Cardiovascular Considerations for Artificial Womb Technologies in the Extremely Premature Infant

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OVERVIEW

Cardiovascular Development

Transition of Circulation to Postnatal Period

Disorders of transition of circulation in Extremely Premature Infants

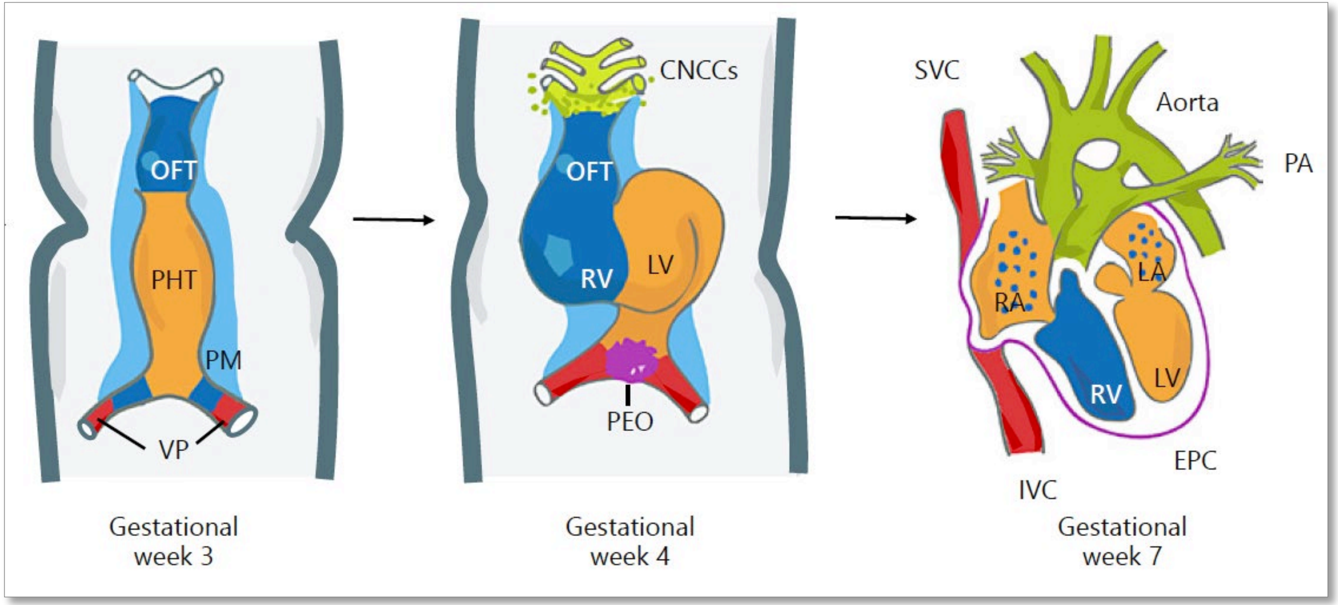
Consequences of ECMO in Small and Premature Infants

Potential Alternatives to ECMO for rescue of Extremely Premature Infants

Preload, Afterload and Ventricular Function during prolonged support

Monitoring Considerations

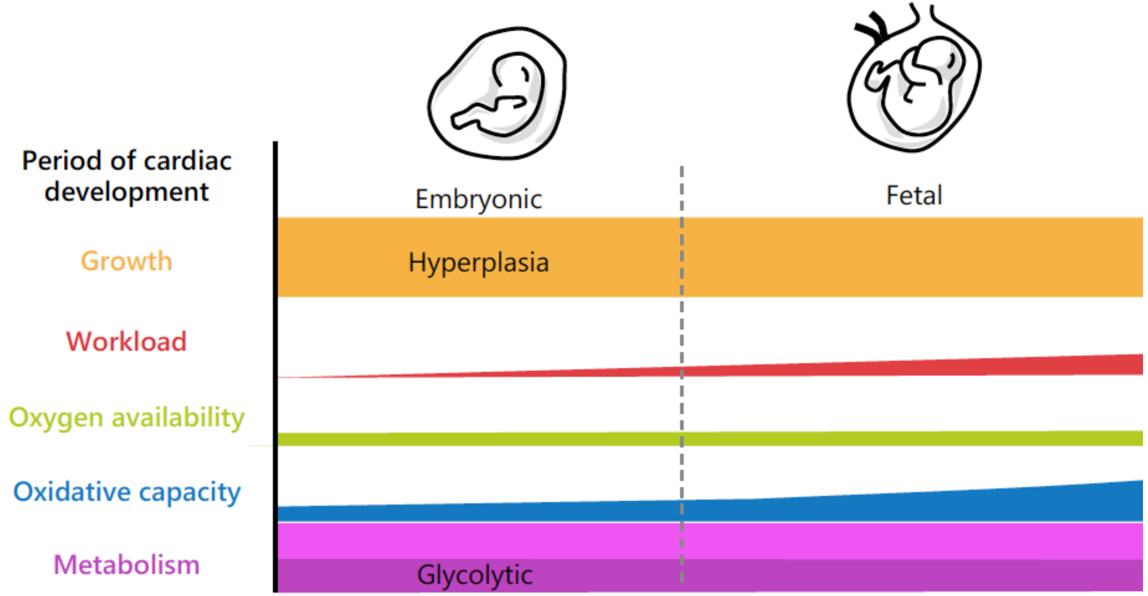
CARDIOVASCULAR DEVELOPMENT



The 4-chambered heart is developed by gestational week 7 and contributes to oxygen and nutrient distribution to the developing embryo

Fetal Diagn Ther 2020;47:373–386

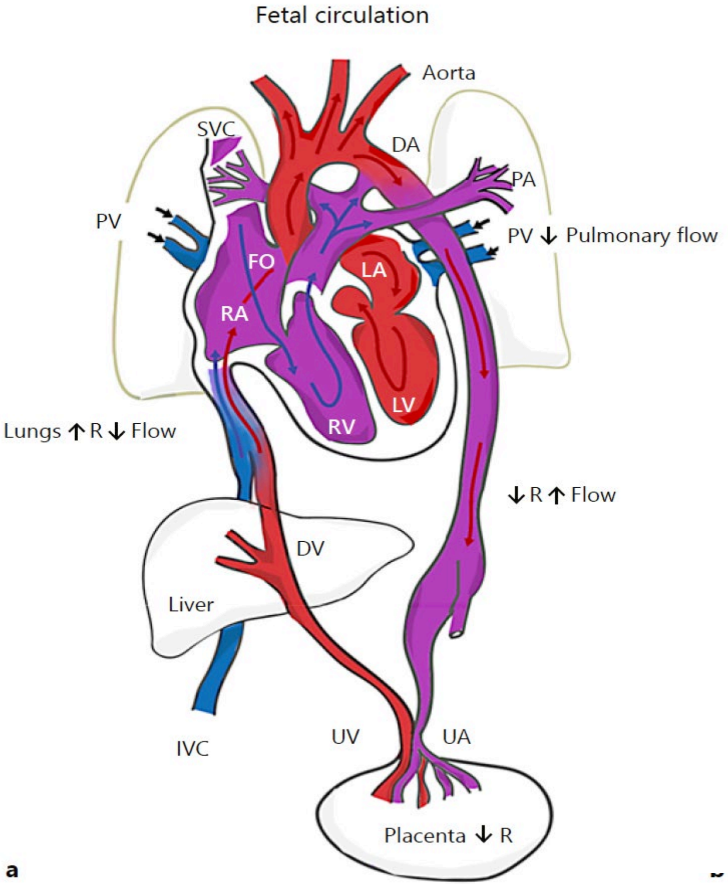
CARDIOVASCULAR DEVELOPMENT



The fetal cardiovascular system gradually increases workload through the second and third trimesters, with increasing oxidative capacity and workload

Fetal Diagn Ther 2020;47:373–386

FETAL CIRCULATION



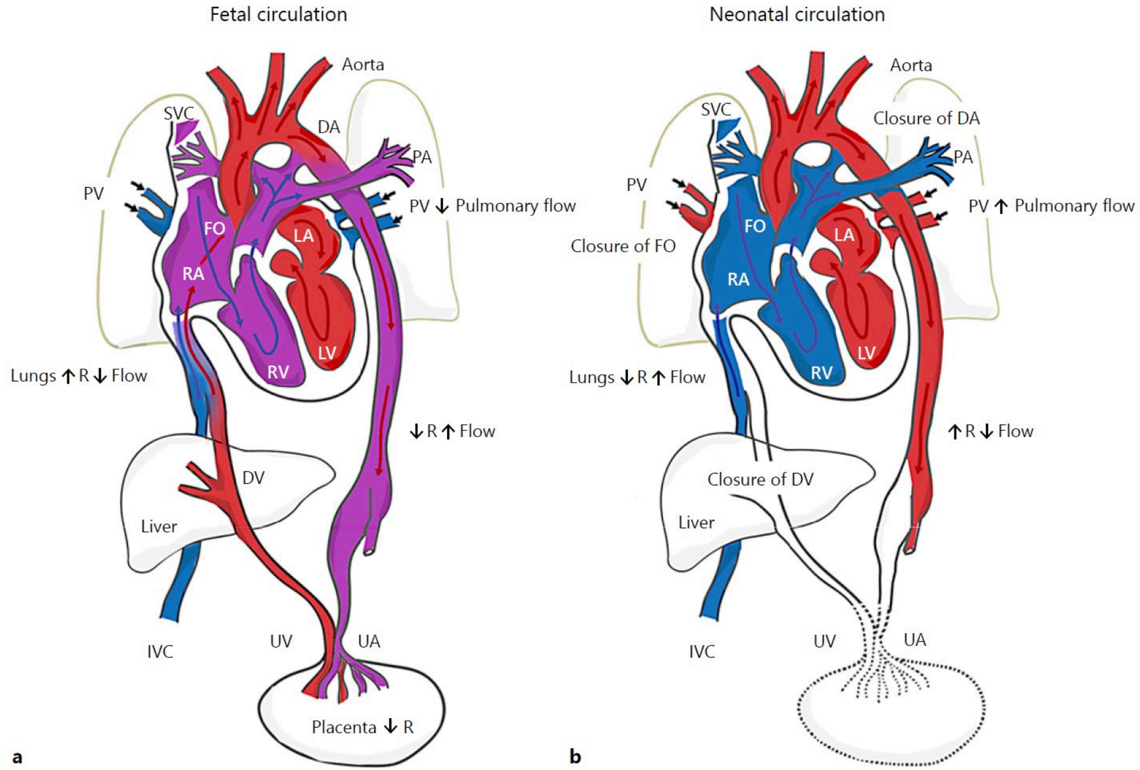
Oxygenated blood from the placenta is delivered to heart and brain.

Biochemical factors
– endothelin-1 and prostaglandins

Anatomical factors
- Vascular shunts include low resistance placenta, ductus venosus, ductus arteriosus and foramen ovale

Fetal Diagn Ther 2020;47:373–386

TRANSITION TO POSTNATAL PERIOD



Increased lung oxygenation and decreased pulmonary vascular resistance -> increase pulmonary blood flow

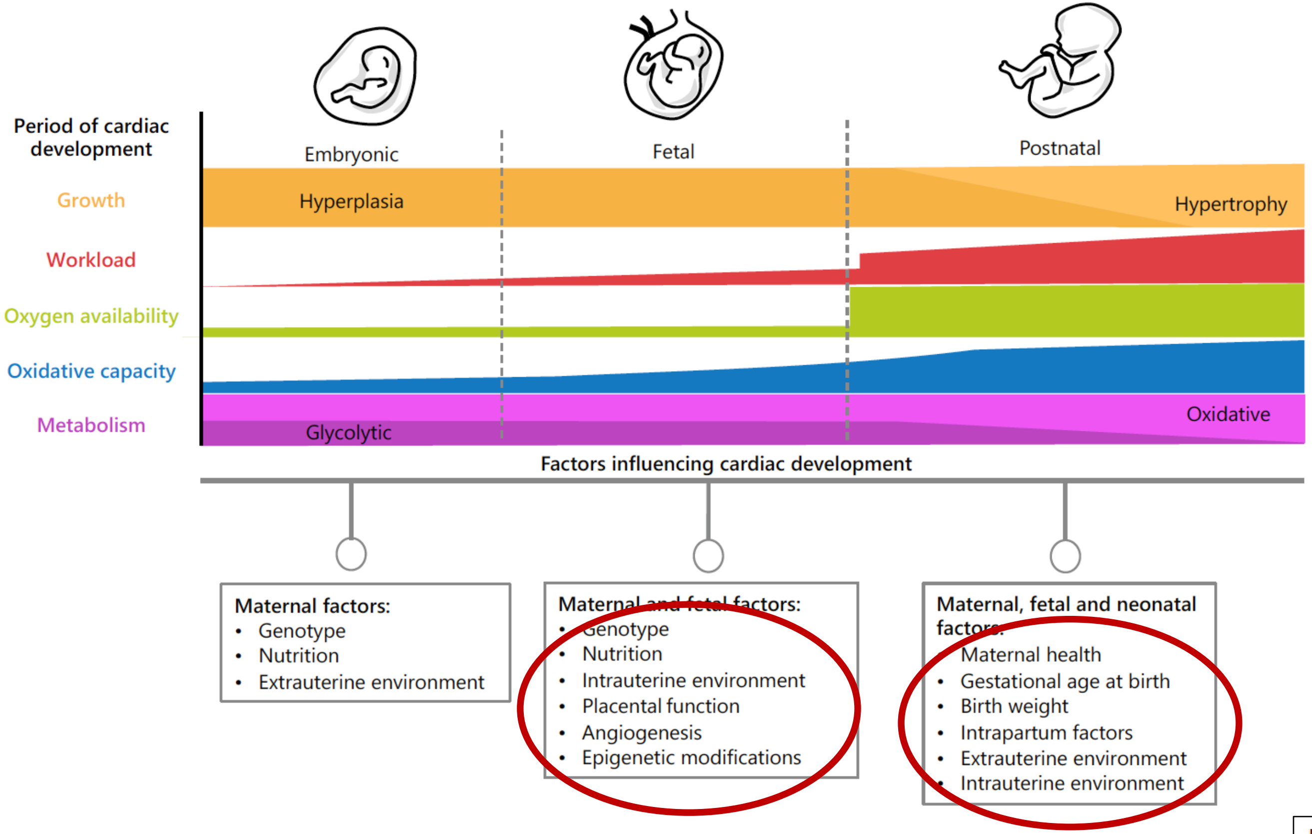
Increase left atrial pressure, closure of foramen ovale

Increased oxygenation and loss of placental prostaglandins – closure of ductus arteriosus

Increased cardiac output

Fetal Diagn Ther 2020;47:373–386

TRANSITION TO POSTNATAL PERIOD



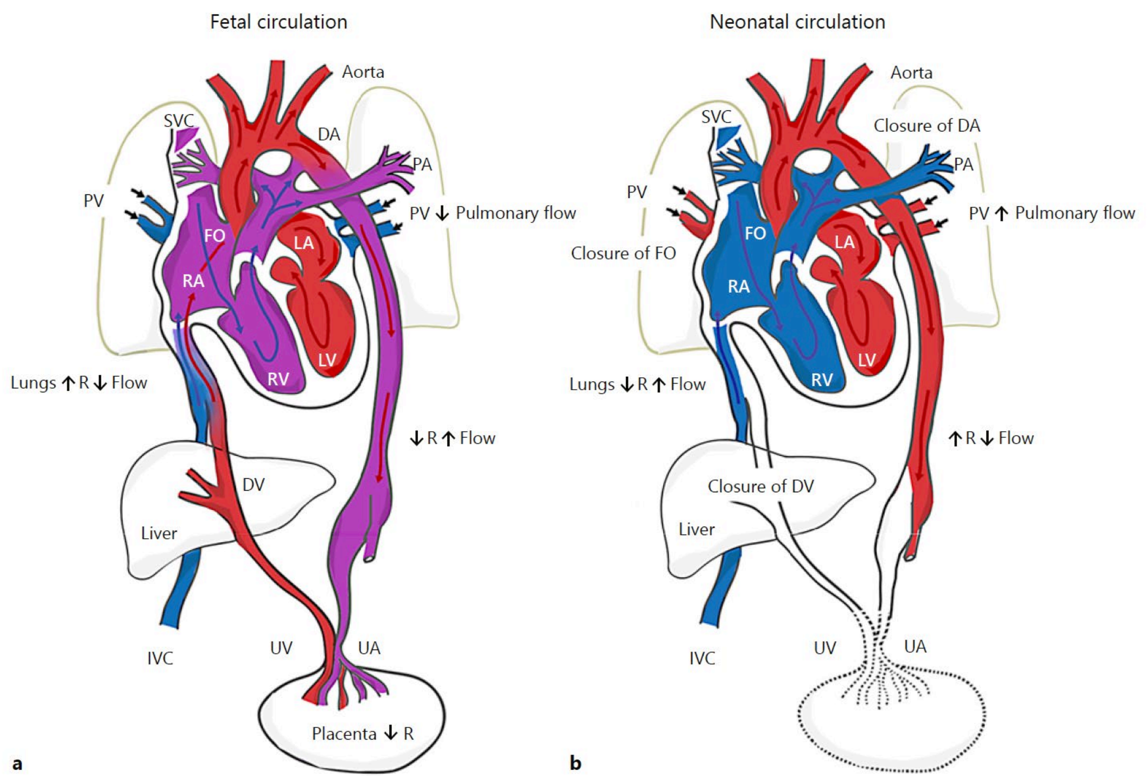
Catecholamines increase HR and contractility

Oxygenation of pulmonary vascular bed

Loss of placental prostaglandins

Fetal Diagn Ther 2020;47:373–386

EXTREMELY PREMATURE INFANTS



Immature cardiovascular system impacts transition to neonatal circulation

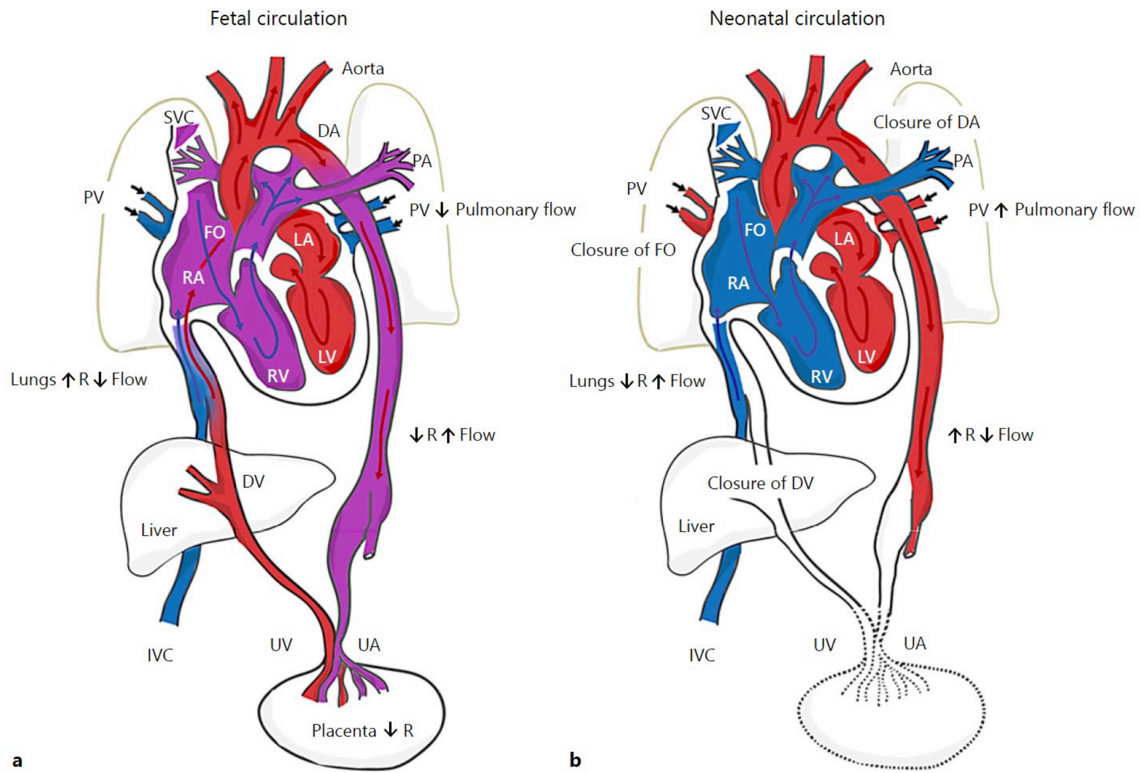
Unresponsive ductus arteriosus constriction

Foramen ovale may remain open

In combination, can result in pulmonary congestion (L->R flow) and systemic hypoperfusion

Fetal Diagn Ther 2020;47:373–386

EXTREMELY PREMATURE INFANTS



Prematurity impacts myocardial structural development altering cardiomyocyte maturation

High systemic vascular resistance and hyperoxia leads to hypertrophy of cardiomyocytes and abnormal post-natal development

Resulting in impaired LV diastolic dysfunction and persistent reduction in RV systolic function

Fetal Diagn Ther 2020;47:373–386

The Extracorporeal Life Support Organization Maastricht Treaty for Nomenclature in Extracorporeal Life Support

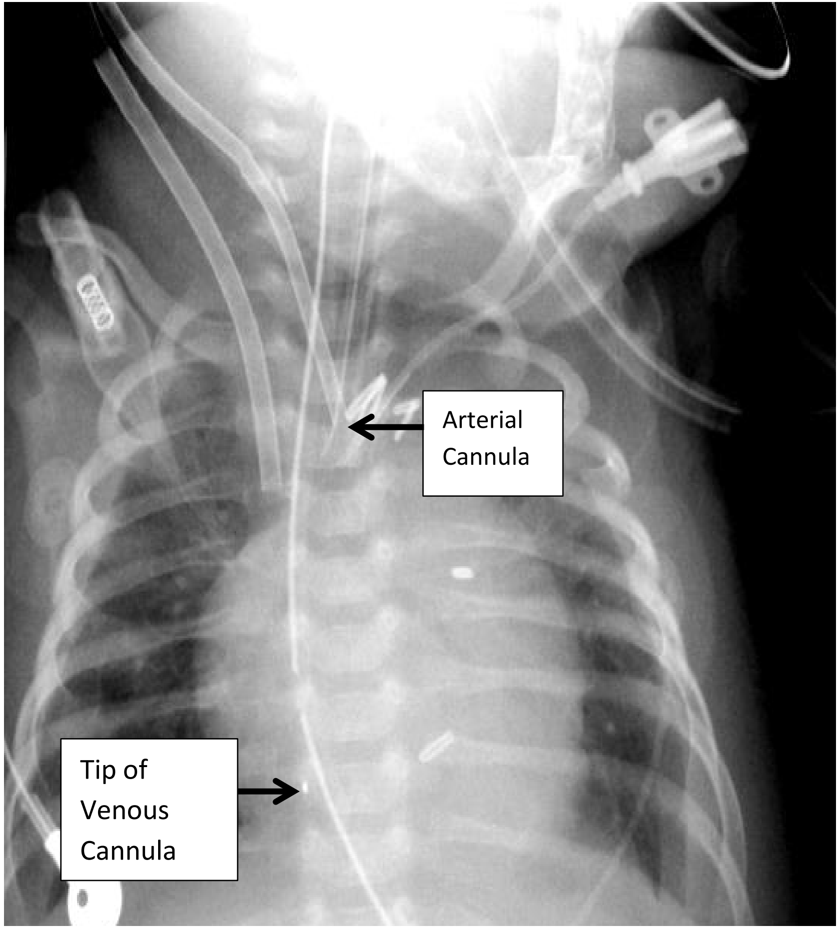
A Position Paper of the Extracorporeal Life Support Organization

Steven A. Conrad[1,2,3], L. Mikael Broman[4,5], Fabio S. Taccone[6], Roberto Lorusso[7], Maximilian V. Malfertheiner[8], Federico Pappalardo[9], Matteo Di Nardo[10], Mirko Belliato[11], Lorenzo Grazioli[12], Ryan P. Barbaro[13], D. Michael McMullan[14], Vincent Pellegrino[15], Daniel Brodie[16], Melania M. Bembea[17], Eddy Fan[18], Malaika Mendonca[19], Rodrigo Diaz[20], and Robert H. Bartlett[21]

Am J Respir Crit Care Med Vol 198, Iss 4, pp 447–451, Aug 15, 2018

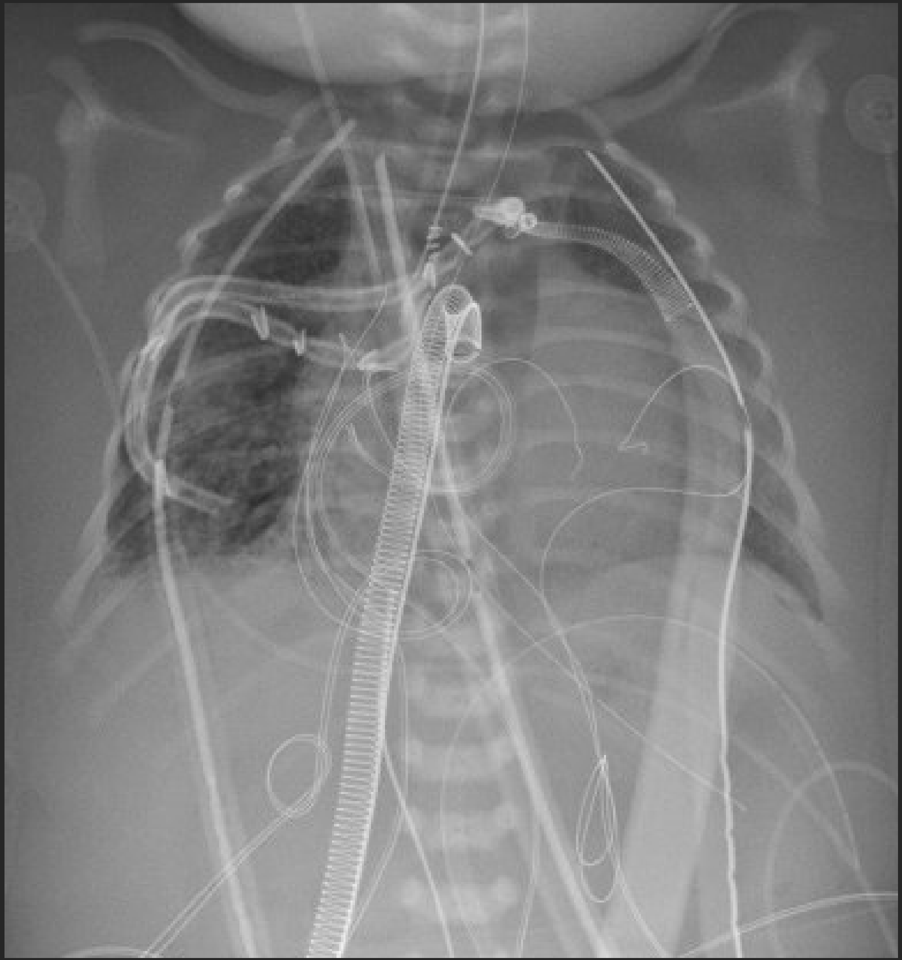
ECLS can be used in different configurations to support the most critically ill patients with pulmonary or cardiopulmonary disease

Most commonly in veno-arterial configuration (VA ECMO) in cardiac population, but has been considered for pulmonary support (veno-venous, VV ECMO) of the extremely premature infant

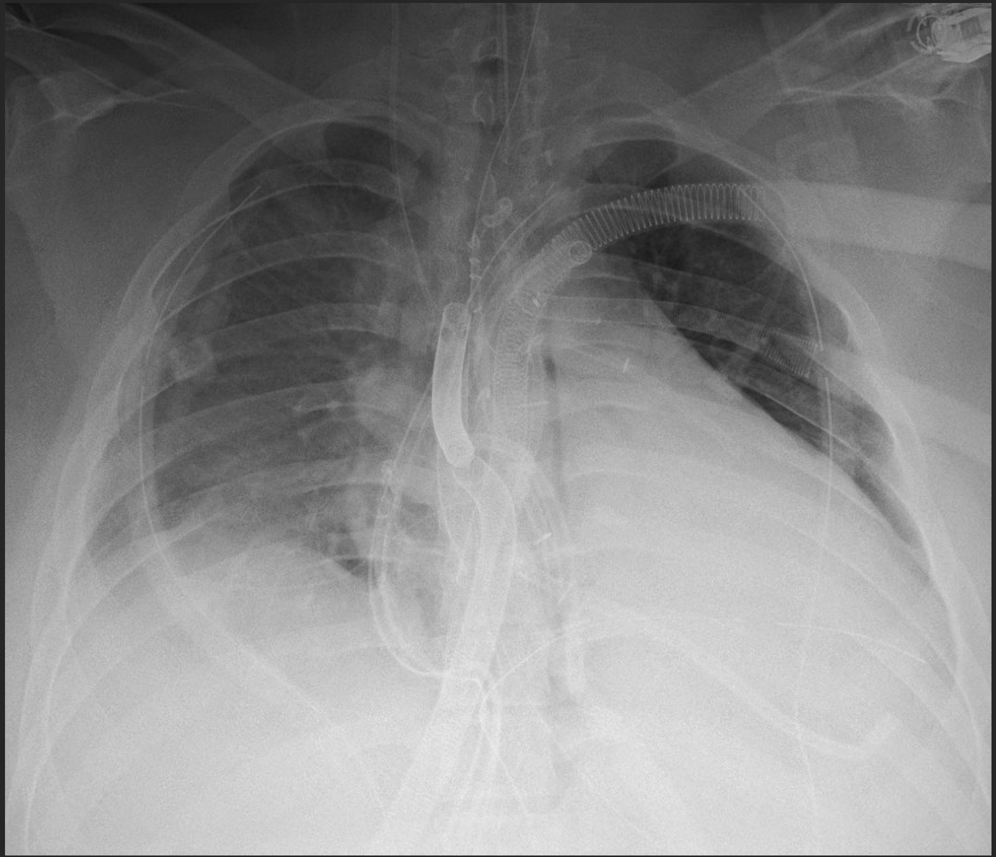



C.E.P

PATIENT DIMENSIONS



1.8kg with 12Fr RA - 6Fr Ao

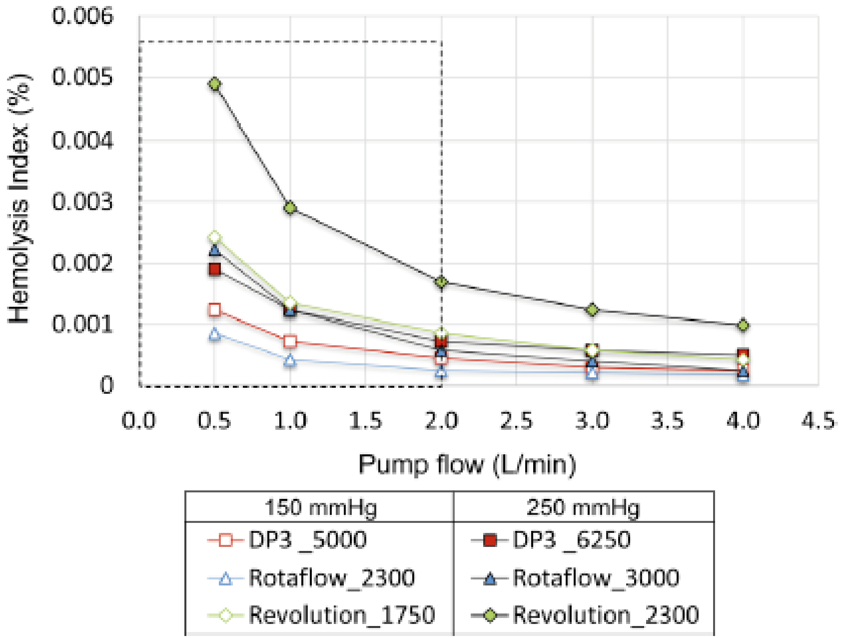


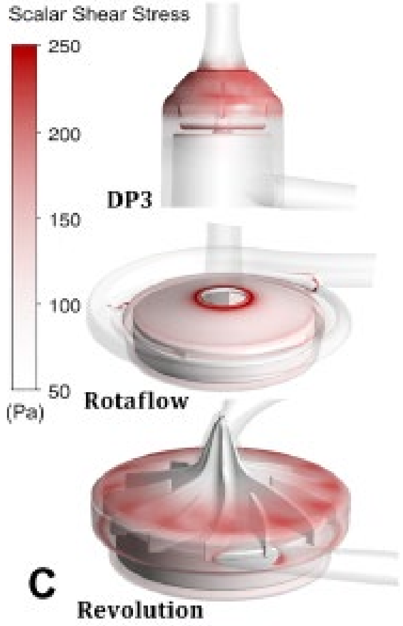
>100kg with 28Fr RA-SVC; 29Fr IVC; 20Fr LV – 22Fr Ao

Low-flow assessment of current ECMO/ $ECCO_2R$ rotary blood pumps and the potential effect on hemocompatibility

Sascha Gross-Hardt[1], Felix Hesselmann[1], Jutta Arens[1], Ulrich Steinseifer[1], Leen Vercaemst[2], Wolfram Windisch[3], Daniel Brodie[4] and Christian Karagiannidis[3*]

Critical Care (2019) 23:348



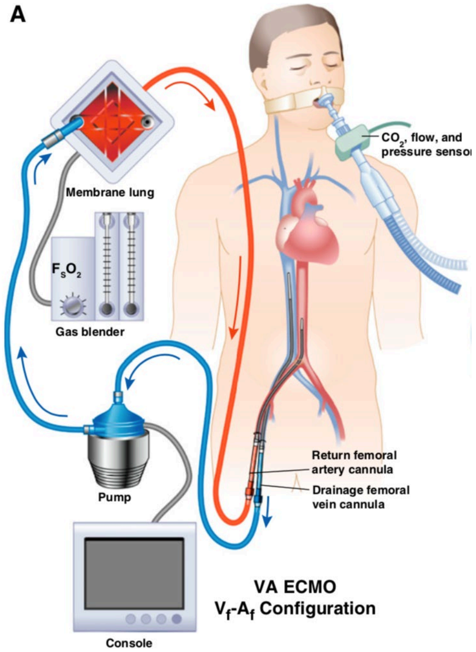


ECMO circuit components are generally not optimized for the pump flows used for neonatal and pediatric ECMO

CONSEQUENCES OF ECMO

occur more frequently in children

DEVICE ASSOCIATED	Neonate	Child	Adult
Cannula malfunction	9.4%	7.4%	3.4%
Circuit hemolysis	4.6%	3%	0.8%
Circuit change	13.8%	12.1%	3.2%
Air in circuit	2.8%	3.1%	0.8%
Oxygenator failure	5.8%	5.7%	3.5%
Pump failure	0.7%	0.6%	0.5%



Rates of select complications in patients supported with ECMO for cardiac indication, 2017-2022

Am J Respir Crit Care Med Vol 198, Iss 4, pp 447–451, Aug 15, 2018

CONSEQUENCES OF ECMO

occur more frequently in children

PATIENT RELATED	Neonate	Child	Adult
Brain hemorrhage	12.1%	5.8%	0.6%
Brain infarction	3.1%	4.5%	3.3%
Seizure	7.4%	3.8%	0.7%
CPR while on ECMO	2.4%	1.8%	2.1%
Lung hemorrhage	2.1%	2.7%	1.4%
Pneumothorax	2%	2%	1.6%
GI hemorrhage	1.3%	2.4%	4.5%

EXTRACORPOREAL LIFE SUPPORT ORGANIZATION ELSO Established 1989 ®

Rates of select complications in patients supported with ECMO for cardiac indication, 2017-2022

Premature and Extracorporeal Life Support: Is it Time? A Systematic Review

Carmen Mesas Burgos,*†‡ Björn Frenckner,*†‡ Lars Mikael Broman†§

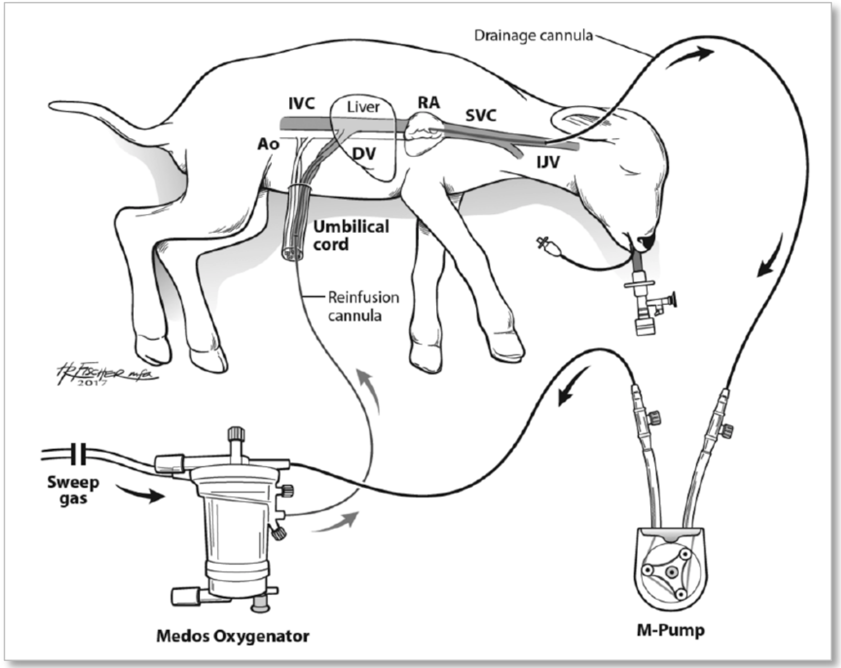
ASAIO Journal 2022; 68;633–645

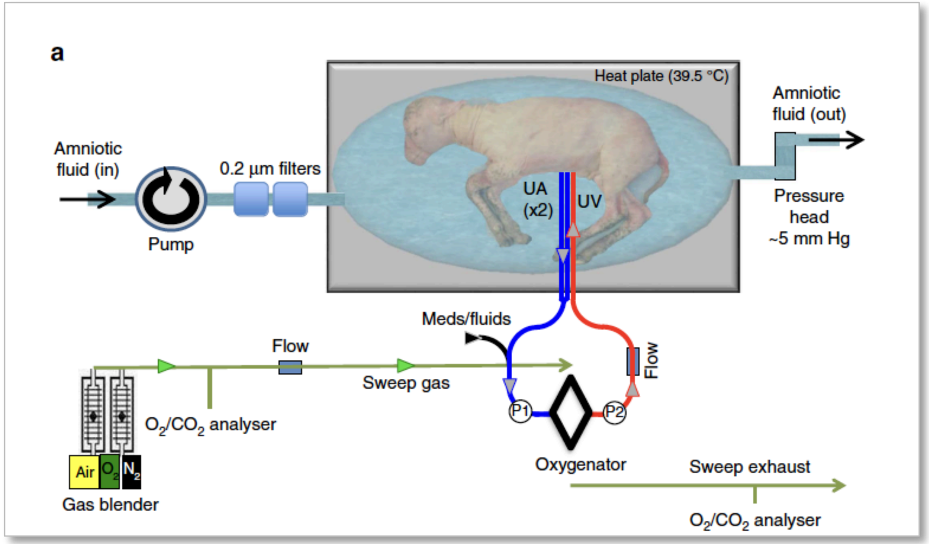
'Over the past decades, the frequency of intracranial hemorrhage has declined (89-21%), survival has increased in both early prematurity (25-76%) and in congenital diaphragmatic hernia (33-75%) with outcome similar to late prematurity (48%)…'

'… At present <34 weeks gestational age might no longer be considered a contraindication for ECMO in premature neonates…'

ALTERNATIVES TO ECMO

artificial womb technology





ASAIO Journal 2019; 65:690–697.

VV ECMO from IJ/RA-UV

NATURE COMMUNICATIONS | DOI: 10.1038/ncomms15112

Oxygenator in line from UA-UV

ALTERNATIVES TO ECMO

Characteristics	VV ECMO from IJ-UV	Oxygenator in line from UA-UV
Cannulation	Surgical cannulation of the IJV and UV at umbilicus	Cannulation of the umbilical vessels without surgical intervention
Anticoagulation	Nitric oxide eluting circuit	Unfractionated heparin in biologically coated circuit
Circulation	100mL/kg/min flow VV ECMO via pumped circuit	AV pumpless circuit connected via umbilical vessels
Ductus arteriosus management	Managed with prostaglandin E1 for ductal patency	Managed with prostaglandin E1 for ductal patency
Circulation Monitoring	Fetal echocardiogram for qualitative biventricular systolic function	Fetal echocardiogram and pulsatility index, normal heart function and growth at 4 weeks

ASAIO Journal 2019; 65:690–697. NATURE COMMUNICATIONS | DOI: 10.1038/

SERIAL CARDIOVASCULAR MONITORING

Fetal vital signs
- Heart rate, mean arterial pressure

General appearance
- Monitor for peripheral edema, ascites, pleural effusions

Fetal ultrasound
- Pulsatility indices of the fetal middle cerebral artery, umbilical artery, ductus venosus

Fetal echocardiography
- Doppler-echocardiography-derived cardiac output (CO)
- Qualitative assessment of biventricular systolic function
- Speckle-tracking derived global longitudinal strain, and strain rate in the RV and LV

Ultrasound Obstet Gynecol 2020; 55: 516–522

SUMMARY

Cardiovascular Immaturity puts extremely premature infants at risk of long-term biventricular dysfunction

Disorders of transition of circulation contribute to complexity of care for extremely premature infants

ECMO is associated with complications in small children

Alternative ECLS modes for rescue of extremely premature infants are in evolution

Preload, Afterload and Ventricular Function during prolonged support depend on strategy

Monitoring Considerations

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