

## ORIGINAL ARTICLE

# Clinical detection of low upper body blood flow in very premature infants using blood pressure, capillary refill time, and central-peripheral temperature difference

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**Objective:** To determine the accuracy of blood pressure (BP), capillary refill time (CRT), and central-peripheral temperature difference (CPTd) for detecting low upper body blood flow in the first day after birth.

**Methods:** A prospective, two centre cohort study of 128 infants born at < 30 weeks gestation. Invasive BP (n = 108), CRT (n = 128), and CPTd (n = 46) were performed immediately before echocardiographic measurement of superior vena cava (SVC) flow at three, 5–10, and 24 hours after birth.

**Results:** Forty four (34%) infants had low SVC flow (< 41 ml/kg/min) in the first day, 13/122 (11%) at three hours, 39/126 (31%) at 5–10 hours, and 4/119 (3%) at 24 hours. CPTd did not detect infants with low flows. Combining all observations in the first 24 hours, CRT  $\geq$  3 seconds had 55% sensitivity and 81% specificity, mean BP < 30 mm Hg had 59% sensitivity and 77% specificity, and systolic BP < 40 mm Hg had 76% sensitivity and 68% specificity for detecting low SVC flow. Combining a mean BP < 30 mm Hg and/or central CRT  $\geq$  3 seconds increases the sensitivity to 78%.

**Conclusions:** Low upper body blood flow is common in the first day after birth and strongly associated with peri/intraventricular haemorrhage. BP and CRT are imperfect bedside tests for detecting low blood flow in the first day after birth.

Organ damage from circulatory compromise occurs when tissue oxygen demand exceeds delivery. The two main determinants of oxygen delivery are arterial oxygen concentration, which is easy to measure, and systemic blood flow (SBF), which is difficult to measure. Because SBF is difficult to measure, various surrogates are widely used in clinical practice to direct circulatory support therapies. These surrogates include blood pressure,<sup>1–6</sup> skin capillary refill time,<sup>7,8</sup> and core peripheral temperature difference.<sup>9–10</sup> Despite their widespread clinical use, there are almost no data validating the accuracy of these tests for detecting low SBF, particularly in preterm infants. Low SBF in the first day after birth is strongly implicated in the development of cerebral injury in preterm infants.<sup>11–15</sup> So clinically detecting low SBF in preterm infants has the potential to allow effective targeting of cardiovascular interventions aimed at improving blood flow and important clinical outcomes.

Doppler echocardiographic measures of ventricular outputs can be used to assess SBF. However, measuring SBF in this way in preterm infants on the first day after birth is complicated by the presence of shunts across the adapting heart (foramen ovale and ductus arteriosus).<sup>16–18</sup> These shunts can cause measurements of ventricular outputs to overestimate SBF by up to 100%.<sup>18</sup> To overcome this problem, we have previously described and validated a novel method of measuring SBF in premature infants in the first days after birth by measuring superior vena cava (SVC) flow, which measures flow returning from the upper body and brain.<sup>19</sup> This must be the same as the blood flow to this important region of the body. Low SVC flow was common in the first 24 hours after birth in extremely premature infants,<sup>11–13</sup> and is strongly and independently associated with subsequent peri/intraventricular haemorrhage (P/IVH),<sup>11–13,14</sup> low urine output and hyperkalaemia,<sup>20</sup> mortality,<sup>13</sup> and poor neurodevelopmental outcome.<sup>15</sup> Low SVC flow was a better

predictor of P/IVH<sup>14</sup> and poor neurodevelopmental outcome<sup>15</sup> than blood pressure. Therefore, accurate clinical detection of low SVC flow is an important clinical goal.

The aim of this study was to determine the accuracy of capillary refill time (CRT), central-peripheral temperature difference (CPTd), and blood pressure (BP) for detecting low blood flow to the brain and upper body in premature infants in the first day after birth.

## METHODS

The study was a two centre, prospective cohort study of premature infants born at < 30 weeks gestation. The study was carried out in the Royal Prince Alfred and Royal North Shore Hospital neonatal intensive care units, Sydney, Australia between October 1998 and December 1999. The ethics committees of Central Sydney and Northern Sydney Area Health Services approved the study. Informed consent was obtained from all parents.

## Infants

Infants born at < 30 weeks gestation and < 12 hours of age were eligible. Informed consent was obtained antenatally where possible. Infants were excluded if parental consent was refused, a major congenital abnormality or cardiac abnormality was identified, the infant was considered by the attending clinician to be non-viable, or if inotrope or indomethacin had been given before three hours after birth. Most infants were nursed in humidified cribs to maintain

**Abbreviations:** BP, blood pressure; CPTd, central peripheral temperature difference; CRT, capillary refill time; LR+, positive likelihood ratio; LR–, negative likelihood ratio; NPV, negative predictive value; P/IVH, peri/intraventricular haemorrhage; PPV, positive predictive value; ROC, receiver operator curve; SBF, systemic blood flow; Sn, sensitivity; Sp, specificity; SVC, superior vena cava

central temperature  $\geq 36.5^{\circ}\text{C}$  and with humidity  $\geq 80\%$ . CPTd was not used to adjust crib temperature.

### Clinical and physiological data

CRT, CPTd, and systolic and mean BP measurements were taken before each scan. A single investigator (DO) performed all clinical measurements after a period of thermal stability (undisturbed for at least 15 minutes). CRT was measured in all 128 enrolled infants, centrally on the anterior chest and peripherally on the palm of the hand. An index finger was used to apply sufficient pressure to blanch the skin for five seconds, and a stopwatch was used to time return to normal skin colour. Two consecutive reproducible results were taken as the true CRT.

Central-peripheral temperature was monitored in a subgroup of 46 infants enrolled at one centre (Royal Prince Alfred Hospital) and nursed in Dräger 8000ic humidicribs. Dräger Thermoview continuous central and peripheral temperature monitoring was used. Central temperature was recorded by placing the sensor at the thorax/bed interface, which has been shown to be an accurate measure of core temperature.<sup>21</sup> Peripheral temperature was recorded by placing the sensor on the sole of the infant's foot. The temperature probes were secured using a hydrocolloid transparent dressing. CPTd was recorded after a 15 minute period of stability before echocardiography.

Invasive arterial monitoring using umbilical or peripheral arterial catheters was available in 108 of the 128 infants enrolled. Systolic and mean BP were recorded over 10 cardiac cycles before echocardiography.

### Echocardiographic monitoring, blood flow measurement, and cardiovascular support

Echocardiographic monitoring was performed routinely at three, 5–10, and 24 hours of age. The 5–10 hour scan is taken as the scan before the start of volume expansion and inotropes if used, or the scan closest to 10 hours of age. Low SBF was defined as SVC flow  $< 41$  ml/kg/min from previous data in healthy preterm babies.<sup>19</sup> An Acuson (Mountain View, California, USA) 128/XP10 ultrasound scanner was used with a 7 MHz vector array transducer incorporating colour flow and pulsed wave Doppler. The scan was recorded on to VHS videotape, and the measurements then taken from the videotape. Structural normality of the heart was established on the initial scan. SVC flow was determined as described previously.<sup>19</sup> A clinically significant patent ductus arteriosus was defined as a ductus with a colour Doppler diameter  $> 1.6$  mm from previous studies.<sup>22–24</sup>

Infants who were identified on echocardiography as having a ductus arteriosus  $> 1.6$  mm were given indomethacin.<sup>25</sup> Infants who were identified as having low SVC flow ( $< 41$  ml/kg/min) were treated with volume expansion (normal saline 10 ml/kg) and inotropes (dopamine and/or dobutamine).<sup>26</sup>

### Statistical analysis

Data were analysed with a PC based statistics package (SPSS release 10.0.7 for Windows) using *t* test for continuous variables, and the two sided  $\chi^2$  test or Fisher exact test where appropriate for dichotomous variables. The Pearson correlation coefficient was used to assess the linear correlation between variables where appropriate. Confidence intervals for diagnostic test accuracy were calculated using the Newcombe-Wilson hybrid score (not continuity corrected).<sup>27</sup> Receiver operator curves (ROC) and area under the ROC (with 95% confidence interval (CI)) were calculated using SPSS.

## RESULTS

### Study population

Between October 1998 and December 1999, 160 infants from 23 to 29 weeks gestation were admitted to the neonatal units (100 to Royal Prince Alfred Hospital and 60 to Royal North Shore Hospital). Consent was not obtained or an investigator was not available for 32 (20%) infants. The mean gestation (27.1 v 26.8 weeks) and birth weight (1078 v 986 g) of non-enrolled infants was not significantly higher than enrolled infants. A total of 128 infants with consent underwent clinical and echocardiographic monitoring in the first 24 hours after birth.

Echocardiography was performed on 122 infants at three hours, 126 at 5–10 hours, and 119 infants at 24 hours. A total of 80 infants (63%) with a significant ductus arteriosus (colour Doppler diameter  $> 1.6$  mm) received indomethacin. Forty four (34%) of 128 infants were identified with low SVC flow in the first 24 hours after birth (table 1). Low SVC flow was identified in 13/122 (11%) at three hours, 39/126 (31%) at 5–10 hours, and 4/119 (3%) at 24 hours. All 44 infants (34%) with low SVC flow in the first 24 hours after birth received volume expansion and inotropes, either dopamine and/or dobutamine. Therefore, no infant had received indomethacin or inotropes at the three hour measurement. At 5–10 hours, 79/126 infants had received indomethacin, and seven infants were receiving inotrope. At 24 hours, 75/119 had received indomethacin, and 39 were receiving inotropes (14 dobutamine, 16 dopamine, and nine both dobutamine and dopamine).

### Central-peripheral temperature difference

Forty six infants had central-peripheral temperature measurements taken before flow measurements (table 2). SVC flow  $< 41$  ml/kg/min was present in 7/43 (16%) infants at three hours, 17/46 (37%) infants at 5–10 hours, and 1/43 (2%) at 24 hours. Combining the three sets of observations (fig 1) results in a pretest probability of low flow of 19% (25/132). There was no correlation between CPTd and SVC flow (Pearson  $r = 0.02$ ,  $p = 0.8$ ). The area under the ROC was 0.47 (95% CI 0.35 to 0.61). The post-test probabilities of low flow were not significantly different from the pretest probabilities (table 3).

**Table 1** Perinatal variables and outcomes of preterm infants with low superior vena cava flow ( $< 41$  ml/kg/min) detected in the first 24 hours after birth

	Normal flow (n = 84)	Low flow (n = 44)	p Value
Mean (SD) gestation (weeks)	27.4 (1.6)	25.8 (1.8)	$< 0.001$
Mean (SD) birth weight (g)	1027 (276)	916 (271)	0.03
$\leq 10$ th percentile	11 (13%)	1 (2%)	0.06
Male	36 (43%)	23 (52%)	0.3
Antenatal steroids			
Any	81 (96%)	37 (84%)	0.03
Complete	60 (71%)	21 (48%)	0.008
Antihypertensives	21 (25%)	2 (5%)	0.004
Labour	56 (67%)	34 (77%)	0.2
Caesarean	50 (60%)	23 (52%)	0.4
Ex utero	6 (7%)	8 (18%)	0.08
Apgar $\leq 4$ at 1 minute	29 (35%)	22 (50%)	0.09
Ventilated	71 (85%)	44 (100%)	0.004
Respiratory distress syndrome	57 (68%)	36 (82%)	0.09
Patent ductus arteriosus	47 (56%)	33 (75%)	0.03
Peri/intraventricular haemorrhage			
Any grade	17 (20%)	21 (48%)	0.001
Grade 3–4	5 (6%)	12 (27%)	0.001
Died	11 (13%)	25 (57%)	$< 0.001$

**Table 2** Use of central-peripheral temperature difference (CPTd), capillary refill time (CRT), mean and systolic blood pressure (BP) to predict low superior vena cava flow (< 41 ml/kg/min) in preterm infants < 30 weeks gestation. Combined observations and conditional likelihood ratios in first 24 hours

	Normal flow	Low flow	Total
<b>CPTd</b>			
< 2°C	74	15	89
≥ 2°C	33	10	43
Total	107	25	132
<b>CRT</b>			
< 3 seconds	249	25	274
3–3.9 seconds	49	15	64
≥ 4 seconds	13	16	29
Total	311	56	367
<b>Systolic BP</b>			
≥ 48 mm Hg	89	4	93
40–47.9 mm Hg	81	9	90
< 40 mm Hg	81	41	122
Total	251	54	305
<b>Mean BP</b>			
≥ 30 mm Hg	193	22	215
< 30 mm Hg	58	32	90
Total	251	54	305
> Gestation	220	38	258
≤ Gestation*	31	16	47
Total	251	54	305

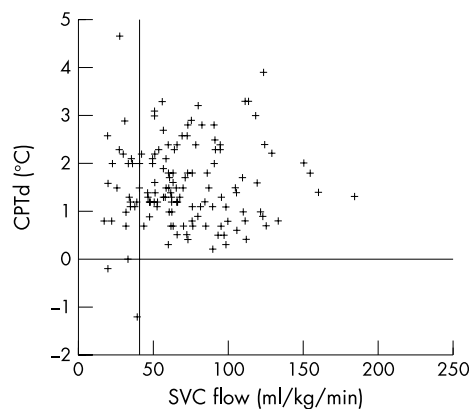
\*Mean blood pressure ≤ gestation in weeks.

### Capillary refill time

Central and peripheral CRT were measured in all 128 infants before flow measurements (table 2), with 13/122 (11%) at three hours, 39/126 (31%) at 5–10 hours, and 4/119 (3%) at 24 hours having low SVC flow. The sensitivity and specificity of the CRT at three and 5–10 hours were similar, as were the results of the central and peripheral CRT. Combining the three sets of observations (fig 2) results in a pretest probability of low flow of 15% (56/367). There was a significant correlation between both central (Pearson  $r = 0.42$ ,  $p < 0.001$ ) and peripheral (Pearson  $r = 0.38$ ,  $p < 0.001$ ) CRT and SVC flow. A central CRT ≥ 3 seconds had a sensitivity of 55% and specificity of 80% for low SVC flow (table 3). The confidence intervals of the positive predictive value (PPV) (33%, 95% CI 29 to 38%) and negative predictive value (NPV) (91%, 95% CI 88 to 94%) values do not include the pretest probabilities. A central CRT ≥ 4 seconds increased the specificity (96%) and PPV (55%) but reduced the sensitivity (29%). The area under the ROC was 0.72 (95% CI 0.64 to 0.80). A sensitivity of 90% was produced at a central CRT ≥ 1.9 seconds, but resulted in only 19% specificity.

### Blood pressure

Invasive BP measurements (table 3) were performed on 108 infants before flow measurements, with 13/97 (13%) at three hours, 37/108 (34%) at 5–10 hours, and 4/100 (4%) at 24 hours having low flow. Combining the three sets of observations (mean BP (fig 3); systolic BP (fig 4)) results in a pretest probability of low flow of 18% (54/305). There was a weak but significant correlation between both mean (Pearson  $r = 0.23$ ,  $p < 0.001$ ) and systolic (Pearson  $r = 0.26$ ,  $p < 0.001$ ) BP and SVC flow in the first 24 hours. The area under the ROC was 0.78 (95% CI 0.64 to 0.80) for systolic BP and 0.75 (95% CI 0.67 to 0.82) for mean BP. At 90% sensitivity, a systolic BP < 47 mm Hg resulted in 35% specificity, similar to a mean BP < 37 mm Hg with 33% specificity.



**Figure 1** Scatter plot of central-peripheral temperature difference (CPTd) against superior vena cava (SVC) flow for all observations. Reference lines represent SVC flow of 41 ml/kg/min and zero CPTd.

A mean BP < 30 mm Hg had 59% sensitivity and 77% specificity for low SVC flow (table 4). The confidence intervals of the PPV (36%, 95% CI 30 to 41%) and NPV (90%, 95% CI 86 to 93%) did not include the pretest probabilities. Using a mean BP ≤ gestation in weeks reduced the sensitivity to 30% but increased the specificity to 88% for low SVC flow.

A systolic BP < 40 mm Hg had 76% sensitivity and 68% specificity for low SVC flow. The confidence intervals of the PPV (34%, 95% CI 28 to 39%) and NPV (93%, 95% CI 90 to 96%) do not include the pretest probabilities. Using a systolic BP < 48 mm Hg increases the sensitivity to 93% but reduces the specificity to 35%. The NPV (96%) means an infant with a systolic BP ≥ 48 mm Hg is unlikely to have low flows.

Using a criterion of a mean BP < 30 mm Hg and/or central CRT ≥ 3 seconds has a similar diagnostic accuracy to a systolic BP < 40 mm Hg with 78% sensitivity, 63% specificity, PPV 31% and NPV 88%.

### DISCUSSION

Detecting low SBF early and accurately in the first day has the potential to allow effective targeting of cardiovascular interventions aimed at improving blood flow and reducing neonatal mortality and morbidity. This study found that systolic and mean BP have clinical utility but are imperfect predictors of low SVC flow. A mean BP ≤ gestation in weeks detects only 30% of infants with low flow. Increasing the cut off to < 30 mm Hg detects nearly twice as many infants. This may be a better cut off, as it has been associated with neonatal mortality and cerebral injury.<sup>28</sup> However, the PPV is still low. Slightly better was using a systolic BP < 40 mm Hg, which detected 76% of infants with low SVC flow, but again the PPV is low. More useful for its “rule out” value is that an infant is unlikely to have low SVC flow if the systolic BP is above 48 mm Hg or mean BP above 40 mm Hg.

Both central and peripheral CRT had similar utility but are also imperfect predictors of low SVC flow. A central CRT ≥ 3 seconds detected 55% of infants with low SVC flow but had low PPV, with only a third of the infants above this level having low flow. Increasing the cut off to four seconds increases the PPV to 55%. There are no previous data in newborn infants relating the CRT to a measure of SBF. A study in healthy term infants in a well baby nursery in the first days after birth showed that values varied widely and depended on environmental and skin temperatures.<sup>8</sup> In our study, an attempt was made to minimise the effect of the environment by nursing the infants in a humidified crib in

**Table 3** Diagnostic accuracy of central-peripheral temperature difference (CPTd) and capillary refill time (CRT) for prediction of low superior vena cava flow in preterm infants < 30 weeks gestation

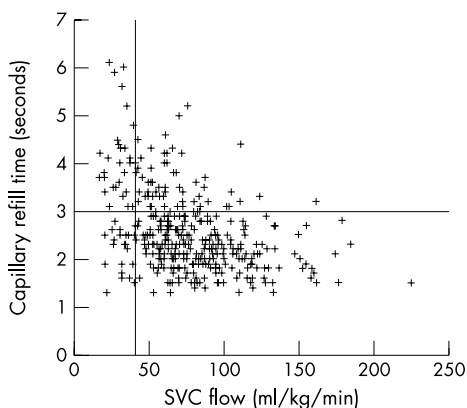
	Sn	Sp	PPV	NPV	LR+	LR-
<b>CPTd ≥ 2°C</b>						
3 hours	29 (15 to 42)	78 (65 to 90)	20 (8 to 32)	85 (74 to 96)	1.29	0.92
10 hours	41 (27 to 55)	66 (52 to 79)	41 (27 to 55)	66 (52 to 79)	1.19	0.90
All observations	40 (32 to 48)	69 (61 to 77)	23 (16 to 30)	83 (77 to 90)	1.30	0.87
<b>CRT ≥ 3 seconds</b>						
3 hours	54 (45 to 63)	79 (72 to 86)	23 (16 to 31)	93 (89 to 98)	2.55	0.58
10 hours	59 (50 to 68)	75 (67 to 82)	51 (42 to 60)	80 (73 to 87)	2.33	0.55
All observations	55 (50 to 60)	80 (76 to 84)	33 (29 to 38)	91 (88 to 94)	2.78	0.56
<b>CRT ≥ 4 seconds</b>						
3 hours	38 (30 to 47)	93 (88 to 97)	38 (30 to 47)	93 (88 to 97)	5.24	0.66
10 hours	26 (18 to 33)	97 (93 to 100)	77 (70 to 84)	74 (67 to 82)	7.44	0.77
All observations	29 (24 to 33)	96 (94 to 98)	55 (50 to 60)	88 (85 to 91)	6.84	0.75

Values in parentheses are 95% confidence intervals. LR+, Positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; Sn, sensitivity; Sp, specificity.

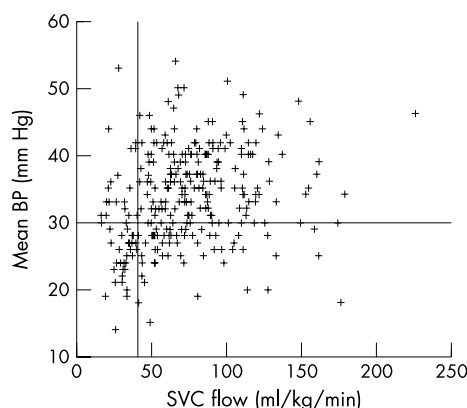
their neutral thermal zone. Although CRT is a continuous variable, cut offs at three and four seconds were used, as this reflects the clinical accuracy of the technique. Used alone, the CRT has limited clinical utility. Combining criteria of a mean BP < 30 mm Hg or central CRT ≥ 3 seconds increases the sensitivity, with 78% of infants with low flow detected. However, again the PPV is low.

In this study, CPTd did not correlate with low SVC flow in the first day after birth. To try to avoid environmental confounders, we nursed infants in their neutral thermal zones and waited 15 minutes without disturbance before measurement and avoided measurement when temperatures were changing rapidly. A previous study has suggested that CPTd is a potential early marker of cold stress after the first two to three days after birth in infants born weighing < 1000 g.<sup>9</sup> They noted a relatively small CPTd in the first day after birth, frequent CPTd reversals, and increased temperature fluctuations outside the normal range. No measure of blood flow was obtained. In a second study, CPTd showed a significant correlation with plasma arginine vasopressin concentration in a group of sick, very preterm infants before and after they were given volume expansion on the basis of clinically suspected hypovolaemia.<sup>10</sup> Again no measure of circulatory filling or SBF was obtained. This study finds a complete lack of clinical utility of CPTd in the first day after birth for detecting infants with low SVC flow.

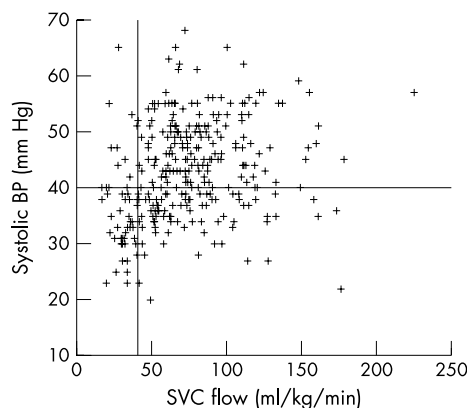
An important question is whether low SVC flow is a valid yardstick. This raises questions of the reliability of measuring SVC flow and the predictive value of low SVC flow for adverse clinical outcomes. Median intraobserver and interobserver variability for SVC flows were previously reported as 8.0% and 14% respectively.<sup>19</sup> Although it must be acknowledged



**Figure 2** Scatter plot of capillary refill time against superior vena cava (SVC) flow for all observations. Reference lines represent SVC flow of 41 ml/kg/min and capillary refill time of three seconds.



**Figure 3** Scatter plot of mean blood pressure (BP) against superior vena cava (SVC) flow for all observations. Reference lines represent SVC flow of 41 ml/kg/min and mean BP of 30 mm Hg.



**Figure 4** Scatter plot of systolic blood pressure (BP) against superior vena cava (SVC) flow for all observations. Reference lines represent SVC flow of 41 ml/kg/min and systolic BP of 40 mm Hg.

**Table 4** Diagnostic accuracy of mean and systolic blood pressure for prediction of low superior vena cava flow in preterm infants < 30 weeks gestation

	Sn	Sp	PPV	NPV	LR+	LR-
<b>Systolic BP &lt; 48 mm Hg</b>						
3 hours	100 (100 to 100)	14 (7 to 21)	15 (8 to 22)	100 (100 to 100)	1.17	0
10 hours	92 (87 to 97)	39 (30 to 49)	44 (35 to 54)	90 (85 to 96)	1.52	0.21
All observations	93 (90 to 96)	35 (30 to 41)	24 (19 to 28)	96 (93 to 98)	1.43	0.21
<b>Systolic BP &lt; 40 mm Hg</b>						
3 hours	69 (60 to 78)	51 (41 to 61)	18 (10 to 26)	91 (86 to 97)	1.42	0.60
10 hours	81 (74 to 88)	65 (56 to 74)	55 (45 to 64)	87 (80 to 93)	2.30	0.29
All observations	76 (71 to 81)	68 (62 to 73)	34 (28 to 39)	93 (90 to 96)	2.35	0.36
<b>Mean BP &lt; 30 mm Hg</b>						
3 hours	62 (57 to 71)	58 (49 to 68)	19 (11 to 26)	91 (85 to 97)	1.48	0.66
10 hours	62 (53 to 71)	82 (74 to 89)	64 (55 to 73)	81 (73 to 88)	3.40	0.46
All observations	59 (54 to 65)	77 (72 to 82)	36 (30 to 41)	90 (86 to 93)	2.56	0.53
<b>Mean BP ≤ gestation (in weeks) mm Hg</b>						
3 hours	38 (29 to 48)	76 (68 to 85)	20 (12 to 28)	89 (83 to 95)	1.62	0.81
10 hours	27 (19 to 35)	92 (86 to 97)	63 (53 to 72)	71 (62 to 79)	3.2	0.8
All observations	30 (25 to 35)	88 (84 to 91)	34 (29 to 39)	85 (81 to 89)	2.40	0.80

Values in parentheses are 95% confidence intervals.

BP, Blood pressure; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; Sn, sensitivity; Sp, specificity.

that this reliability is that of experienced operators in neonatal echocardiography, the techniques for measuring SVC flow are relatively simple, and the vessel was chosen for its ease of measurement in the first day after birth. Low SVC flow is common in the first 24 hours after birth in extremely premature infants,<sup>11 13</sup> and is strongly and independently associated with subsequent P/IVH,<sup>11 13 14</sup> low urine output and hyperkalaemia,<sup>20</sup> mortality,<sup>13</sup> and poor neurodevelopmental outcome.<sup>15</sup> Low SVC flow was a better predictor of P/IVH<sup>14</sup> and poor neurodevelopmental outcome<sup>15</sup> than BP. Clearly, current evidence suggests that it is important to detect low SVC flow. All non-invasive measures have limitations to their accuracy, and SVC flow is no exception. We would argue that neonatology currently has no clinically usable haemodynamic measure that has been better validated for use as a yardstick.

However, most clinical centres do not use echocardiography in the first day after birth to determine cardiovascular status. In addition, most studies of cardiovascular interventions in preterm infants have enrolled hypotensive preterm infants and used blood pressure to determine success of treatment.<sup>1-6</sup> Commonly used criteria for hypotension and cardiovascular intervention have included a mean BP < 30 mm Hg,<sup>2 3 29</sup> which was associated with increased mortality and cerebral injury in a cohort study.<sup>28</sup> Other studies<sup>4 5 30-32</sup> have defined hypotension as below the range (usually the 10th centile) seen in population studies<sup>33 34</sup> of preterm infants. A commonly used bedside approximation of the 10th centile is a mean BP less than the gestational age in weeks or a systolic BP < 40 mm Hg.<sup>33</sup>

The low correlation between blood pressure and SBF in the first days after birth has been reported previously in very premature infants.<sup>35 36</sup> In view of the inaccuracy of using blood pressure to identify preterm infants with low blood flow and the strong association between low upper body blood flow and adverse outcomes,<sup>11 13-15</sup> future studies of cardiovascular interventions in preterm infants should measure SBF. In clinical practice, no bedside test accurately identifies infants with and without low SVC flow, and reliance on these tests is likely to result in inappropriate use of cardiovascular interventions. In Australia and New Zealand, 40% of units have a neonatologist who provides an echocardiographic service that would facilitate the measurement of blood flow.<sup>37</sup>

In conclusion, CPTd did not correlate with low SVC flow in the first day after birth. BP and CRT are imperfect predictors

of low SVC flow. Future studies of cardiovascular interventions in very preterm infants should measure SBF.

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