Non Invasive Estimation of End-systolic Blood Pressure in Babies

GA Pearson1, P Burton2 and D Field3

1Department of Paediatric Intensive Care, Birmingham Children’s Hospital, UK
2Department of Infrastructural Epidemiology, University of Bristol, UK
3Department of Neonatal Medicine, University of Leicester, UK

Abstract

Conventional measurements of systolic cardiac function and cardiac output may be influenced by loading conditions. The presence of extra-cardiac shunts in the transitional circulation limits the application of such measures in a neonatal population. An accurate method to assess neonatal myocardial function is required that takes account of cardiac loading conditions. One option is to correlate conventional echocardiographic indices with end systolic stress, an index of afterload derived from measurements of the thickness of the ventricular wall and the end systolic blood pressure. We hypothesised that this could be done on-invasively and sought to compare such a method to a gold standard. In this study, end systolic blood pressure was derived from calibrated axillary artery pulse wave traces, made using hand held external pressure transducers. These were compared to pressures simultaneously recorded directly from a catheter in the aortic arch. 195 synchronous measurements were analysed (by assessment of bias and components of variance) in a population of 17 infants (<4 months). The results show a fixed bias of 1.23mmHg and 95% confidence limits of +/-5.56mmHg if five consecutive beats are analysed. These levels of agreement validate the method and demonstrate a degree of accuracy and precision that suggest that the technique may be clinically useful when used in a clinical setting without simultaneous cardiac catheterisation.

INTRODUCTION

“Cardiac function” is a global concept which incorporates volumetric indices (such as the cardiac output) and mechanical forces of loading and contractility. Invasive haemodynamic assessment is often restricted or precluded in neonatal intensive care because of the size of the patient. In the presence of apparent circulatory insufficiency the choice between cardio-tropic support and intravascular volume loading may be difficult or made in the absence of accurate information about cardiac function. There is therefore a need for an accurate and precise but non-invasive method of assaying cardiac function on the neonatal intensive care unit.

Ventricular function may be assessed by a variety of techniques during both systolic and diastolic phases of the cardiac cycle. The choice depends upon the clinical situation and the question posed. The indices are influenced to varying extents by changes in cardiac loading conditions. The end systolic point can be recognised for each heart beat on a pulse pressure trace since it occurs at the dichrotic notch. The significance of the end systolic point is its stability in the face of acute variation in loading conditions and its reaction to changes in contractility [1]. At end systole, preload influences are at a minimum. Ventricular wall stress derived at end systole is an accurate expression of after load.

End systolic wall stress (ESS) has been shown to allow comparisons to be drawn between ventricles which have compensated for chronic loading conditions [2], as well as acute changes [3]. Its determination relies upon the accurate measurement of end systolic blood pressure (ESBP). Non-invasive methods have been described for use in neonates and small children [4], and have been used in studies of Paediatric populations since the 1980s [5]. These methods have been shown to bear a positive correlation with catheter data but their accuracy (agreement with a gold standard) has not been determined. Difficulties in the non-invasive measurement of ESBP have led several authors to substitute peak systolic pressure in their calculations [6], but the assertion that peak systolic pressure bears a linear relationship to ESBP between patients in the neonatal population is counterintuitive. We assessed a simple non-invasive technique of determining ESBP in babies less than six months of age and less than 5kg. Hypothesising that
the non-invasive method would agree with the invasive method and hence prove clinically useful. The study received local ethical approval.

**METHODS**

**Patients and Methods**

Seventeen infants aged 0-6 months undergoing cardiac catheterisation for a variety of indications were studied. These patients could be anticipated to demonstrate a diverse relationship between systolic and ESBP as they were not preselected by cardiac lesion. The study group included patients with persistent ductus arteriosus, aortic stenosis and aortic and mitral regurgitation. The investigator was kept blind to the patient diagnosis and subsequent data analysis performed upon anonymous records.

All the studies were performed by one investigator blinded to the cardiac diagnosis. During the cardiac catheterisation, the investigator applied a hand held external pressure transducer to the axilla. This was used to sense the pulse in the axillary artery (where it crosses the humeral head) and to generate a trace on a chart recorder without the necessity for an arterial line. The end systolic pressure (the base of the dicrotic notch) was determined by interpolation once the trace was calibrated. Calibration was achieved by ascribing values to the maxima and minima of the trace from the systolic and diastolic measurements of cuff blood pressure determined from a simultaneous oscillometric measurement. Three consecutive automated cuff blood pressure measurements (Dynamap – Critikon 8100 1986) were made during the pressure tracing using a cuff size sufficient to cover two thirds of the upper arm of the infant. The subsequently ascribed systolic and diastolic values were the average of these measurements.

The external trace was charted simultaneously with that from a calibrated side hole pressure line in the aortic arch. The data were analysed to estimate the components of variance (defining the precision of the non-invasive technique) and the bias, (defining its accuracy), treating the catheter measurement as the gold standard. Data derived from cardiac catheterisation may itself be subject to measurement error. However, for the purpose of comparative analysis, catheter derived data was used as a reference standard i.e., was assumed to represent the true value of the ESBP. These results were then processed to predict the number of beats necessary in each recording required to produce a clinically useful result.

**Statistical Methods**

Data derived from cardiac catheterisation may itself be subject to measurement error. However for the purposes of comparative analysis catheter data was used as a reference standard i.e., it was assumed to represent the true value of the blood pressure at any point in the cardiac cycle. Consequently the catheter data alone were used to determine the limits of agreement and correlation between end systolic and peak systolic blood pressure to assess whether the two values can or should be used interchangeably in arithmetic calculations such as the determination of end systolic stress.

The observed variability of a non-invasive measurement of end systolic blood pressure (NIESBP) may rationally be resolved into four components.

(a) Random variation of the true mean ESBP between individuals

(b) Random variation of the true ESBP from beat to beat within an individual

(c) Random variation of the non invasive measurement error between individuals

(d) Random variation of the non invasive measurement error from beat to beat within an individual

There may also be a systematic bias associated with the non-invasive measurement.

The random and fixed components contributing to an observed NIESBP value at a given beat were represented by a linear model. Given that the catheter measurement of ESBP at a particular beat may reasonably be viewed as being "correct", components (a) and (b) may be estimated using the observed catheter measured ESBP values only. These estimates may reasonably be obtained from standard components of variance analysis, simply viewed as being an extension of one way analysis of variance. Components (c) and (d) may then be estimated in an analogous manner using the differences between the non-invasive and catheter measurements at each beat. Finally the systematic bias of the cuff (λ) was estimated using standard maximum likelihood methods.

Having calculated the relevant fixed and random effects, estimates were made of the expected variation of an observed non-invasive (or catheter) based ESBP measurement - based upon an observed heart beat value - about the true mean ESBP in a given individual. Finally, tables were constructed detailing the expected variances standard errors and equivalent 95% confidence intervals for a variety of different values of n.

One assumption of the stated method is that there is no important correlation between the (NIESBP - Catheter ESBP) differences and the actual values of the catheter ESBP. This assumption was tested and found to be acceptable.

**RESULTS**

A total of 195 synchronous measurements were made from 17 patients. Mean weight of the patients was 3.4kg and mean age 6 weeks.

No linear relationship was found between peak and end-systolic blood pressure [correlation within individuals varied from $r=0.43+0.92$. There was also no useful level of agreement [7], between the two (mean difference $+24.7mmHg$, limits of agreement 4.9 to 44.9mmHg) showing that the measures cannot be used interchangeably. By contrast, when compared to the catheter data, the non-invasively determined end systolic blood pressure showed a fixed bias of 1.23mmHg (95% CI +/- 5.56 mmHg).

The estimates of components of variance were as follows:

(a) Variance of the true ESBP between individuals = 84.67mmHg$^2$. 


Email: GALE.PEARSON@bch.nhs.uk
(β) Variance of the true ESBP from beat to beat within an individual = 13.3mmHg².

(γ) Variance of non-invasive methods’ measurement error between individuals = 3.86mmHg².

(δ) Variance of non-invasive methods’ measurement error from beat to beat within individuals = 5.98mmHg².

(λ) Estimated cuff measurement bias (λ) = 1.23mmHg.

Variance of estimated cuff bias = 0.27mmHg².

The linear model representing the fixed and random contributions to the observed NIESBP measurement at a given pulse beat in an individual infant may be represented as follows:

\[ \text{Observed NIESBP} = \mu + \alpha + \beta + \gamma + \delta + \lambda \]

Where \( \mu \) = The fixed component representing the true mean ESBP in the relevant population as a whole. Ignoring the variance of the systematic bias, we calculated the overall variance for the mean of the 10 observations as follows:

\[ 1.67 + 3.86 + \frac{13.3 + 5.98}{10} = 90.46 \]

This is equivalent to a standard error of the mean of \( \sqrt{90.46} = 9.51 \) or an approximate 95% confidence interval of the estimated mean of +/-2 X 9.51 = +/- 19.02. However this estimate of the variability includes the random component (α) which estimates the variation of the true ESBP between individuals in the population. In any realistic clinical setting one is usually interested in the potential variability of measured ESBP about the true ESBP of the individual being investigated. That being the case one simply needs to remove the term (α) from the sum in order to estimate variability about the true mean, and so the relevant variance estimate for 10 observations would be:

\[ 1.86 + \frac{13.3 + 5.98}{10} = 5.79 \text{mmHg}^2 \]

which is equivalent to a standard error of 2.41 mmHg and a 95% confidence interval width of approximately +/-4.82 mmHg.

Table 1 details the estimated variability of a NIESBP measurement given a variety of different numbers of observed pulses. (Table 2) details the equivalent estimates for a catheter based ESBP measurement.

If the non-invasive method has a consistent bias, the estimates of variability detailed in (Table 1) would be completely appropriate for situations where one wished to make a comparison between different individuals or within one individual over time (using only the non-invasive technique) as any fixed bias would then be the same at each measurement and would therefore cancel. However in order to make definitive statements about the absolute variability of observed NIESBP and true ESBP, one ought to really take account of the uncertainty inherent to the estimated value of the bias i.e. the variance (λ) ought to be taken into consideration. (Table 3) is equivalent to table one but the contribution of the Var (λ) has been taken into account in all estimates. It is clear from the similarity of tables one and three that this component of variance is relatively unimportant in comparison to the other components considered.

On the basis of the results of this study the best estimate of true ESBP given a non-invasive measured ESBP of θ would be: θ - λ = θ - 1.23 mmHg and given that this was based upon 1, 5, 10 or 20 pulses, the variability of this estimate could be obtained from table three (for other values of n the variability could be estimated using the same methods). It would be useful to refine this estimate of bias using further data.

DISCUSSION

The use of indices of cardiac output and/or cardiac function in neonates may be difficult to interpret. Cardiac loading conditions may be profoundly affected by transitional circulation and the presence of extracardiac shunts. The persistence of a ductus arteriosus is a common phenomenon in neonatal intensive care and can allow a left-to-right or right-to-left extracardiac shunt depending upon the balance of pulmonary and systematic vascular resistance. Increases in pulmonary blood flow create a hyperdynamic state and right to left shunts cause systemic

<table>
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<th>Variance about the mean for the individual</th>
<th>Standard error about the true mean</th>
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desaturation. The sources of left ventricular blood are the pulmonary blood flow plus or minus a contribution from any atrial shunt through the foramen ovale. The fate of the cardiac output is similarly divided according to the balance of vascular resistance across persistent foetal connections. A large “run-off” for example may lead to low ends systolic and diastolic blood pressure. Our data failed to show a linear relation between peaks and end systolic blood pressure implying that one should not be used as a substitute for the other. The dynamics of the cardiac output in such circumstances cannot be used to derive information about the systemic delivery of oxygenated blood. Nor do they reliably reveal detail of cardiac function since no account is taken of loading conditions. Alternative methods of assessing oxygen delivery and consumption such as mixed venous oxygen saturation are of limited use without knowledge of cardiac function. In addition the insertion of pulmonary arterial lines is prohibitively difficult in neonatal intensive care which consequently proceeds without an accurate method of estimating cardiac function. Difficulties in measuring indices of cardiac function in small patients have led to neonatal clinical reliance on Doppler and protocol driven strategies of cardiovascular support that differ from those in older age groups where more invasive measurement is possible [8].

One drawback of this study is that all the investigations were performed by one individual. Hence inter-user variability was not assessed. Nevertheless it seems clear that the apparent variability of the non-invasive method would frequently be acceptable in the clinical or research setting particularly if 5 or 10 pulses are simultaneously performed without an accurate method of estimating cardiac function. Difficulties in measuring indices of cardiac function in small patients have led to neonatal clinical reliance on Doppler and protocol driven strategies of cardiovascular support that differ from those in older age groups where more invasive measurement is possible [8].

The reliability of a method of measuring cardiac function may be increased by its expression as a ratio with a measure of loading conditions. The end systolic stress (derived from the ESBP) and echocardiographic measurements of ventricular wall thickness is such a measure of afterload used to enhance systolic indices such as the mean velocity of circumferential fibre shortening (VmCFS) and fractional shortening index. The ratio of the VmCFS: ESS ratio is a preload independent index of systolic cardiac function that incorporates afterload and is sensitive to preload. The echocardiographic measurements can be made from a simple M mode of the left ventricle during systole. A high degree of echocardiographic skill is not required [9].

The appropriate use of indices of myocardial contractility may be clinically useful when choosing between volume loading and inotropes and between different inotropes. We have demonstrated that a non-invasive assessment of end systolic blood pressure made on the basis of five or ten consecutive beats can be accurate and precise enough to make these indices accessible. The peak systolic blood pressure is an inappropriate clinical or numerical substitute.

ACKNOWLEDGEMENT

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REFERENCES


Table 3: The estimated variability of a NIESBP measurement given that the measurement is based upon n individual pulse beats, taking into account the variance of the estimated bias.

<table>
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