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ORIGINAL RESEARCH

Pediatric blood pressures during anesthesia assessed using normalization and principal component analysis techniques

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Abstract

Expected values for blood pressure are known for both unanesthetized and anesthetized children. The statistics of changes in blood pressure during anesthesia, which may have important diagnostic significance, have not been reported. The purpose of this study was to report the variation in changes in blood pressure in four pediatric age groups, undergoing both cardiac and non-cardiac surgery. An analysis of the changes in blood pressure using normalization and principal component analysis techniques was performed using an existing electronic dataset of intra-arterial pediatric blood pressure values during anesthesia. Cardiac and noncardiac cases were analyzed separately. For 1361 non-cardiac cases, the average systolic blood pressure increased from 55.2 (17.6) mmHg in the first month of life to 85.4 (17.7) mmHg at 5–6 years. For 912 cardiac cases, the average systolic blood pressure increased from 55.7 (16.7) to 71.8 (24.8) mmHg in these cohorts. For non-cardiac cases in the first month, the mean (SD) for change in blood pressure over a 30 s period was 0.00 (8.8), for 5–6 year olds 0.0 (7.4); for cardiac cases, 0.1 (9.2) to − 0.1 (9.2). Variations in systolic blood pressure over a 5-min period were wider: in non-cardiac from 0.1 (12.2) mmHg (first month) to 0.4 (11.5) mmHg (5–6 year old) and from 0.2 (12.5) to 0.4 (14.2) mmHg in cardiac cases. Absolute blood pressures and changes in blood pressure during anesthesia in pediatric cardiac and non-cardiac surgical cases have been analyzed from a population database. Using these values, the quantitative methods of normalization and principal component analysis allow the identification of statistically significant changes.

Keywords Pediatrics · Blood pressure · General anesthesia · Monitoring · Normalization · Principal component analysis

1 Introduction

Blood pressure values for the pediatric population are well documented and are used in standardized clinical charts. However, the range of blood pressures of children under general anesthesia has only recently been published [1]; the data used for this study were from the same database. Absolute values for blood pressure are important for baseline evaluation of the anesthetized patient, but changes in blood pressure are also important as these can be of broad and of considerable diagnostic significance. An increase in blood pressure may be indicative of a sympathetic response in the setting of inadequate anesthesia; a decrease may represent the onset of hypovolemia or perhaps too deep a state of anesthesia.

Alarms based on absolute blood pressure thresholds are technically simple but have obvious limitations. An alarm should, ideally, draw the anesthetist's attention to a clinically significant change in the patient's condition. Consider, however, a blood pressure alarm that is triggered below a systolic blood pressure (SBP) of 85 mmHg. An alarm would be produced if a patient's blood pressure was to fall from 85 to 84 mmHg, and yet no alarm would be produced if the blood pressure fell from 140 to 86 mmHg. This threshold alarm behavior is therefore exactly the opposite of what is desired: the change in the latter instance is almost certainly clinically significant, but the change in the former is not.

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A study of adult patients by Harrison and Connor [2] described an alarm system that made use of both current and recent past blood pressures. Using a normalization or principal component analysis (PCA) methodology, an alarm algorithm was created that favored detection of significant changes in blood pressure in which sensitivity was set by standard deviations from the mean rather than relying on absolute pressure levels alone. A subsequent paper by Connor et al. [3] illustrated the concept further. However, pediatric cardiac physiology features notable differences from adult cardiac physiology, such as incomplete sympathetic innervations [4] and a reduced ability to increase stroke volume [5]. These differences suggest that a distinct analysis for blood pressure monitoring in pediatric patients under general anesthesia is desirable.

2 Methods

The pediatric database of blood pressures during anesthesia used by Sottas et al. [1] was used for analysis using the techniques of normalization and PCA. The SaferSleep database of 55,896 anesthetic cases included 2645 cases with intra-arterial blood pressure measurements, of these 2273 had sufficient data for analysis. The data were subdivided into cardiac and non-cardiac cases. The SaferSleep system (SaferSleep LLC, Nashville, TN, USA) is used routinely for intra-operative records and monitoring at Starship Children's Hospital, a tertiary referral centre, Auckland, New Zealand. The system collects and stores arterial blood pressure measurements every 30 s. The data were extracted from the central hospital database with ethical approval, de-identified, and reformatted for use in this study.

Data were subset by the following patient ages: 1–30 days, 1 month to 1 year, 1–5 years, and 5–6 years. A simple band-pass filter was applied to remove artifact in the blood pressure recordings: SBPs below 30 mmHg or above 200 mmHg were excluded from the records. The changes in arterial SBP were assessed over two measurement intervals, 30 s and 300 s. These data were obtained by appropriately sub-sampling the raw arterial pressure data. The data in the 30 s and 300 s dataset are therefore derived from the same patient population and can be compared in a paired fashion.

For both normalization and PCA techniques it is necessary to know the current SBP and the immediate past blood pressure at some fixed time interval (e.g. up to 300 s) from which the change in pressure is calculated. The normalization technique depends on the mean and standard deviations of the SBP and also the mean and standard deviation of the changes over the specified time interval. Absolute blood pressure values and changes in blood pressure are converted to equivalent values in units of the underlying standard deviation. An alarm is generated when the Pythagorean sum of these normalized values exceeds a set threshold such as 2 standard deviations (the Pythagorean sum is the square root of the sum of the squares; for example, the Pythagorean sum of 3 and 4 is 5). This may occur when the current absolute pressure is far from the mean average, or when the blood pressure is changing rapidly, or a combination of these two events. A detailed description of the analysis is in Harrison and Connor [2].

The PCA technique is based upon the same principle but also includes the angle of the slope that best captures the alignment between current and past BPs, i.e. the principal component of this dataset, see analysis details in Harrison and Connor [2]. PCA emphasizes variation and brings out major factors in the data. The Pythagorean sum of the two orthogonal standard deviations, which can be different, is used to determine if the change exceeds the clinician's set threshold.

3 Results

The ASA status of the cardiac and non-cardiac patients are presented in Table 1 and the population systolic BP values for the two data subsets are presented in Table 2. The changes in SBP are presented for two measurement intervals, 30 s and 300 s. As specified, these data are derived from the same underlying population and can therefore be analyzed statistically as such.

The average SBP was calculated for each group over the entire observation period, which is from the start of the procedure to the end. For the cardiac patients the average population SBP increased from 55.7 to 71.8 mmHg. The values for the non-cardiac patients were 55.2–85.4 mmHg. Separation between these mean SBPs for each class of patient, as shown in Fig. 1, was tested with a one-way ANOVA using the standard Tukey–Kramer correction for multiple comparisons. For both cardiac and non-cardiac patients, mean blood pressure increased with age. There was a strong statistical separation ($p < 0.0001$) between the 1–30 days, 1 month to 1 year and 1–5 years groups for both cardiac and non-cardiac patients. The difference

Table 1 ASA status of cardiac and non-cardiac patients

ASA	Cardiac (n)	Non-cardiac (n)
1	0 (0.0%)	83 (7.2%)
2	78 (10.9%)	246 (21.4%)
3	456 (63.5%)	603 (52.4%)
4	183 (25.5%)	214 (18.6%)
5	1 (0.1%)	4 (0.3%)
Not recorded	194	211
Total	912	1361

Table 2 SBPs and changes in blood pressures over 30 s and 300 s for subsets of cardiac (a) and non-cardiac (b) pediatric patients

	Measurements n	Average BP mmHg (SD)	Average dBP 30 s (SD)	Average dBP 300 s (SD)
(a) Cardiac cases				
Patients 1–30 days n = 209				
	n_1 117,670	55.7 (16.7)	0.1 (9.2)	0.2 (12.5)
	n_2 98,989			
	n_3 80,119			
Patient 1 month to 1 year n = 395				
	n_1 192,580	64.8 (23.2)	0.1 (8.8)	0.3 (13.4)
	n_2 166,192			
	n_3 137,826			
Patients 1–5 year n = 264				
	n_1 121,732	68.6 (23.5)	0.00 (8.6)	0.3 (13.9)
	n_2 98,466			
	n_3 82,990			
Patients 5–6 year n = 44				
	n_1 21,913	71.8 (24.8)	−0.1 (9.2)	0.4 (14.2)
	n_2 17,128			
	n_3 14,305			
(b) Non-cardiac cases				
Patients 1–30 days n = 207				
	n_1 75,020	55.2 (17.6)	0.00 (8.8)	0.1 (12.2)
	n_2 61,235			
	n_3 48,044			
Patient 1 month to 1 year n = 457				
	n_1 157,437	70.6 (21.6)	0.00 (8.4)	0.2 (13.5)
	n_2 136,604			
	n_3 111,140			
Patients 1–5 year n = 623				
	n_1 215,419	80.1 (18.8)	0.00 (7.1)	0.1 (12.2)
	n_2 185,054			
	n_3 155,281			
Patients 5–6 year n = 74				
	n_1 23,130	85.4 (17.7)	0.00 (7.4)	0.4 (11.5)
	n_2 17,808			
	n_3 14,768			

n data points are presented for all blood pressure measurements (n_1), for 30 s (n_2) and 300 s (n_3) intervals

between 1–5 and 5–6 years was not statistically significant ($p = 0.39$ for cardiac patients, $p = 0.14$ for non-cardiac patients). In each of the four age groups, cardiac patients had a lower mean blood pressure than non-cardiac patients. This cardiac versus non-cardiac difference was strongly significant in each age group, with the exception of the 1–30 days group ($p = 0.66$, $p < 0.0001$, $p < 0.0001$, $p = 0.0012$ respectively).

There is no statistical difference between the changes in SBP between either of the measurement intervals or

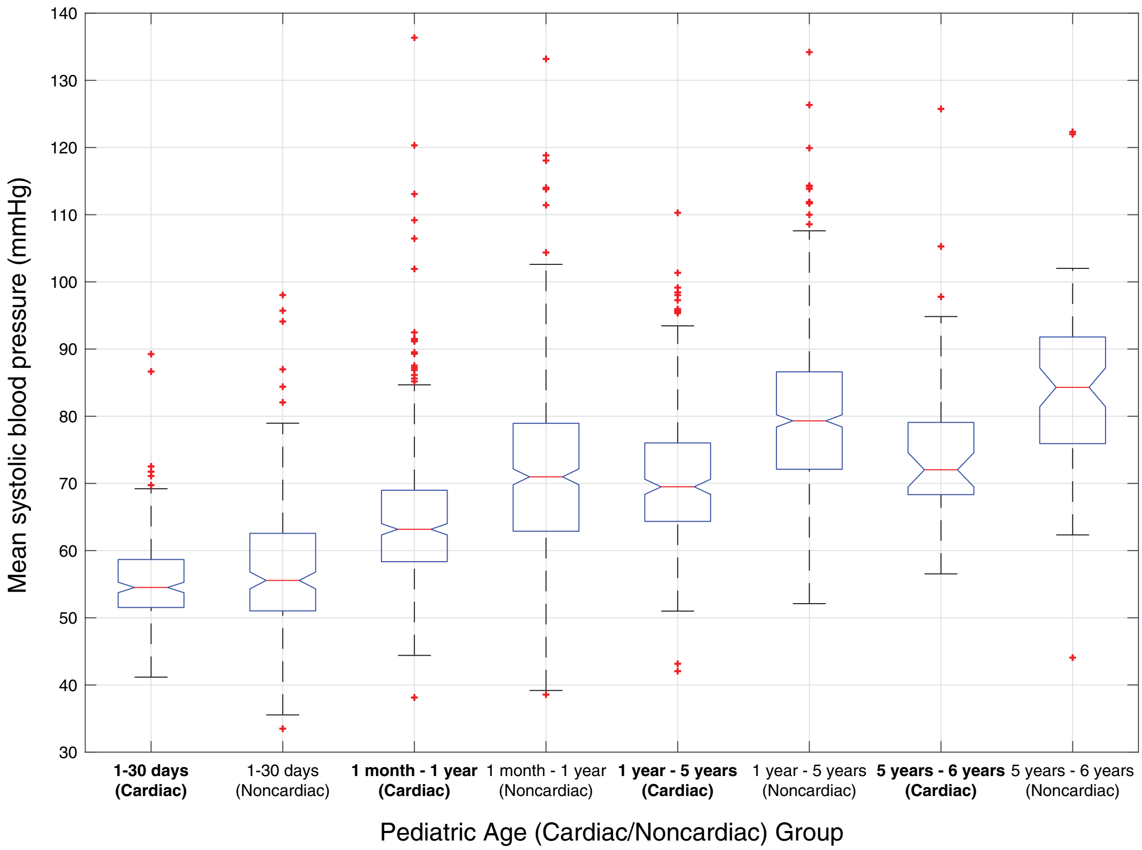

Fig. 1 Box plots of the separation of mean SBP for each age group of cardiac and non-cardiac patients

between any of the pediatric age groups. The mean value for change in systolic BP is close to zero.

To determine the Pythagorean value using the normalization technique, suppose that the systolic BP of a 2 year old non-cardiac patient is 89 mmHg. Measured in terms of standard deviations (SD), this blood pressure is + 0.47 SD, since $\frac{89-80.1}{18.8} = 0.47$.

If, over 30 s, the BP were to increase to 115 mmHg then the SD value for this change would be + 3.45 SD, since $\frac{(115-89)-0.0}{7.1} = 3.66$.

The combined SD, using Pythagoras' theorem, is $\sqrt{0.47^2 + 3.66^2} = 3.7$.

Such a change in 30 s would trigger an alarm set at the 2 SD level.

Figure 2 displays the blood pressure distribution used in the PCA technique. It shows the data for SBP changes over 300 s in the 5–6 year cohort, in which the SBP from 300 s before is plotted on the x axis and the current blood pressure is plotted on the y axis. The ellipse represents the 2 SD alarm boundary. As an example, a blood pressure increase from 80 to 110 mmHg over 300 s lies outside this alarm perimeter and would therefore also trigger an alarm at this level.

The current SBP and its recent change are represented on orthogonal axes. PCA allows a rotation to be applied to these axes, which tends to reflect a natural homeostatic tendency for the SBP to regress towards the mean.

In adults, as the time interval between measurements increases, the prior measurement becomes appreciably less predictive of the subsequent measurement and the principal component angle is used to refine the normalization alarm accordingly [2]. However, in the pediatric dataset, the data disperse in a somewhat symmetric manner as the time interval increases. The principal component angle, therefore, remains close to 45° with increasing measurement interval, as shown in Fig. 3, unlike the adult case [2, 3]. This demonstrates the relative cardiovascular stability of pediatric patients under anesthesia when compared to adults.

4 Discussion

The results of our analysis of the dataset of blood pressures during anesthesia in the first 6 years of life reinforce the view that pediatric patients have very stable cardiovascular systems. The average SBP during anesthesia does increase

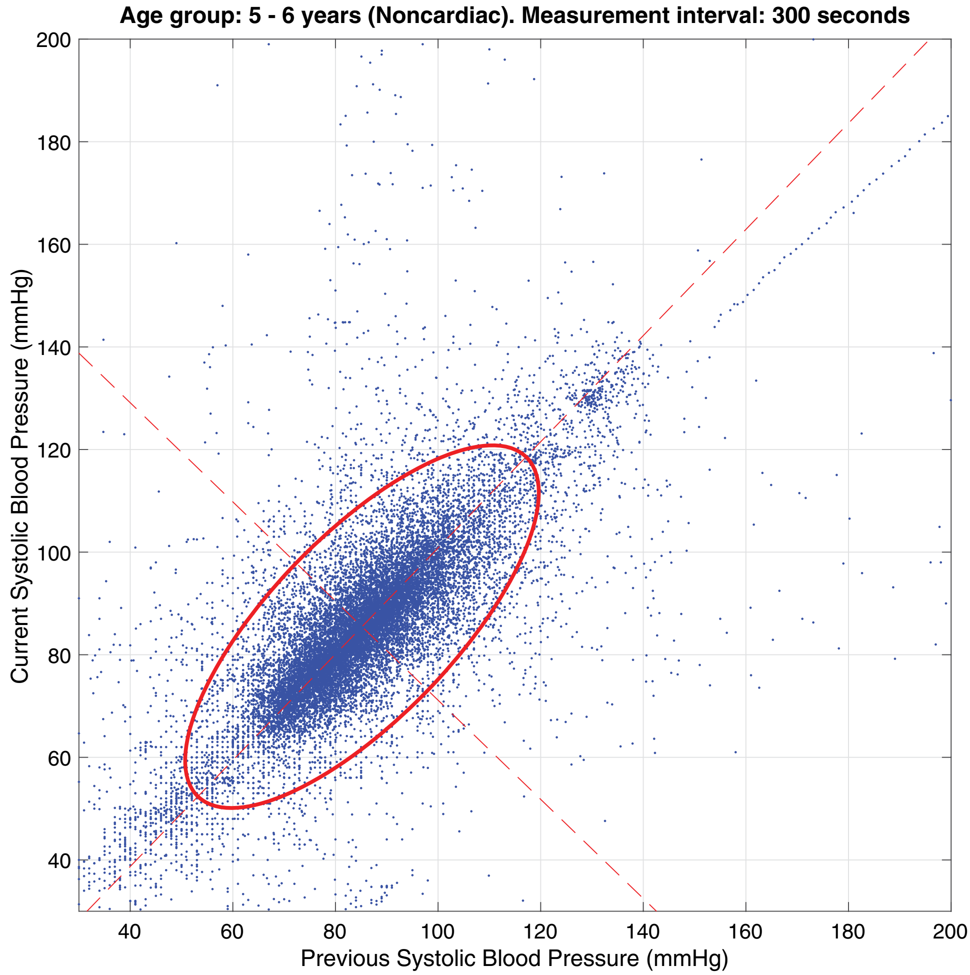

Fig. 2 Data for SBP measurements, separated by 300 s, in the non-cardiac 5–6 years age group. The PCA axes are represented by the dashed lines: the principal component angle is 46.0°. The average SBP, at the intersection of the PCA axes, is 85.4 mmHg. The standard deviations of the data along the principal and secondary component axes are 23.0 mmHg and 8.9 mmHg respectively. The solid red ellipse denotes the 2 SD alarm boundary

with age but the changes in blood pressure, for the different age groups, over two intervals of time (30 s and 300 s) do not change significantly.

Threshold blood pressure alarms have the disadvantage that a blood pressure has to be set as indicative of hypotension, but the definition of hypotension is difficult [6]. The degree to which the blood pressure is allowed fall depends on both age and pathophysiology, aortic stenosis being a prime example. A system that monitors changes in blood pressure has the ability to discriminate between a moderate fall in blood pressure from an above average blood pressure and the same decrease from a lower blood pressure. An alert can therefore be generated before significant hypotension occurs. It does not negate the need for a low blood pressure alarm. Any monitoring systems that were to use this method to assess BP changes would need to have datasets suitable for the age of the child. As Fig. 1 demonstrates, there is a qualitative difference between the behavior of SBP under anesthesia in children [1] and the adults previously studied [2, 3].

A limitation of the dataset is that the nature of the anesthetic is unknown. It is likely that the anesthesia techniques used were very variable. The blood pressure values do represent all the values collected from each patient.

The introduction of a monitoring system based on blood pressure changes does not preclude the on-going use of traditional threshold alarms for high and low absolute blood pressure values. Both monitoring alarm systems can coexist, working in parallel. A statistics-based alarm system adds diagnostic information, especially when combined with other physiological parameters. A significant change in blood pressure associated with a change in heart rate and a change in pulse volume can be diagnostic of sympathetic activity [7], perhaps inadequate anesthesia, or hypovolemia [8]. The monitoring system could select the correct reference dataset automatically based upon the non-invasive blood pressure (NIBP) device settings or default to 30 s if invasive monitoring is used. The configuration of such a monitoring system would therefore not create an additional burden on the anesthetist.

One obvious feature of this analysis is that pediatric patients appear to have a more stable cardiovascular system. However, the adult data in the previous studies were

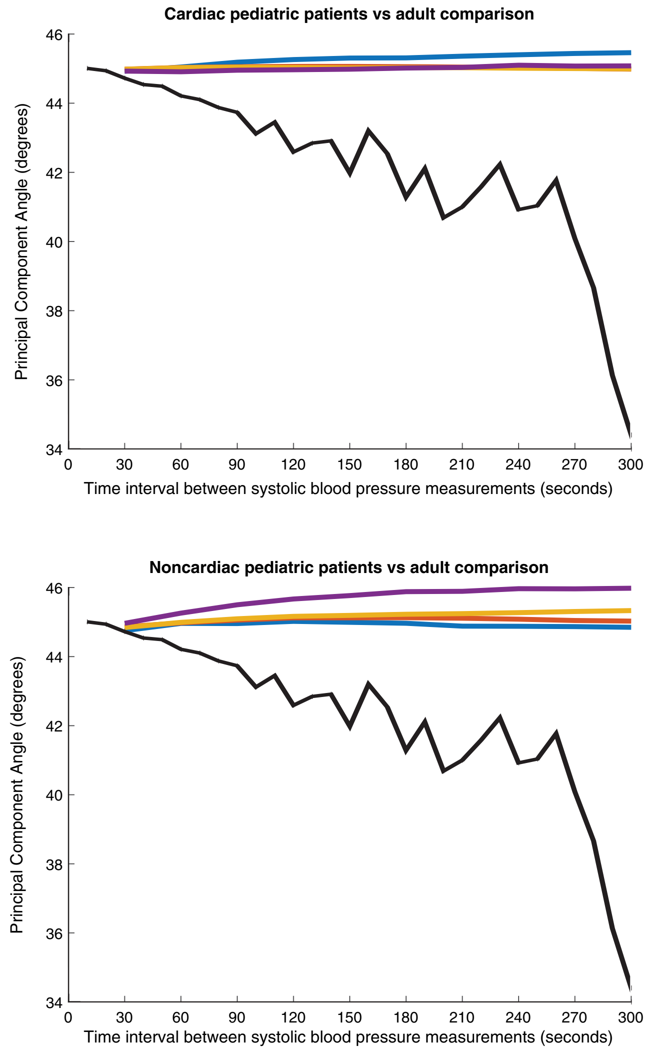

Fig. 3 The homeostatic angle for SBP measurements in adults and in cardiac and non-cardiac subsets. In the adult it decreases over increasing intervals of time. In the pediatric subsets the angle is maintained at about 45°. Blue: 1–30 days, orange: 1 month to 1 year, yellow: 1–5 years, purple: 5–6 years and black: adults

obtained during surgeries in which hemodynamic instability was considered more likely—hence their planned invasive arterial monitoring. These higher risk patients might be expected to be less stable than the average adult undergoing comparably routine surgeries. It would also be of interest to study adults with less stable cardiovascular response systems due to co-morbidities such as diabetes or heart failure. Adult heart failure is characterized by a progressive and ultimately pathological stimulation of the sympathetic nervous system [9]. In contrast, parasympathetic and vagal responses are more characteristic of cardiac physiology in the pediatric population. Further studies on the optimum monitoring strategy for intraoperative hemodynamic should include these groups, and such studies would go a long way to complete the picture of blood pressure response under general anesthesia.

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Compliance with ethical standards

Conflict of interest Michael Harrison is the designer of EBMi anesthesia monitoring software. The other authors declare that they have no conflict of interest.

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