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# **Assessment of Systemic Blood Flow in the Newborn Infant**

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## **Abstract**

Preterm infants are vulnerable to brain injury which is thought to be caused partly by abnormalities in cerebral perfusion. However the accurate assessment of cerebral and general systemic perfusion remains a challenge in the newborn infant. Commonly used clinical parameters such as blood pressure and blood lactate concentrations are imperfect predictors of blood flow. Cardiac output measurements used in older children do not reflect true systemic perfusion in the neonate due to shunting of blood through persisting fetal pathways. Echocardiographic measurements of descending aortic (DAo) and superior vena caval (SVC) blood flow may provide more reliable assessment of neonatal systemic perfusion. This thesis evaluates these techniques in the first days of postnatal life.

Measures of flow volume in the SVC and DAo were found to be feasible in the vast majority of infants, and were performed without significantly affecting cardiorespiratory status. Assessment of SVC flow volume showed similar repeatability to other measures of blood flow in neonates when assessed by a single observer, as did assessment of velocity of flow in the DAo.

We then used these techniques to further assess the transitional circulation, and found no evidence of a positive association between arterial blood pressure and volume of systemic perfusion. Contrary to previous assumptions that ductal shunting compromises systemic perfusion, we found that left ventricular output tended to increase with increasing shunt through the ductus arteriosus, thereby maintaining upper, though not necessarily lower, body perfusion.

There was an association between very low levels of flow in individuals and some adverse outcomes that had a strong circulatory component to their pathophysiology (periventricular haemorrhage and necrotising enterocolitis). However low blood flow in the SVC or DAo did not predict poor outcome within the entire cohort.

Assessments of SVC and DAo flow in the neonate are feasible, relatively repeatable and have already enhanced our understanding of the pathophysiology of the transitional circulation. These and other techniques to monitor systemic blood flow in the neonate may aid identification of circulatory failure, act as short-term endpoints in clinical trials of interventions supporting the circulation, and eventually improve neurodevelopmental outcome in preterm infants.

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This thesis is dedicated to my family and in particular to my parents who have always been there for me. Likewise to my brother, sister and my friends both in New Zealand and the UK, who helped me keep my 'work life balance'.

## **Preface**

The incidence of premature birth in industrialised nations shows no signs of decreasing(1). While survival rates have improved dramatically in recent decades there is little or no evidence for similar improvements in neurodevelopmental outcome(2). Many of the causes of adverse neurodevelopmental outcome are poorly understood. However there is increasing evidence that circulatory factors may play a critical role in the pathophysiology of brain injuries in preterm infants(3).

The circulation of the newborn infant undergoes a transition from the fetal to the adult pattern in early extra-uterine life. In the fetus the ductus arteriosus carries deoxygenated blood from the pulmonary artery away from the high resistance pulmonary circulation towards the placenta for oxygenation. Oxygenated blood returning to the right atrium from the placenta is diverted by the foramen ovale towards the brain and upper body via the left atrium, left ventricle and ascending aorta. The central features of the transitional circulation are the removal of the low resistance placental circulation by clamping of the umbilical cord, and an abrupt increase in pulmonary blood flow due to falling pulmonary artery pressure as the lungs take on the role of gaseous exchange. In term infants the fetal shunt pathways of the ductus arteriosus and foramen ovale are generally functionally closed within 24 hours of birth(4).

In term infants the changes occurring in the transitional circulation are rapid and lead to significant increases in cardiac output to match metabolic demand(4). In the extremely preterm infant the heart, like many other organs, may not be adequately prepared for the rigours of extra-uterine life. The immature myocardium may be less able to contract against the increase in vascular resistance produced by removal of the low resistance

placental bed(5). The fall in pulmonary vascular resistance is often delayed(6), as is functional closure of the fetal shunt pathways(4). Severe respiratory disease and the requirement for mechanical ventilation may further impair cardiac function in preterm infants(5).

Attempts to monitor cardiac function during this transitional period in preterm infants are hindered by the persistence of the fetal shunt pathways. Measurements of left and right ventricular output are useful in assessing systemic perfusion in older children and adults. However in the presence of shunting through the ductus arteriosus and foramen ovale, neither left nor right ventricular output assesses the volume of blood actually reaching the tissues.

In the absence of reliable guides to systemic perfusion, clinicians have limited ability to detect circulatory failure in preterm infants. Furthermore, even if circulatory failure was to be detected, the optimal treatment required to support the circulation is unclear, since adequacy of perfusion cannot easily be assessed as an outcome measure in clinical trials.

The work described in this thesis was prompted by a series of journal articles published in 2000-2001. These highlighted the vascular component of the pathophysiology of preterm brain injury(7), the importance of provision of appropriate cardiovascular monitoring and support to preterm infants(4, 8) and the potential for superior vena cava (SVC) flow to be measured as a marker of systemic perfusion that was unaffected by fetal shunt pathways(9) and that predicted subsequent brain injury(10).

We elected to use echocardiography to study a cohort of preterm infants born at the National Women's Hospital, Auckland, New Zealand. By studying a large cohort of



preterm infants we aimed to evaluate the feasibility of using echocardiography to make repeated haemodynamic measures in the early postnatal period in preterm infants.

A principle objective of the study was to further examine the utility of the technique of measurement of SVC flow volume. It was important to establish whether this measure was feasible and reproducible in the hands of a group of researchers distinct from those who first described the technique. As volume of descending aorta (DAo) flow is increasingly being monitored in paediatric(11) and adult(12) intensive care units, we also undertook the first systematic evaluation of this technique in preterm infants to assess its suitability as a further marker of systemic perfusion unaffected by fetal shunt pathways.

We aimed to assess the safety of these echocardiographic techniques, to establish reference ranges for SVC and DAo flow, and to carefully assess the repeatability of the measurements.

To allow interpretation of the patterns of SVC and DAo flow volume in the unique context of the transitional circulation we also quantified left and right ventricular outputs, assessed ductal and atrial shunt patterns and quantified arterial blood pressure. We were particularly interested in whether findings from our cohort of infants studied during the transition from the fetal to the adult circulations would provide further insights into the relationship between arterial blood pressure and systemic blood flow, and the impact of shunting through the fetal channels on adequacy of systemic perfusion during this critical time.

Finally, and perhaps most importantly, we hoped to further assess the association between markers of blood flow and outcome following preterm birth, particularly the association between early low SVC flow and subsequent brain injury. Specifically we

aimed to examine whether use of echocardiographic markers of perfusion in clinical practice could add to the information obtained through the currently routine practice of monitoring of arterial blood pressure.

The aim of the research described in this thesis is above all to increase awareness and understanding of the pathophysiology of the transitional circulation. In the future we hope to continue working to improve cardiovascular monitoring and support in preterm infants with the goal of improving long term neurodevelopmental outcome.

## Table of Contents

<b>1</b>	<b>Literature Review .....</b>	<b>1</b>
1.2	Role of the ductus arteriosus .....	9
1.3	Assessment of systemic and cerebral perfusion	20
1.4	Cerebral blood flow and neurodevelopmental outcome .....	34
1.5	The transitional circulation in the preterm infant	50
1.6	Echocardiography in the assessment of neonatal haemodynamics .....	61
1.7	Summary of literature review.....	73
<b>2</b>	<b>Methods .....</b>	<b>75</b>
2.1	Recruitment.....	75
2.2	Data collection .....	76
2.3	Echocardiography techniques .....	79
2.4	Statistical analysis.....	96
<b>3</b>	<b>Cardiorespiratory Stability during Echocardiography in Preterm Infants.....</b>	<b>97</b>
3.1	Introduction.....	97
3.2	Methods.....	98
3.3	Results.....	99
3.4	Discussion .....	101
3.5	Conclusion .....	103
<b>4</b>	<b>Repeatability of Measurement of Flow Volume in the Superior Vena Cava and Descending Aorta .....</b>	<b>104</b>
4.1	Introduction.....	104
4.2	Methods.....	106
4.3	Results.....	107
4.4	Discussion .....	115
4.5	Conclusion .....	120
<b>5</b>	<b>Reference Ranges of Flow Volume in the Superior Vena Cava and Descending Aorta in Healthy Preterm and Term Neonates .....</b>	<b>122</b>
5.1	Introduction.....	122

5.2	Methods .....	123
5.3	Results in term infants .....	123
5.4	Results in preterm infants .....	125
5.5	Discussion .....	129
5.6	Conclusion .....	134
<b>6</b>	<b>Flow Volume in the Superior Vena Cava and Descending Aorta in Sick Preterm Neonates .....</b>	<b>136</b>
6.1	Introduction.....	136
6.2	Methods .....	137
6.3	Results.....	138
6.4	Discussion .....	148
6.5	Conclusion .....	154
<b>7</b>	<b>Relationship between Blood Pressure and Blood Flow in Sick Preterm Neonates.....</b>	<b>155</b>
7.1	Introduction.....	155
7.2	Methods .....	156
7.3	Results.....	157
7.4	Discussion .....	160
7.5	Conclusions .....	167
<b>8</b>	<b>Impact of the Ductus Arteriosus on Systemic Perfusion in Preterm Infants in the First 48 Hours of Postnatal Life.....</b>	<b>168</b>
8.1	Introduction.....	168
8.2	Methods .....	170
8.3	Results.....	171
8.4	Discussion .....	179
8.5	Conclusion .....	189
<b>9</b>	<b>Relationship between Markers of Systemic Blood Flow and Clinical Outcome in Preterm Neonates ..</b>	<b>190</b>
9.1	Introduction.....	190
9.2	Methods .....	191
9.3	Results.....	193
9.4	Discussion .....	214
9.5	Conclusion .....	222

<b>10</b>	<b>Conclusions and Future Directions .....</b>	<b>224</b>
<b>11</b>	<b>Appendices .....</b>	<b>229</b>
<b>12</b>	<b>References .....</b>	<b>235</b>

## List of Figures

Figure 2.1 - Transducer position for SVC diameter measurement.....	85
Figure 2.2 - M mode imaging for SVC diameter measurement .....	85
Figure 2.3 - Transducer position for SVC flow velocity measurement.....	86
Figure 2.4 - Pulsed wave Doppler imaging for SVC flow velocity measurement .....	86
Figure 2.5 - Transducer position for DAo diameter measurement .....	87
Figure 2.6 - M mode imaging for DAo diameter measurement .....	87
Figure 2.7 - Transducer position for subcostal DAo flow velocity measurement.....	88
Figure 2.8 - Pulsed wave Doppler imaging for subcostal DAo flow velocity measurement .....	88
Figure 2.9 - Transducer position for suprasternal DAo flow velocity measurement .....	89
Figure 2.10 - Pulsed wave Doppler imaging for suprasternal DAo flow velocity measurement .....	89
Figure 4.1 - Bland-Altman plot of intra-observer difference between two measures of SVC flow for 18 scans in 13 infants .....	108
Figure 4.2 - Bland-Altman plot of inter-observer difference between two measures of SVC flow for 11 scans in eight preterm infants.....	110
Figure 4.3 - Bland-Altman plot of intra-observer difference between two measures of DAo flow for 18 scans in 13 preterm infants.....	111
Figure 4.4 - Bland-Altman plot of inter-observer difference between two measures of DAo flow for 11 scans in eight preterm infants.....	113
Figure 6.1 - Box and whisker plot of SVC flow at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants .....	143
Figure 6.2 - Box and whisker plot of DAo flow at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants .....	145
Figure 6.3 - Box and whisker plot of LVO at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.....	146
Figure 6.4 - Box and whisker plot of RVO at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.....	147
Figure 7.1 - Inverse relationship between SVC flow and continuously monitored mean blood pressure in 30 preterm infants at 5 hours postnatal age.....	158
Figure 7.2 - Inverse relationship between SVC flow and continuously monitored mean blood pressure in 32 preterm infants at 12 hours postnatal age.....	159
Figure 8.1 - Presence of reversal of diastolic DAo flow is associated with increased LVO in infants with duct diameter >1.5 mm at 12 Hours .....	174
Figure 8.2 - Degree of reversal of diastolic DAo flow is not associated with SVC flow in infants with duct diameter >1.5 mm at 12 Hours. ....	175
Figure 8.3 - Increased degree of reversal of diastolic DAo flow is associated with decreased DAo flow in infants with duct diameter >1.5 mm at 12 Hours. ....	175

## List of Tables

Table 3.1 - Systolic, diastolic and mean blood pressure (BP), heart rate and oxygen saturation during scan and control periods for 40 scans in 17 infants.	100
Table 3.2 - Coefficients of variation for systolic, diastolic and mean blood pressure, heart rate and oxygen saturation during scan and control periods.....	101
Table 4.1 - Intra-observer repeatability for SVC diameter, velocity time integral, heart rate and flow volume for 18 scans in 13 preterm infants.....	109
Table 4.2 - Inter-observer repeatability for SVC diameter, velocity time integral, heart rate and flow volume for 11 scans in eight preterm infants.....	110
Table 4.3 - Intra-observer repeatability data for DAo diameter, velocity time integral, heart rate and flow volume for 18 scans in 13 preterm infants.....	112
Table 4.4 - Inter-observer repeatability data for DAo diameter, velocity time integral, heart rate and flow volume for 11 scans in eight preterm infants.....	114
Table 5.1 - Values for SVC studies in 13 healthy term infants. ....	124
Table 5.2 - Values for DAo studies in 13 healthy term infants .....	125
Table 5.3 - Values for SVC studies in 14 healthy preterm infants.....	127
Table 5.4 - Values for DAo studies in 14 healthy preterm infants.....	128
Table 6.1 - Characteristics of included infants .....	139
Table 6.2 - Postnatal age at echocardiography in 80 preterm infants.....	141
Table 6.3 - Scans in which satisfactory images were gained at echocardiography .....	142
Table 6.4 - Values for SVC flow at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.. .....	143
Table 6.5 - Values for DAo flow at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.. .....	144
Table 6.6 - Values for LVO at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.. .....	145
Table 6.7 - Values for RVO at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.. .....	146
Table 6.8 - Ductal diameter at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.. .....	147
Table 6.9 - Mean arterial blood pressure at 5-48 hours postnatal age in 14 healthy and 66 sick preterm infants.....	148
Table 8.1 - Duct diameter and direction of shunt in 80 preterm infants.....	172
Table 8.2 - Associations of ductal size and DAo flow reversal at 5, 12, 24 and 48 hours postnatal age in 80 preterm infants.. .....	179
Table 9.1 - Timing of periventricular haemorrhage and occurrence of low blood flow in the first 24 hours in the 13 preterm infants of the 80 studied. ....	195
Table 9.2 - Timing of symptom onset and occurrence of low blood flow in the first 24 hours in the 5 preterm infants with abdominal pathology of the 80 studied. ....	198
Table 9.3 - Outcomes in ten premature infants with very low SVC flow .....	208
Table 9.4 - Outcomes in ten premature infants with very low DAo flow .....	209
Table 9.5 - Sensitivity, specificity, positive predictive value and negative predictive value of a single episode of each of low SVC or DAo flow, LVO or RVO for predicting the combined outcomes of death/PVH/NEC/CLD in 80 preterm infants .....	213
Table 9.6 - Sensitivity, specificity, positive predictive value and negative predictive value of a single episode of each of low SVC or DAo flow, LVO or RVO for predicting the narrower combined outcomes of new PVH or NEC in 80 preterm infants.....	214