Indications for Cardiopulmonary Bypass During Pregnancy and Impact on Fetal Outcomes

Indikationen für kardiopulmonalen Bypass in der Schwangerschaft und Auswirkung auf fetale Sterblichkeit

Abstract

Background: Cardiac operations in pregnant patients are a challenge for physicians in multidisciplinary teams due to the complexity of the condition which affects both mother and baby. Management strategies vary on a case-by-case basis. Feto-neonatal and maternal outcomes after cardiopulmonary bypass (CPB) in pregnancy, especially long-term follow-up results, have not been sufficiently described.

Methods: This review was based on a complete literature retrieval of articles published between 1991 and April 30, 2013.

Results: Indications for CPB during pregnancy were cardiac surgery in 150 (96.8%) patients, most of which consisted of valve replacements for mitral and/or aortic valve disorders, resuscitation due to amniotic fluid embolism, autotransfusion, and circulatory support during cesarean section to improve patient survival in 5 (3.2%) patients. During CPB, fetuses showed either a brief heart rate drop with natural recovery after surgery or, in most cases, fetal heart rate remained normal throughout the whole course of CPB. Overall feto-neonatal mortality was 18.6%. In comparison with pregnant patients whose baby survived, feto-neonatal death occurred after a significantly shorter gestational period at the time of onset of cardiac symptoms, cardiac surgery/resuscitation under CPB in the whole patient setting, or cardiac surgery/resuscitation with CPB prior to delivery.

Conclusions: The most common surgical indications for CPB during pregnancy were cardiac surgery, followed by resuscitation for cardiopulmonary collapse. CPB was used most frequently in maternal cardiac surgery/resuscitation in the second trimester. Improved CPB conditions including high flow, high pressure and normothermia or mild hypothermia during pregnancy have benefited maternal and feto-neonatal outcomes. A

Zusammenfassung


Schlussfolgerung: Die häufigsten chirurgischen Indikationen für CPB während der Schwangerschaft waren Herzoperationen, gefolgt von Reanimationen wegen kardiopulmonalem Kollaps. Die
shorter gestational period and the use of CPB during pregnancy were closely associated with feto-neonatal mortality. It is therefore important to attempt delivery ahead of surgery/CPB or to defer surgery till late pregnancy.

**Introduction**

In 1958, Dubourg et al. [1] first reported on a repair of tetralogy of Fallot under cardiopulmonary bypass (CPB) in a pregnant patient (10th week of gestation), who unfortunately had a spontaneous abortion at 6 months’ gestation. Since then, cardiac surgery with CPB has increasingly been performed in pregnant patients, with premature babies more likely to survive as medical skill and experience has improved, even though fetuses remain at high risk during maternal cardiac surgery [2]. Clinical reports have shown that cardiac surgery under CPB during pregnancy is associated with a maternal mortality of around 3%, similar to that of non-pregnant patients [3, 4]. Fetal demise was more likely with urgent, high-risk cardiac surgery and maternal co-morbidities and if surgery was carried out in the early gestational period [5]. Fetal morbidity and mortality during maternal cardiac surgery were as high as 9 and 30%, respectively [6], and fetal mortality was much higher prior to 15 weeks’ gestation compared to after 15 weeks’ gestation (17 vs. 2.4%) [7]. There is evidence that profound hypothermia with total circulatory arrest could lead to even higher fetal mortality rates [8]. A comprehensive survey revealed that fetal mortality varies during different periods of gestation; fetal mortality was 29, 3 and 0%, respectively, for pre-pregnant patients who had cardiac surgery with CPB during pregnancy, immediately after delivery, or delayed until after delivery [5].

Many case reports have described their individual experiences with cardiac surgery and CPB in pregnant patients and the feto-neonatal outcomes. CPB during pregnancy has been debated in a series of publications [4, 6, 9–14]. However, reviews were mostly narrative, and case reports were anecdotal. Few expressed their results with sufficient statistical support. A few surveys [2, 5, 7, 15] have comprehensively analyzed the published materials, offering interesting information on the topic. The excellent survey by Weiss et al. [5] was of particular interest with regard to maternal outcomes after cardiac surgery during pregnancy with or without CPB, but their consensus on feto-neonatal outcomes may warrant further examination. At all events, feto-neonatal mortality remains a problem. In order to offer optimal care to mother and fetus, the present article aims to examine the indications for CPB during pregnancy and the impact of CPB on fetal outcome by reviewing the available data.

**Materials and Methods**

Relevant literature published in English between 1991 and April 30, 2013 was retrieved from MEDLINE, Highwire Press and using the Google search engine. The search terms included “pregnancy” and “cardiopulmonary bypass”, “cardiac surgical procedures”, “congenital heart defects”, “heart valves” “aortic operation”, “coronary artery bypass”, “cardiac neoplasms”, “thrombectomy”, or “amniotic fluid embolism”. Information from cited references helped complete the collection of literature. Using this retrieval policy, a total of 157 articles were collected. Patients who developed aortic dissection during pregnancy and had surgery with CPB with or without profound hypothermic circulatory arrest, and patients with onset of cardiac symptoms after delivery who were managed surgically with CPB were not included. Pregnant patients who received off-pump coronary artery bypass were excluded from this study. After these articles had been omitted, a total of 76 reports remained [16–91]. Information on each individual case was carefully abstracted from the reports and tabulated to facilitate statistical analysis. Information collected included patients’ age, gestation period at the time of onset of symptoms, gestation period at the time of CPB, duration of gestation from onset of symptoms to CPB, indications for CPB, types of cardiac surgery/resuscitation, CPB conditions (arterial pressure, flow rate, minimum core temperature, CPB time and cross-clamping time), mode of delivery, gestation period at delivery, fetal heart rate (FHR), prognoses and follow-up periods for mother and baby.

Measurement data and enumeration data were expressed as mean ± standard deviation or frequencies, and compared using paired or unpaired t-test and $\chi^2$ test, respectively. Two-tailed $p < 0.05$ was considered statistically significant.

**Results**

**Patient information**

A total of 76 reports with 155 patients [16–91] met the retrieval policy. Patients were aged between 28.6 ± 5.9 (range, 17–45; median, 28) years (n = 145). Their pregnancy was in the 22.3 ± 9.2 (range, 3–41; median, 22) week of gestation (n = 146), with 28 (19.2%), 72 (49.3%) and 46 (31.5%) cases, respectively, in each of the three trimesters at the time of onset of cardiac symptoms. The pregnancy was in the 23.3 ± 9.2 (range, 3–41; median, 24) week of gestation (n = 144), with 23 (16.0%), 67 (46.5%) and 54 (37.5%), respectively, in each of the three trimesters at the time of cardiac surgery/CPB. Three (1.9%) patients were current or previous drug abusers.

**Indications for CPB**

In this patient setting, 150 (96.8%) patients had cardiac surgery: 108 (69.7%) patients had cardiac surgery at 16.1 ± 8.4 (range, 0.024–8; median, 17) weeks of gestation prior to delivery (n = 77), 34 (22.7%) patients had one-stage consecutive delivery and cardiac surgery, and 10 (7.2%) patients had cardiac surgery performed at 0.9 ± 1.3 (range, 0.012–3; median, 0.1) weeks after.

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Yuan S-M Indications for Cardiopulmonary... Geburtsfr Frauenheilk 2014; 74: 55–62
Table 1  Indications for CPB in 155 pregnant patients.

<table>
<thead>
<tr>
<th>Indication</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvular disorder</td>
<td>57 (36.8)</td>
</tr>
<tr>
<td>MS</td>
<td>28 (18.1)</td>
</tr>
<tr>
<td>MR</td>
<td>9 (5.8)</td>
</tr>
<tr>
<td>MR, MS</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Mitral valve disorder (pathology not stated)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>AS</td>
<td>10 (6.5)</td>
</tr>
<tr>
<td>AR, MR</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>AS, MR, MS</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Aortic valve disorder (pathology not stated)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>TR, MR post-ASD &amp; pulmonary stenosis repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Congenital heart defects</td>
<td>19 (12.3)</td>
</tr>
<tr>
<td>Atrioventricular canal defect, perforated mitral valve</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Cor triatriatum</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>ASD</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>AS, bicuspid aortic valve</td>
<td>6 (3.9)</td>
</tr>
<tr>
<td>Unicuspid aortic valve</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>ASD, AS</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Ebstein’s anomaly, Wolff-Parkinson-White syndrome</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Ruptured sinus of Valsalva of the right coronary cusp</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>PFO</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>PFO, paradoxical embolism</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>PFO, paradoxical embolism, DIC</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>PFO, paradoxical embolism, cardiopulmonary collapse, DIC, amniotic fluid embolism</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Prosthetic valve disorders</td>
<td>29 (18.7)</td>
</tr>
<tr>
<td>Prosthetic valve thrombus</td>
<td>14 (8.0)</td>
</tr>
<tr>
<td>Prosthetic AV stuck</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>MS post-MVR</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Biologic prosthetic aortic valve deterioration</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>MS, MR post-AVR+MVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Prosthetic AS</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>LA thrombus post-AVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Prosthetic valve problem (pathology not given)</td>
<td>4 (2.6)</td>
</tr>
</tbody>
</table>

Aortic disorders: 10 (6.5)

- Aortic aneurysm: 8 (5.2)
  - Aortic root 2 (1.3), ascending aorta 2 (1.3), aortic arch 2 (1.3), descending aorta 1 (0.7), and thoracoabdominal aorta 1 (0.7)
- Ascending aortic aneurysm, mitral valve prolapse: 1 (0.7)
- Traumatic thoracic aortic rupture: 1 (0.7)
- Pulmonary artery embolism: 5 (3.2)
  - Amniotic fluid embolism, cardiopulmonary collapse: 5 (3.2)
    - (1 [0.7%] patient had presumed amniotic fluid embolism and 1 [0.7%] patient had PFO as listed above)
- Coronary artery disease: 1 (0.7)
- Annuloaortic ectasia in Marfan syndrome: 1 (0.7)
- Hypertrophic cardiomyopathy (HCM), systolic anterior motion of the mitral valve (SAM): 1 (0.7)
- Synchronous autotransfusion: 1 (0.7)


delivery. Five (3.2%) patients did not have cardiac surgery but required CPB during resuscitation (Tables 1 and 2).

Modes of CPB

Standard CPB was established in 150 (96.8%) patients (deep hypothermic circulatory arrest was instituted in 2 patients for 24 and 37 minutes, respectively; intraaortic balloon pump was used in 3 patients), right femoral artery-right atrium bypass in 2 (1.3%) patients, right femoral vein bypass (details not given) in 1 (0.7%) patient, extracorporeal membrane oxygenation (left femoral artery-right femoral vein bypass) with intraaortic balloon pump in 1 (0.7%) patient in whom right ventricular assist device was used for successful weaning from CPB. The flow rate was 3.4 ± 1.3 (range, 1.7–6.8; median, 2.5) ml/kg/min (n = 75), arterial pressure was 70.7 ± 7.1 (range, 50–90; median, 70) mmHg (n = 67), and minimum core temperature was 32.7 ± 3.8 (range, 19–38.3; median, 33) (n = 115). CPB time was 89.5 ± 50.6 (range, 16–340; median, 78) min (n = 113), and duration of cross-clamping time was 64.1 ± 35.2 (range, 0–170; median, 55) min (n = 63). A total of 131 pregnant patients delivered 132 babies at 36.3 ± 4.2 weeks of gestation (n = 108). Two (1.5%) babies died after delivery. In addition, 27 fetuses died at 20.1 ± 7.3 (range, 7–35.4; median, 22) weeks of gestation (n = 21) (Table 3). Overall feto-neonatal mortality was 18.6% (29/156).

Fetal monitoring

Use of fetal monitoring during cardiac surgery was reported in 27 cases: there was fetal heart asystole during aortic cross-clamping in 2 (7.4%) cases, limited fetal movement in 1 (3.7%), brief FHR drop during CPB with gradual recovery after cardiac operation in 12 (44.4%), transient FHR drop during CPB with subsequent resolution by increasing the flow rate or temperature in 2 (7.4%), and normal FHR throughout the CPB course in 10 (37.0%) cases (χ² = 25.3, p < 0.0001).
Cardiac surgery or resuscitation with cardiopulmonary bypass.

<table>
<thead>
<tr>
<th>Major operation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve surgery</td>
<td></td>
</tr>
<tr>
<td>1. MVR</td>
<td>34 (21.9)</td>
</tr>
<tr>
<td>2. Mitral valve repair</td>
<td>10 (6.5)</td>
</tr>
<tr>
<td>3. MVR, tricuspid valve repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>4. MVR, TVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>5. AVR, MVR</td>
<td>21 (13.5)</td>
</tr>
<tr>
<td>6. AVR, MVR</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>7. AVR, ascending aorta replacement</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>8. AVR, mitral valve anuloplasty</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>9. AVR, ruptured sinus of Valsalva repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>10. AVR, coronary artery bypass grafting</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>11. Composite AVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>12. TVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>13. Redo MVR</td>
<td>18 (11.6)</td>
</tr>
<tr>
<td>14. Redo AVR</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Cardiac tumor resection</td>
<td></td>
</tr>
<tr>
<td>15. Cardiac myxoma excision</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>16. Cardiac myxoma excision, MVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>17. Cardiac myxoma excision, mitral valve repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>18. Cardiac lipoma excision</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>19. Cardiac leiomyomatosis excision</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>20. Cardiac osteosarcoma excision</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>21. Incomplete resection of cardiac sarcoma, MVR, modified De Vega tricuspid anuloplasty</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Thrombectomy</td>
<td></td>
</tr>
<tr>
<td>22. Pulmonary artery embolectomy</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>23. Pulmonary artery embolectomy &amp; atrial septal defect repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>24. Thrombectomy of the left atrium</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>25. Embolectomy (right atrium, bilateral pulmonary arteries and common iliac arteries)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>26. Prosthetic mitral valve debridement &amp; declotting</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>27. Prosthetic aortic valve thrombectomy</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>28. Prosthetic aortic valve debridement</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Congenital heart defect surgery</td>
<td></td>
</tr>
<tr>
<td>29. Patent fossa ovalis closure</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>30. Patent fossa ovalis closure, paradoxical embolism removal</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>31. Tetralogy of Fallot repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>32. Atrial septal defect closure</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>33. Atrial septal defect closure, MVR</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>34. Accessory pathway ablation, tricuspid anuloplasty</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>35. Cor triatriatum repair</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Coronary surgery</td>
<td></td>
</tr>
<tr>
<td>36. Coronary artery bypass grafting × 2, intraaortic balloon pump</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Other cardiac surgery</td>
<td></td>
</tr>
<tr>
<td>37. Aortic aneurysm repair</td>
<td>5 (3.2)</td>
</tr>
<tr>
<td>38. Descending aorta-innominate artery bypass</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>39. Extra-anatomic bypass graft</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>40. Septal myxoma</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>No cardiac operation</td>
<td></td>
</tr>
<tr>
<td>41. Cesarean section under cardiopulmonary bypass (circulatory support during surgery to improve the patient’s chances of survival)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>42. Open chest cardiac massage (no evidence of pulmonary artery thrombosis)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>43. Placement of a right ventricular assist device</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>44. Resuscitation with extracorporeal membrane oxygenation, intraaortic balloon pump</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>45. Synchronous autotransfusion</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>

FHR monitoring was reported in 29 cases. Brief FHR drop occurred in 17 (58.6%) cases, with a drop from 140 ± 23.2 (range, 120–180; median, 135) beats per minute (bpm) to 63.2 ± 10.5 (range, 40–80; median, 65) bpm (n = 13) (p < 0.0001). FHR remained normal at 132.5 ± 16.6 (range, 110–135; median, 135) bpm (n = 4) during cardiac surgery in 10 (34.5%) cases. Fetal heart asystole during CPB was noted in two (6.9%) cases (χ² = 17.5, p = 0.0002).

Feto-neonatal outcomes

Follow-up was 15.5 ± 16.0 (range, 3–54; median, 9) months (n = 22) for the mothers and 14.7 ± 13.3 (range, 3–48; median, 10.5) months (n = 10) for the neonates. There were eight hospital maternal deaths out of 155 pregnant patients, resulting in an early mortality of 5.2%.

Feto-neonatal outcomes were compared between two groups: one consisting of the patients whose baby survived and the other of patients whose babies/fetuses died. Gestation periods for pregnant patients with feto-neonatal death were significantly shorter at the onset of cardiac symptoms, at cardiac surgery/resuscitation with CPB in the whole patient setting, and at cardiac surgery/resuscitation under CPB performed prior to delivery compared to patients whose baby survived. A significant difference in rates of surviving and dead fetuses/babies was also noted in terms of the gestation period at the time of delivery. There was no statistically significant difference in CPB conditions, including arterial pressure, flow rate and minimum core temperature, between patients whose baby survived and those whose baby/fetus died, and there were no differences with regard to CPB times or cross-clamping times (Table 4).

Comparisons of gestation times among the three trimesters between patients whose baby survived and those whose baby/fetus died showed significant differences. However, no differences were found between the two groups with regard to CPB times and the time of delivery (Table 5).

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean section</td>
<td>65 (41.9)</td>
</tr>
<tr>
<td>Vacuum delivery</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Stillborn</td>
<td>6 (3.9)</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Operative death</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Cesarean section &amp; hysterectomy</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Delivery method not stated</td>
<td>30 (19.4)</td>
</tr>
<tr>
<td>Induced labor</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Forceps delivery</td>
<td>3 (1.9)</td>
</tr>
</tbody>
</table>

vascular resistance [95]. Pulsatile perfusion may reduce uterine 
steroids administration during bypass may attenuate placental 
tion may be mediated by prostaglandins and indomethacin, and 
tive factors for uterine contractions [11]. Placental vasoconstric-
ors to placental dysfunction following CPB [94]. During CPB, 
prime volumes have been evidenced as potential contribu-
tants uterine contractions during CPB are considered risk fac-
Uteroplacental hypoperfusion and fetal hypoxia subjected to sus-
exosomes and particulates [93].

Alterations to maternal physiology regulate the development of 
integrated functional unit called the feto-placento-maternal unit. 
The fetus, placenta, and mother constitute an 
patients under CPB: uterine contraction, placental hypoperfusion 
particulate and air embolism, nonpulsatile flow, hypothermia and 
coagulation and blood component alterations, the release of 
vasoactive substances from leukocytes, complement activation, 
particulate and air embolism, nonpulsatile flow, hypothermia and 

Three main pathophysiological changes can occur in pregnant 
patients under CPB: uterine contraction, placental hypoperfusion 
and fetal hypoxia. The fetus, placenta, and mother constitute an 
integrated functional unit called the feto-placento-maternal unit. 
Alterations to maternal physiology regulate the development of 
the fetus and placenta through products derived from the feto-
placento-maternal unit, including microchimeric cells, placental 
exosomes and particulates [93]. 
Uteroplacental hypoperfusion and fetal hypoxia subjected to s-
tained uterine contractions during CPB are considered risk fac-
tors for fetal death. Large extracorporeal surface contact areas 
and prime volumes have been evidenced as potential contribu-
tors to placental dysfunction following CPB [94]. During CPB, 
prostaglandin synthesis may cause an early vasoactive response, 
and severe acidosis may trigger fetal stress response [9]. Dilution 
of progestrone, cooling and rewarming processes can be causa-
tive factors for uterine contractions [11]. Placental vasoconstric-
tion may be mediated by prostaglandins and indomethacin, and 
steroids administration during bypass may attenuate placental 
vascular resistance [95]. Pulsatile perfusion may reduce uterine 

contractions by releasing endothelial-derived growth factors 
from the vascular endothelium [48,96]. Infusion of cold cardio-
plegia may induce brief fetal bradycardia, which could be re-
versed by increased pump flow and core temperature [25]. 
Bradycardia is often the first response of the fetus to hypothermia 
and hypoperfusion during normal FHR ranges (120–160 bpm), 
wheras a FHR of 70–80 bpm represents fetal distress. During 
CPB, FHR usually decreases to 100–115 bpm, but this decrease 
may occasionally be severe, dropping to 70–80 bpm, which rep-
resents considerable fetal distress [97]. Elevating perfusion flow 
and increasing the maternal oxygen partial pressure to 300– 
400 mmHg can be a solution for fetal distress [10]. The bradycar-
dia often appears at the beginning of CPB in the event of hypoxia, 
secondary to decreased fetal oxygenation, placental hypotension, 
or acid-base imbalance, and can persist for the total duration of 
CPB but may be reversible by increasing perfusion flow [9]. Fetal 

Table 5 Comparisons between pregnant patients whose baby survived and those whose fetus/baby died (Part 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survived</th>
<th>Died</th>
<th>χ²</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of gestation at onset of cardiac symptoms, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st trimester</td>
<td>20 (69.0)</td>
<td>9 (31.0)</td>
<td>7.86</td>
<td>0.0196</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>59 (80.8)</td>
<td>14 (19.2)</td>
<td>7.86</td>
<td>0.0196</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>44 (93.6)</td>
<td>3 (6.4)</td>
<td>9.42</td>
<td>0.0090</td>
</tr>
<tr>
<td>Time of gestation at cardiac surgery, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st trimester</td>
<td>17 (70.8)</td>
<td>7 (29.2)</td>
<td>9.42</td>
<td>0.0090</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>52 (76.5)</td>
<td>16 (23.5)</td>
<td>4.82</td>
<td>0.0302</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>52 (94.5)</td>
<td>3 (5.5)</td>
<td>12.24</td>
<td>0.0004</td>
</tr>
<tr>
<td>Association between use of CPB and delivery, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPB ahead of delivery</td>
<td>94 (85.5)</td>
<td>16 (14.5)</td>
<td>1.65</td>
<td>0.4382</td>
</tr>
<tr>
<td>One-stage</td>
<td>27 (77.1)</td>
<td>8 (22.9)</td>
<td>1.65</td>
<td>0.4382</td>
</tr>
<tr>
<td>CPB post-delivery</td>
<td>9 (90)</td>
<td>1 (10)</td>
<td>1.65</td>
<td>0.4382</td>
</tr>
</tbody>
</table>

Discussion

Pregnancies prior to cardiac surgery are associated with signifi-
cantly increased rates of miscarriage, preterm delivery and onset 
of cardiac events [92]. CPB can compromise uteroplacental perfu-
sion and fetal development by potential adverse effects such as 
coagulation and blood component alterations, the release of 
vasoactive substances from leukocytes, complement activation, 
particulate and air embolism, nonpulsatile flow, hypothermia and hypotension [7].

Three main pathophysiological changes can occur in pregnant 
patients under CPB: uterine contraction, placental hypoperfusion 
and fetal hypoxia. The fetus, placenta, and mother constitute an 
integrated functional unit called the feto-placento-maternal unit. 
Alterations to maternal physiology regulate the development of 
the fetus and placenta through products derived from the feto-
placento-maternal unit, including microchimeric cells, placental 
exosomes and particulates [93]. 
Uteroplacental hypoperfusion and fetal hypoxia subjected to s-
tained uterine contractions during CPB are considered risk fac-
tors for fetal death. Large extracorporeal surface contact areas 
and prime volumes have been evidenced as potential contribu-
tors to placental dysfunction following CPB [94]. During CPB, 
prostaglandin synthesis may cause an early vasoactive response, 
and severe acidosis may trigger fetal stress response [9]. Dilution 
of progestrone, cooling and rewarming processes can be causa-
tive factors for uterine contractions [11]. Placental vasoconstric-
tion may be mediated by prostaglandins and indomethacin, and 
steroids administration during bypass may attenuate placental 
vascular resistance [95]. Pulsatile perfusion may reduce uterine 

contractions by releasing endothelial-derived growth factors 
from the vascular endothelium [48,96]. Infusion of cold cardio-
plegia may induce brief fetal bradycardia, which could be re-
versed by increased pump flow and core temperature [25]. 
Bradycardia is often the first response of the fetus to hypothermia 
and hypoperfusion during normal FHR ranges (120–160 bpm), 
wheras a FHR of 70–80 bpm represents fetal distress. During 
CPB, FHR usually decreases to 100–115 bpm, but this decrease 
may occasionally be severe, dropping to 70–80 bpm, which rep-
resents considerable fetal distress [97]. Elevating perfusion flow 
and increasing the maternal oxygen partial pressure to 300– 
400 mmHg can be a solution for fetal distress [10]. The bradycar-
dia often appears at the beginning of CPB in the event of hypoxia, 
secondary to decreased fetal oxygenation, placental hypotension, 
or acid-base imbalance, and can persist for the total duration of 
CPB but may be reversible by increasing perfusion flow [9]. Fetal 

Bradycardia and demise may also be attributable to the use of 
nonpulsatile perfusion [98]. In addition, uterine contractions are 
particularly common during the rewarming phase after moder-
ate or profound hypothermia [99]. However, experimental and 
clinical observations revealed hypothermia cooling to as low as 
25°C could still result in successful pregnancies [7]. Pregnant pa-
nents undergoing valve replacement may have higher fetal mor-
tality rates. An increased severity of the valvular pathology with 
advanced pregnancy and longer bypass times during cardiac sur-
gery were considered the underlying risk factors [2]. Hyperventi-
lation and the use of adrenaline and noradrenaline should be 
avoided during cardiac surgery to prevent excessive vasocon-
striction [100]. But in a critical case, ephedrine and phenyleph-
rine were exceptionally used for 5 minutes after removal of the
aortic cross-clamp to increase maternal arterial pressure and counter the FHR drop, but inotropic administration did not have a negative effect on the fetus [27].

Teratogenic effects due to drug administration during CPB can be the main concern during the first trimester of pregnancy. CPB can be associated with a high incidence of premature labor in the third trimester, while uterine excitability and fetal malformations could be reduced during the second trimester [15]. If cardiac surgery could be delayed to allow the fetus to mature, fetal mortality would be lower. To avoid the deleterious effect of CPB on fetal outcomes, delivery can be done by cesarean section immediately prior to cardiac surgery. Alternatively, in the third trimester, delivery can be advocated before CPB is started to avoid fetal distress from perfusion. However, from the maternal point of view, cardiac surgery may be tolerated better during early pregnancy [5].

A short CPB time, normothermia, the maintenance of high flow rates and perfusion pressure play important roles in fetal perfusion. Therefore, a high flow ≥ 5L/min, high pressure of 70–75 mmHg, adequate hematocrit levels (25–27%) and mild hypothermia or normothermia, at least for a brief period during CPB, have been advocated [2,20,99,101]. Increasing the flow rate of CPB to 3100–3600 mL/min may significantly improve FHR. Occasionally, increasing the pump flow did not consistently improve FHR, whereas, occasionally, successful outcomes were obtained for both mother and fetus after profound hypothermic circulatory arrest [21]. However, hydrocephalus and hydrops were observed on postoperative day 2 even with nonpulsatile perfusion at a mean arterial pressure of 77–90 mmHg, a peak flow rate of 3.5–4.0 L/min/m² and a core temperature of 34–35 °C during cardiac surgery [27]. Accordingly, the reliability of nonpulsatile normothermic CPB has been questioned and whether it can meet the needs of fetoplacental circulation. Tocodynamometer monitoring appears imperative to obtain sufficient information about the uterus to intervene where necessary [98].

Cesarean section after heparinization and cannulation of the mother before the start of CPB is another alternative to improve fetal outcome [17]. If fetal distress occurs during cardiac operation under CPB, emergent cesarean section may save the lives of both the mother and baby [102]. Delivery prior to cardiac surgery under CPB during the third trimester can be a solution. Moreover, the cesarean incision can be left unsutured to allow further exploration of the uterus for potential hemorrhage or hematoma at a later stage [9]. In such patients, blood loss could be slightly higher and additional blood product infusions may be required [96].

The present study demonstrated that mitral and/or aortic valve disorders were the most common surgical indications for CPB during pregnancy, although it has been recognized that coronary artery disease is increasingly prevalent in gynecological patients [103]. The latter, however, could be managed interventionally in most patients, avoiding the risk associated with CPB for feto-neonatal outcome. In addition to cardiac surgery, resuscitation for cardiopulmonary collapse due to amniotic fluid embolism, auto-transfusion and circulatory support during cesarean section to improve patient survival were alternative indications for CPB. CPB was most frequently instituted during maternal cardiac surgery/resuscitation in the second trimester, and there were significant differences between the three trimesters in terms of feto-neonatal survival. Other main findings of this report were the disparities in the week of gestation at the time of onset of cardiac symptoms, time of cardiac surgery/resuscitation under CPB, and time of delivery between patients whose baby survived and those whose fetus/baby died. This showed, on the one hand, that the onset of cardiac symptoms and cardiac surgery/CPB during the early period of pregnancy can lead to higher feto-neonatal mortality rates. On the other hand, fetal demise was often associated with premature delivery. There were no intergroup differences with regard to CPB conditions, including high flow, high perfusion pressure, mild hypothermia or normothermia, CPB and cross-clamping times, between patients whose baby survived and those whose baby/fetus died. CPB duration and temperature did not have a significant influence on feto-neonatal outcome in this study, which was consistent with the literature [5]. Contrary to what was reported by Weiss et al. [5], the time since gestation greatly influenced feto-neonatal outcomes. Feto-neonatal death was associated with much shorter gestation periods, whether at the time of onset of cardiac symptoms, at cardiac surgery, at cardiac surgery under CPB prior to delivery, or at delivery. Feto-neonatal mortality rates successively decreased from the first through to the third trimesters. It is plausible that insufficient intrauterine development of fetuses could be a predictive risk factor for feto-neonatal morbidity and mortality. Patients who had one-stage delivery with cardiac surgery had higher feto-neonatal mortality rates than those who had CPB ahead of delivery or those who had CPB post-delivery, but the difference did not reach a statistical significance.

Although data from different studies served as a basis for statistical analysis, the main drawback of this study was the inhomogeneity of the data. Moreover, there is still not enough information from the long-term follow-up of both mother and baby after maternal cardiac surgery/resuscitation under CPB. These could be subjects for further study.

In conclusion, valve replacement for valvular disorder was the most common indication for maternal cardiac surgery with CPB during pregnancy. Resuscitation for cardiopulmonary collapse was an alternative indication for the initiation of CPB during pregnancy. Improved CPB conditions have led to improved feto-neonatal outcomes in pregnant patients undergoing CPB. The period of gestation and the timing of CPB during pregnancy are closely correlated with feto-neonatal mortality. Therefore, it is important to either deliver the baby prior to surgery/CPB or to defer surgery till late pregnancy.

Conflict of Interest

No conflict or financial support.

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