Indications for Cardiopulmonary Bypass During Pregnancy and Impact on Fetal Outcomes

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

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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

Einleitung: Herzoperationen an schwangeren Patientinnen stellen wegen der damit verbunden Komplexität, die Mutter und Kind gleichermaßen betreffen, eine Herausforderung für Chirurgen in interdisziplinären Teams dar. Die Behandlungsentscheidung hängt von der Einzelfallbewertung ab. Bislang wurden Müttersterblichkeit sowie das Überleben von Feten/Neugeborenen nach kardiopulmonalem Bypass („cardiopulmonary bypass" CPB) der Mutter nicht ausreichend in der Literatur beschrieben, es fehlen insbesondere Ergebnisse der Langzeit-Verlaufsbeobachtung.
Methodik: Dieser Übersichtsartikel basiert auf einer umfassenden Literaturrecherche für den Zeitraum von 1991 bis zum 30. April 2013.
Ergebnisse: Die Indikation für den Einsatz von CPB während der Schwangerschaft stellten Herzoperationen in 150 (96,8%) Patientinnen dar. Die häufigsten Eingriffe waren Herzklappenersatzoperationen wegen Aorten- und Mitralklappeninsuffizienz, Reanimation wegen Fruchtwasserembolie, Autotransfusion sowie Kreislaufunterstützung während des Kaiserschnitts in 5 Patientinnen. Während des CPB war entweder ein kurzer Abfall der fetalen Herzfrequenz zu verzeichnen, die sich nach der Operation wieder von selbst normalisierte, oder die fetale Herzfrequenz blieb während des ganzen CPB im Normalbereich. Die Gesamtsterblichkeit von Feten und Neugeborenen betrug 18,6%. Verglichen mit Müttern, deren Feten/Kinder überlebten, war die fetale/neugeborenen Sterblichkeit signifikant höher, wenn mütterliche Herzinsuffizienzsymptome schon im früheren Gestationsalter auftraten bzw. bei kürzerer Schwangerschaftsdauer zum Operationszeitpunkt mit CPB.
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.

häufigsten Eingriffe mit CPB wurden während des 2. Trimesters vorgenommen. Bessere CPB-Bedingungen, darunter höhere Fließgeschwindigkeiten, höhere Blutdruckwerte und Normothermie, oder nur milde Hypothermie haben zu einer Verbesserung der mütterlichen und fetalen Ergebnisse geführt. Kurze Schwangerschaftsdauer zum Zeitpunkt des CPB war eng mit fetaler/neugeborener Sterblichkeit korreliert. Es wird empfohlen, die Entbindung vor dem Eingriff mit CPB vorzunehmen oder aber den Eingriff mit CPB auf einem möglichst späten Zeitpunkt zu verschieben.

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 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 χ^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, 0.024–34; 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

Table 1 Indications for CPB in 155 pregnant patients.

Indication	n (%)
Valvular disorder	**57 (36.8)**
MS	28 (18.1)
MR	9 (5.8)
MR, MS	2 (1.3)
Mitral valve disorder (pathology not stated)	3 (1.9)
AS	10 (6.5)
AR, MR	2 (1.3)
AS, MR, MS	1 (0.7)
Aortic valve disorder (pathology not stated)	1 (0.7)
TR, MR post-ASD & pulmonary stenosis repair	1 (0.7)
Congenital heart defects	**19 (12.3)**
Atrioventricular canal defect, perforated mitral valve	1 (0.7)
Cor triatriatum	1 (0.7)
ASD	1 (0.7)
AS, bicuspid aortic valve	6 (3.9)
Unicuspid aortic valve	1 (0.7)
ASD, AS	1 (0.7)
Ebstein's anomaly, Wolff-Parkinson-White syndrome	1 (0.7)
Ruptured sinus of Valsalva of the right coronary cusp	1 (0.7)
Tetralogy of Fallot	2 (1.3)
PFO	1 (0.7)
PFO, paradoxical embolism	1 (0.7)
PFO, paradoxical embolism, DIC	1 (0.7)
PFO, paradoxical embolism, cardiopulmonary collapse, DIC, amniotic fluid embolism	1 (0.7)
Prosthetic valve disorders	**29 (18.7)**
Prosthetic valve thrombus	14 (9.0)
Prosthetic AV stuck	3 (1.9)
MS post-MVR	3 (1.9)
Biologic prosthetic aortic valve deterioration	2 (1.3)
MS, MR post-AVR+MVR	1 (0.7)
Prosthetic AS	1 (0.7)
LA thrombus post-AVR	1 (0.7)
Prosthetic valve problem (pathology was not given)	4 (2.6)
Cardiac tumors	**14 (9.0)**
Myxoma	8 (5.2) (6 [3.9] in the LA, 1 [0.7] in the right ventricle, and 1 [0.7] in the right atrium)
Right atrial lipoma	1 (0.7)
Right ventricular lipoma, paroxysmal tachycardias	1 (0.7)
Recurrent LA myxoma 8 years after initial myxoma resection	1 (0.7)
LA osteosarcoma	1 (0.7)
LA sarcoma spreading to mitral leaflet and annulus	1 (0.7)
Intravenous leiomyomatosis of uterine origin with extension into the pelvic veins, inferior vena cava, right atrium & right ventricle	1 (0.7)
Infective endocarditis	**12 (7.7)**
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 aorta aneurysm, mitral valve prolapse	1 (0.7)
Traumatic thoracic aorta 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)**

AR: aortic valve regurgitation; AS: aortic valve stenosis; ASD: atrial septal defect; AVR: aortic valve replacement; DIC: disseminated intravascular coagulation; LA: left atrium; MR: mitral valve regurgitation; MS: mitral valve stenosis; MVR: mitral valve replacement; PFO: patent fossa ovalis; TR: tricuspid valve regurgitation.

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 the right femoral artery) in 1 (0.7%) patient, and right atrium (inflow) – main pulmonary artery (outflow) CPB 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 (range, 25–42; median, 38) 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 ($\chi^2 = 25.3$, $p < 0.0001$).

Table 2 Cardiac surgery or resuscitation with cardiopulmonary bypass.

Major operation	n (%)
Valve surgery	105 (67.7)
1. MVR	34 (21.9)
2. Mitral valve repair	10 (6.5)
3. MVR, tricuspid valve repair	1 (0.7)
4. MVR, TVR	1 (0.7)
5. AVR	21 (13.5)
6. AVR, MVR	4 (2.6)
7. AVR, ascending aorta replacement	4 (2.6)
8. AVR, mitral valve annuloplasty	1 (0.7)
9. AVR, ruptured sinus of Valsalva repair	1 (0.7)
10. AVR, coronary artery bypass grafting	1 (0.7)
11. Composite AVR	1 (0.7)
12. TVR	1 (0.7)
13. Redo MVR	18 (11.6)
14. Redo AVR	7 (4.5)
Cardiac tumor resection	14 (9.0)
15. Cardiac myxoma excision	7 (4.5)
16. Cardiac myxoma excision, MVR	1 (0.7)
17. Cardiac myxoma excision, mitral valve repair	1 (0.7)
18. Cardiac lipoma excision	2 (1.3)
19. Cardiac leiomyomatosis excision	1 (0.7)
20. Cardiac osteosarcoma excision	1 (0.7)
21. Incomplete resection of cardiac sarcoma, MVR, modified De Vega tricuspid annuloplasty	1 (0.7)
Thrombectomy	13 (8.4)
22. Pulmonary artery embolectomy	4 (2.6)
23. Pulmonary artery embolectomy & atrial septal defect repair	1 (0.7)
24. Thrombectomy of the left atrium	1 (0.7)
25. Embolectomy (right atrium, bilateral pulmonary arteries and common iliac arteries)	1 (0.7)
26. Prosthetic mitral valve debridement & declotting	3 (1.9)
27. Prosthetic aortic valve thrombectomy	1 (0.7)
28. Prosthetic aortic valve debridement	2 (1.3)
Congenital heart defect surgery	9 (5.8)
29. Patent fossa ovalis closure	2 (1.3)
30. Patent fossa ovalis closure, paradoxical embolism removal	2 (1.3)
31. Tetralogy of Fallot repair	1 (0.7)
32. Atrial septal defect closure	1 (0.7)
33. Atrial septal defect closure, MVR	1 (0.7)
34. Accessory pathway ablation, tricuspid annuloplasty	1 (0.7)
35. Cor triatriatum repair	1 (0.7)
Coronary surgery	1 (0.7)
36. Coronary artery bypass grafting × 2, intraaortic balloon pump	1 (0.7)
Other cardiac surgery	8 (5.2)
37. Aortic aneurysm repair	5 (3.2)
38. Descending aorta-innominate artery bypass	1 (0.7)
39. Extra-anatomic bypass graft	1 (0.7)
40. Septal myectomy	1 (0.7)
No cardiac operation	5 (3.2)
41. Cesarean section under cardiopulmonary bypass (circulatory support during surgery to improve the patient's chances of survival)	1 (0.7)
42. Open chest cardiac massage (no evidence of pulmonary artery thrombosis)	1 (0.7)
43. Placement of a right ventricular assist device	1 (0.7)
44. Resuscitation with extracorporeal membrane oxygenation, intraaortic balloon pump	1 (0.7)
45. Synchronous autotransfusion	1 (0.7)

AVR: aortic valve replacement; MVR: mitral valve replacement; TVR: tricuspid valve replacement.

Table 3 Mode of delivery and feto-neonatal outcomes.

Mode of delivery	n (%)
Cesarean section	65 (41.9) (1 [0.7 %] was cesarean section & hysterectomy, and 1 [0.7 %] fetus died)
Delivery method not stated	30 (19.4) (1 [0.7 %] baby died of acute respiratory distress syndrome)
Forceps delivery	3 (1.9)
Induced labor	3 (1.9)
Spontaneous vaginal delivery	23 (14.8) (2 [1.3 %] stillborn)
Vacuum delivery	1 (0.7)
Still with normal pregnancy when the reports were published	5 (3.2)
Operative death	7 (4.5)
Spontaneous abortion	7 (4.5)
Stillborn	6 (3.9)
Termination of pregnancy	5 (3.2)

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 ($\chi^2 = 17.5$, $p = 0.0002$).

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 4 Comparisons between pregnant patients whose baby survived and those whose fetus/baby died (Part 1).

Variable	Survived	Died	p value
Maternal age (year)	28.5 ± 6.1	28.8 ± 5.4	0.8088
Week of gestation at onset of cardiac symptoms	23.4 ± 9.3	17.8 ± 7.4	0.0047
Week of gestation at cardiac surgery	24.2 ± 9.4	19.0 ± 7.2	0.0075
Week of gestation of patients who underwent cardiac surgery under CPB prior to delivery	17.0 ± 7.7	7.3 ± 10.8	0.0030
Time of delivery (week of gestation)	36.5 ± 4.1	20.1 ± 7.3	< 0.0001
Arterial pressure (mmHg)	70.4 ± 6.6	73.5 ± 11.1	0.1933
Flow rate (ml/kg/min)	3.3 ± 1.2	3.6 ± 1.6	0.4645
Temperature (°C)	32.7 ± 4.0	33.0 ± 3.0	0.6953
Cardiopulmonary bypass time (min)	84.5 ± 45.8	108.2 ± 68.6	0.0678
Cross-clamping time (min)	60.6 ± 35.1	64.9 ± 25.0	0.7011

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

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

Discussion

Pregnancies prior to cardiac surgery are associated with significantly increased rates of miscarriage, preterm delivery and onset of cardiac events [92]. CPB can compromise uteroplacental perfusion 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 sustained uterine contractions during CPB are considered risk factors for fetal death. Large extracorporeal surface contact areas and prime volumes have been evidenced as potential contributors 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 progesterone, cooling and rewarming processes can be causative factors for uterine contractions [11]. Placental vasoconstriction 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 cardioplegia may induce brief fetal bradycardia, which could be reversed 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), whereas 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 represents 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 bradycardia 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 moderate 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 patients undergoing valve replacement may have higher fetal mortality rates. An increased severity of the valvular pathology with advanced pregnancy and longer bypass times during cardiac surgery were considered the underlying risk factors [2]. Hyperventilation and the use of adrenaline and noradrenaline should be avoided during cardiac surgery to prevent excessive vasoconstriction [100]. But in a critical case, ephedrine and phenylephrine 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 ≥ 5 L/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/m^2 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, autotransfusion 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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