>—</td>
<td>1·4</td>
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<tr>
<td>Farhat[70]</td>
<td>36</td>
<td>26</td>
<td>26</td>
<td>28</td>
<td>14</td>
<td>0·9</td>
</tr>
<tr>
<td>Born[71]</td>
<td>16</td>
<td>—</td>
<td>—</td>
<td>19</td>
<td>5</td>
<td>0·9</td>
</tr>
</tbody>
</table>

Balloon inflation generally causes transient maternal hypotension and a transient decrease in fetal heart rate. Both parameters return to baseline within a few seconds of balloon deflation, with no serious fetal distress noted. However, in one case, transient bundle branch block developed an hour after the procedure[48] and in another transient first-degree atrio-ventricular block occurred[49]. During balloon mitral valvuloplasty, the supine position is necessary: this may cause maternal hypotension that can be alleviated by intravenous fluid infusion. The recumbent position causes compression of the gravid uterus on the pelvic vessels that may obstruct the passage of catheters, and the use of fluoroscopy during the procedure carries the risk of fetal radiation exposure (discussed below). In the pregnant patient, the procedure has been performed both with the single- and the double-balloon technique. With the Inoue single-balloon catheter, the process is considerably shorter than with the double-balloon technique, with a reduction in the fluoroscopic time.

Transoesophageal ultrasound can be used during percutaneous balloon valvuloplasty in order to minimize radiation exposure. However, this technique entails a greater need for sedation and has not been shown to improve outcome[62].

The results of the procedure in pregnant women appear to benefit both the mother and fetus, but it should be noted that 12 out of 27 of the cases cited were successful case reports. In our experience with four cases of balloon mitral valvuloplasty in pregnant women, one resulted in severe mitral regurgitation and required urgent surgical mitral valve replacement, with loss of the fetus. The patient had severe, symptomatic mitral stenosis and an echocardiographic score of 12 (thickened and calcific mitral leaflets with involvement of subvalvular apparatus).

At present, all patients with severe mitral stenosis in functional class III/IV New York Heart Association and a favourable valvular anatomy seem to be the best candidates for percutaneous mitral valvuloplasty. In asymptomatic patients, the risk of maternal death is very low. However, deterioration in haemodynamic conditions can be expected and emergency commissurotomy may become necessary. A simple 'rule of thumb' is an increase of one New York Heart Association functional class. In these cases a 'prophylactic' percutaneous mitral valvuloplasty should be considered, provided there is a satisfactory echocardiographic score (<8).

Balloon mitral valvuloplasty in the pregnant patient is a technically complex procedure that needs to be done quickly, that may require subsequent surgery, and should only be attempted in centres that have extensive experience with this procedure.

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Aortic valve stenosis

Severe aortic valve stenosis is very rare during pregnancy, because the congenital form is more commonly found in men. Severe stenosis in the rheumatic form is progressive and is therefore unusual in women of child-bearing age (with average age at clinical presentation of about 48 years).

Although pregnancy necessitates increased cardiac output, this tends to be tolerated in women with mild-to-moderate aortic stenosis. The major problem in the pregnant patient with severe aortic valve stenosis is maintenance of adequate cardiac output across a fixed aortic valve. With severe disease, in which cardiac output is relatively fixed, there is a narrow window of appropriate fluid loading. Small decreases in preload due to haemorrhage or regional anaesthesia may result in decreased cardiac output and dangerous clinical hypotension. On the other hand, small increases in vascular volume may produce dramatic increases in filling pressures, resulting in pulmonary oedema. Since the publication of the review by Arias and Pineda in 1978, which reported a maternal mortality as high as 17% in pregnant patients with aortic stenosis, pregnancies have been discouraged in these patients.

Our series includes 129 pregnancies in 58 patients with valvular aortic stenosis, with complications of 10% and no maternal deaths. A transvalvular gradient greater than 50 mmHg was only present in 14. A very low overall mortality, approaching 0, has also been observed by others recently. The unfavourable outcome reported by Arias and Pineda was most likely because their pregnant patients had a severe form of the disease. Intervention (either surgical with valvotomy or valve replacement, or percutaneous balloon aortic valvuloplasty) is therefore indicated only in severe, symptomatic aortic valve stenosis. During pregnancy, due to the increase in cardiac output, the transvalvular gradient may double its basal value. Aortic stenosis should probably only be considered severe if the gradient is greater than 100 mmHg. In this setting, calculation of aortic valve area provides an index of the stenosis independent of changes in transaortic volume flow. Other useful information can be obtained from clinical indices of severity, such as electrocardiographic and echocardiographic hypertrophy.

Since the first report in 1983, balloon aortic valvuloplasty appears to be an effective and safe technique for treating congenital aortic stenosis in children. However, this procedure in adults does not have as good results as a palliative procedure and is limited to high risk surgical patients. There may be complications with aortic valvuloplasty, such as embolic phenomena, massive aortic regurgitation, aortic rupture and haemopericardium. Transient conduction defects have also been reported. In the literature, only four cases of percutaneous balloon aortic valvuloplasty have been reported during pregnancy in patients with severe and symptomatic congenital aortic valve stenosis.

In each of the four cases, the gradient across the aortic valve was halved (Table 2) and the pregnancy was carried out uneventfully. Aortic balloon valvuloplasty is contraindicated in women with significant aortic regurgitation as well as in those with heavily calcified valves.

The long-term efficiency of percutaneous balloon aortic valvuloplasty has not been established and it must be considered as a palliative procedure, enabling the pregnancy to continue.

Coarctation of the aorta

Coarctation of the aorta is also rare during pregnancy. This congenital cardiac disease accounts for approximately 9% of all congenital cardiac defects and predominates in males, with a sex ratio as high as 3:1. The condition is likely to produce significant symptoms during two stages of life, first in early infancy (when the ductus closes) and second after age 20 to 30 years. Once beyond infancy, patients with coarctation of the aorta are usually asymptomatic when first diagnosed.

The risk to pregnant patients with coarctation of the aorta was found to be as high as 17% in the first published reports (which probably included very sick patients). Uncomplicated, uncorrected coarctation nowadays carries a maternal mortality risk of less than 3%. The four common fatal complications are dissecting aneurysm and rupture of the aorta, congestive heart failure, bacterial endocarditis, and rupture of an intracranial arterial aneurysm.

Pregnancy per se seems to be a condition that predisposes to dissection: biochemical alterations in systemic arterial connective tissue are thought to occur during pregnancy owing to alterations in hormonal levels, especially elevated oestrogen concentrations. In addition, the increase in blood volume and cardiac output may further predispose to dissection.

Table 2  The transvalvular aortic gradient and the aortic valve area are reported before and after percutaneous balloon valvuloplasty in four pregnant patients

<table>
<thead>
<tr>
<th>Study authors</th>
<th>Age (years)</th>
<th>Gestation period (weeks)</th>
<th>Gradient (mmHg) Before</th>
<th>Gradient (mmHg) After</th>
<th>Aortic valve area (cm²) Before</th>
<th>Aortic valve area (cm²) After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angel³⁷⁸</td>
<td>17</td>
<td>19</td>
<td>133</td>
<td>68</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>McIvor³⁷⁹</td>
<td>19</td>
<td>14</td>
<td>64</td>
<td>32</td>
<td>0·67</td>
<td>1·12</td>
</tr>
<tr>
<td>Lao³⁸⁰</td>
<td>26</td>
<td>16</td>
<td>112</td>
<td>42</td>
<td>0·5</td>
<td>1·0</td>
</tr>
<tr>
<td>Perloff³⁸³</td>
<td>26</td>
<td>36</td>
<td>100</td>
<td>30</td>
<td>—</td>
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</tr>
</tbody>
</table>

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output, above all in the third trimester, may increase the risk of aortic rupture. Hypertension, when present during pregnancy, is another known risk factor for dissection.

Left ventricular failure is rare despite the augmented volume imposed upon the pressure-loaded left ventricle.

Since 1982, percutaneous balloon angioplasty of coarctation of the aorta has been performed in a large number of patients with native coarctation and post-operative recoarctation\cite{84-87}. Post dilatation angiography often disclosed intimal tears and long-term follow-up in some patients demonstrated development of saccular or fusiform aortic aneurysms\cite{88-90}. For these reasons percutaneous balloon angioplasty of coarctation of the aorta should be avoided in the pregnant patient and in fact has never been reported in the literature.

**Pulmonary valve stenosis**

Pulmonary valve stenosis is a more common problem because 50% of patients are female and can reach adult life without symptoms, even if the gradient through the stenotic valve is high\cite{91}.

During pregnancy, right ventricular obstruction tends to be well tolerated despite the gestational volume overload imposed on an already pressure-loaded right ventricle. Out of 136 pregnancies reported in the literature and our own series of 60 pregnant women\cite{75,86,92} with pulmonary valve stenosis, no deaths were reported and there was a low incidence of minor maternal complications (about 15%).

Since the first percutaneous balloon pulmonary valvuloplasty, reported by Kan et al. in 1982\cite{93}, this procedure has become the main treatment for children and adults with pulmonary stenosis. Percutaneous balloon pulmonary valvuloplasty was shown to be safe and effective, and the mortality and morbidity associated with it appear to be minimal. The only reported complications have been arrhythmias and hypotension and transient right bundle branch block. Mild postoperative low pressure pulmonary regurgitation is very infrequent and clinically irrelevant. However, percutaneous balloon pulmonary valvuloplasty may be indicated in pregnant women only in very severe (gradient suprasystemic) and/or symptomatic cases. In the literature only two cases are reported. The first case was an 18-year-old pregnant woman, near term, with severe pulmonary stenosis, in which, after balloon dilatation, right ventricular pressure fell from 280 to 60 mmHg, and the right ventricular to pulmonary arterial gradient decreased to 40 mmHg\cite{94}. The second case was a young Indian pregnant woman in her third trimester\cite{95}. The procedure was performed without complications in both cases. In our department we performed a percutaneous balloon pulmonary valvuloplasty in a pregnant woman following the wishes of the mother and the family doctor, with good result and a subsequent natural delivery. The gradient decreased from 130 to 40 mmHg.

**Coronary artery disease**

Coronary artery disease is mainly a disease of elderly women and its incidence in women of child-bearing age is very low. However, pregnancy may create a significant problem in patients with limited coronary reserve because of the haemodynamic changes that increase the myocardial oxygen requirement. The increase in cardiac output, resting heart rate, and total blood volume, and the fact that the absolute rise in cardiac output in response to exercise is higher during pregnancy results in the early appearance of symptoms of myocardial ischaemia; they are also more difficult to manage. In the literature only two successful cases of coronary angioplasty are reported in pregnant patients\cite{94,95}. In both cases, angioplasty was performed because of ongoing angina after acute myocardial infarction. The outcome was good in both mothers and their embryos, without complications.

**Fetal risk of radiation and contrast medium**

Cardiac catheterization in the pregnant patient carries the risk of fetal radiation exposure. The effects of radiation on the fetus depend on the radiation dose and the gestational age at which exposure occurs. The maximal permissible dose of radiation to the pregnant woman has been set at 0.5 rad, but some authors have suggested that a 10 rad exposure is safe\cite{97,98}. If the radiation fetal dose in excess of 25 rad, elective pregnancy termination should be recommended because the risk of adverse outcome is high.

The effects of radiation during pregnancy can be divided into three main phases. Irradiation during the pre-implantation period (0 to 9 days) tends to cause death rather than anomalies. The effects appear to be 'all or none'\cite{99}. The incidence of spontaneous embryo resorption during the first 2 weeks of gestation is approximately 25–50%, and a dose of 10 rad is estimated to increase that number by 0–1%. During the period of active organogenesis (9 to 42 days) radiation causes severe structural anomalies. A dose of 200 rad will produce a 100% incidence of congenital abnormalities, whereas a dose of 10 rad results in a 1% increase in malformations over a baseline of 5–10%. During the second and third trimester, risks are primarily related to the development of childhood leukemia\cite{100} and other malignancies\cite{101}. It has been estimated that a dose of 1 rad increases the risk of childhood cancer by two cases per 100 000 births to a total of six cases in 100 000 live births\cite{102}. Although the development of most organs is complete by 9 to 12 weeks, the brain continues to grow and thus remains sensitive to the effects of radiation. Some reports have correlated radiation exposure to mental retardation and microcephaly\cite{99,103}.

It has been calculated that cardiac catheterization (with the use of fluoroscopy and cineangiography)
causes a mean value of skin dose of 47 rad per examination, a mean radiation exposure to the chest of 1.1 rad, and the unshielded abdomen of 0.15 rad. When there is a direct exposition of the maternal pelvis to radiation, less than 20% of such dose reaches the fetus because of tissutal attenuation. During cardiac catheterization in the pregnant patient some precautions should be taken in order to minimize the fetal risk. The gravid uterus should be shielded from direct radiation with a lead barrier wrapped circumferentially around the mother’s abdomen, from the respiratory diaphragm to the symphysis pubis. Fluoroscopic time should be shortened and cineangiography avoided to keep scattered radiation to a minimum. If possible, the procedure should be performed after the period of major organogenesis (>12 weeks after last menses). The risk of fetal hypothyroidism, for the use of iodine contrast, is present after 25 weeks of gestation when the thyroid becomes active. However, this risk is minimal with the amount of inert iodine dye used during the procedure. The best period for performing percutaneous balloon valvuloplasty is considered to be the 4th month, during which period, the organogenesis is terminated, the thyroid of the fetus is still inactive and the volume of the uterus is small so that there is a greater distance between the fetus and the chest than in the following months. During percutaneous balloon mitral valvuloplasty, the radiation exposure to the fetus has been estimated to be less than 0.2 rad in one study and 0.05 rad in another. This dose is far below the maximum radiation recommended for therapeutic absorption, so we believe that performing cardiac catheterization and interventional procedures during pregnancy is safe for the fetus.

**Conclusions**

Available data suggest that interventional cardiology may have a place in several cardiac diseases in pregnancy, such as the ones discussed, provided such procedures are very carefully evaluated by experienced operators. There are several other conditions that could, theoretically, be treated with transcatheter procedures even during pregnancy. These include obstructions of venous or arterial pathways in complex congenital heart disease, closure of shunts, etc. So far, no such procedures have been carried out in pregnant women and it seems reasonable to suggest that any attempt should be made only in presence of life-threatening situations.

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