

A Simple Method of Blood Pressure Measurement in the Pig Using a Neonatal Cuff

P K H Chow,* M Med (Surg), FRCS (Edin), T H Ng,** DMT, D Heng,*** MRCP, MPhil, P O P Mack,**** FAMS, FRCS (Edin), PhD

Abstract

The pig is a commonly used large animal model in experimental studies. Few non-invasive techniques exist however for the measurement of blood pressure in the porcine model. This study evaluates the novel use of the easily available neonatal blood pressure cuff for measuring blood pressure in the pig.

Six Yorkshire pigs were used for the study. Blood pressure measurements obtained by the application of neonatal blood pressure cuff (Hewlett Packard) around the base of the tail were compared with results obtained from intra-arterial measurements in the normotensive range as well as in experimentally created hypertensive (intravenous dopamine) and hypotensive (hypovolaemic shock) ranges.

Results of the two techniques are closely correlated (Pearson's coefficient = 0.95, 0.97, 0.90). Systematic bias was however detected at the extremes of hypertensive and hypotensive blood pressure. Analysis of the limits of agreement (method of Bland and Altman) showed that neonatal blood pressure cuff measurements fall within 2 to 2.5 mmHg of the readings obtained from the invasive technique (95% confidence interval).

The neonatal blood pressure cuff technique is a good substitute for the standard invasive intra-arterial measurement of blood pressure in the pig model.

Ann Acad Med Singapore 1999; 28: 15-9

Key words: Animal model, Blood pressure cuff, Blood pressure measurement, Pig, Non-invasive technique

Introduction

Blood pressure is an important parameter commonly measured in experimental studies using animal models. Various non-invasive techniques to monitor blood pressure have been described in the literature but most of these are applicable only to small animal models like the rat.^{1,2} Few techniques on non-invasive blood pressure monitoring in large animal models have been described and validated.

The pig is a commonly used model in experimental studies.³ In terms of cardiovascular and gastrointestinal physiology, the pig closely resembles man. The porcine model has therefore been widely used in liver transplantation studies,^{4,6} as hepatectomy models⁷⁻⁹ and as models for haemodynamic studies¹⁰ and in studies on shock.^{11,12}

Invasive blood pressure measurement is the most widely used and accepted method for monitoring blood pressure in the pig or any other large animal model. This

is achieved by connecting a pressure transducer to a cannula inserted into an artery i.e. via an intra-arterial line. Such intra-arterial cannulae may be inserted by either the percutaneous route or by arterial cut-down.

Percutaneous femoral arterial cannulation for blood pressure monitoring can be extremely difficult in the pig as the thick tissue bulk covering the artery hinders localisation of the vessel. Most pigs used for experimental surgery research are in the weight range of 30 to 50 kg and the relatively small size of the femoral arteries in these animals adds to the difficulty of blind cannulation. Inadvertent haematomas are a common occurrence and these could compromise blood flow. Intra-arterial cannulae are therefore commonly inserted by arterial cut-down. Using cut-down techniques for sequential measurement of blood pressure e.g. repeated measurements taken over a number of days, is however difficult. To avoid cannula complications, removal of the intra-

* Senior Registrar

**** Senior Consultant

Department of General Surgery

** Senior Medical Technologist

Department of Experimental Surgery

Singapore General Hospital

*** Clinical Epidemiologist

Clinical Trials and Epidemiology Research Unit

National Medical Research Council, Singapore

Address for Reprints: Dr Pierce Chow, Department of General Surgery, Singapore General Hospital, 1 Hospital Drive, Singapore, 169608

arterial cannula after each period of measurement is necessary and this requires ligation and the subsequent thrombosis of that vessel. A new site and vessel has to be used each time the blood pressure is measured.

In our institution, the pig is widely commonly used in experimental surgery studies and blood pressure monitoring in the pig posed a practical challenge. To circumvent the problems associated with invasive blood pressure monitoring in the pig, an alternative non-invasive technique was therefore sought. Special tail-cuffs have been developed to measure blood pressure in the rat^{1,2} and this includes some commercial models but these are not available for the pig. This study was carried out to evaluate the use of the easily available and common neonatal blood pressure cuff as a non-invasive technique for monitoring blood pressure in a porcine model.

Materials and Method

In the pig, the blood pressure in the caudal artery may be measured by application of a blood pressure cuff of a suitable size around the base of the tail. We used a neonatal blood pressure cuff for this purpose. The aim of this study was to validate this novel technique of monitoring porcine blood pressure against results obtained by the standard invasive intra-arterial technique. All operative procedures were conducted in accordance with International Guidelines for Animal Research.¹³

Six healthy Yorkshire pigs (40 to 50 kg) were used for this study. After an overnight fast, each animal was first sedated with i/m ketamine at 15 mg/kg BW. Anaesthesia was induced with pentobarbitone (10 mg/kg BW) and maintained with 1.5% inhalational halothane.

A neonatal blood pressure cuff (Hewlett Packard, size 1) was applied against the base of the tail of each animal with circumference settings of between 3.1 and 5.7 cm. Open cannulation of the femoral artery was carried out using an 18 G intra-arterial cannula. The cannula was connected to a low-volume miniature strain-gauge transducer and which was then zeroed. Both the neonatal blood pressure cuff and the intra-arterial system were then connected to a Hewlett Packard Patient Monitoring Machine (HP 78354A) which was pre-calibrated for 50 mmHg, 100 mmHg and 150 mmHg using a mercury pressure gauge.

Paired readings from the neonatal blood pressure cuff and the intra-arterial cannula were obtained over 3 ranges of blood pressure namely normotensive blood pressure, dopamine-induced hypertension and hypotension resulting from hypovolaemic shock. In each of these blood pressure ranges, systolic blood pressure, mean arterial pressure (MAP) and diastolic blood pressure were separately recorded.

A total of 5 paired blood base-line pressure readings at

2-minute intervals were first obtained from the anaesthetised animals 15 minutes after all invasive procedures were carried out. These readings therefore reflected the physiological blood pressure of these anaesthetised animals under haemodynamically stable conditions.

Hypertension was then induced in these animals by bolus intravenous injections of 200 mg dopamine. Five pairs of blood pressure readings were then obtained at 5-minute intervals. Twenty minutes was then allowed to pass before hypovolaemic shock was induced by exsanguination of the animal from the internal jugular vein into a transfusion bag. Paired blood pressure readings were obtained at 2-minute intervals starting from the time 200 ml of blood was collected in the transfusion bag. A total of 5 readings were taken.

Results obtained were analysed using the SPSS 7.5 statistical software. The relationship between results obtained from non-invasive blood pressure monitoring using neonatal blood pressure cuff and results from invasive intra-arterial blood pressure measurement was investigated using Pearson's correlation coefficient. The method of Bland and Altman^{14,15} was used to estimate limits of agreement between the two techniques and to evaluate the practical and statistical feasibility of using the neonatal blood pressure cuff technique to replace the standard invasive intra-arterial technique for monitoring blood pressure in this model.

Results

Normotensive MAP in this pig model was 66 to 100 mmHg (mean 85.6, SD 10.2) and 67 to 100 mmHg (mean 85.7, SD 9.9) respectively when measured by the neonatal blood pressure cuff and by the intra-arterial technique. After bolus intravenous injection of 200 mg dopamine, MAP ranged from 96 to 117 mmHg (mean 104.6, SD 4.3) and 104 to 139 mmHg (mean 115.5, SD 10.43) respectively by this two techniques. The range of MAP measured in this study when hypotension was created by exsanguination was from 44 to 66 mmHg (mean 55.3, SD 7.3) and 38 to 67 mmHg (mean 53.3, SD 8.8) respectively. Table I shows the summary statistics for the BP ranges recorded under various conditions.

Correlation between the 2 methods of blood pressure monitoring is illustrated in Figures 1, 2 and 3, which show the scatter plots of paired readings obtained for diastolic, mean and systolic blood pressure respectively. The two methods showed good correlation and Pearson's correlation coefficients were 0.95 ($P < 0.001$), 0.97 ($P < 0.001$) and 0.90 ($P < 0.001$) for the above 3 blood pressures.

Figures 4, 5 and 6 show the difference in the blood pressure readings plotted against the mean of the 2 blood pressure readings (method of Bland and Altman). This type of plot is useful in detecting bias and estimat-

TABLE I: SUMMARY STATISTICS FOR BLOOD PRESSURE RANGES RECORDED UNDER VARIOUS CONDITIONS

Normotensive conditions			
n = 30	Range (mmHg)	Mean (mmHg)	Standard deviation (mmHg)
Diastolic BP			
IABP*	56-87	73.4	9.9
Neonatal cuff	53-84	69.4	9.7
Mean BP			
IABP	67-100	85.7	9.9
Neonatal cuff	66-100	85.6	10.2
Systolic BP			
IABP	83-124	107.1	11.8
Neonatal cuff	84-129	113.17	12.1
Dopamine-induced hypertension			
n = 28	Range (mmHg)	Mean (mmHg)	Standard deviation (mmHg)
Diastolic BP			
IABP	85-128	99.2	12.4
Neonatal cuff	76-104	91.4	7.1
Mean BP			
IABP	104-139	115.5	10.4
Neonatal cuff	96-117	104.6	4.3
Systolic BP			
IABP	126-172	146.0	12.4
Neonatal cuff	107-135	124.0	6.3
Hypotension secondary to hypovolaemia			
n = 30	Range (mmHg)	Mean (mmHg)	Standard deviation (mmHg)
Diastolic BP			
IABP	31-59	43.1	8.8
Neonatal cuff	35-57	44.7	7.3
Mean BP			
IABP	38-67	53.3	8.8
Neonatal cuff	44-66	55.3	7.3
Systolic BP			
IABP	49-88	70.7	10.7
Neonatal cuff	59-100	74.8	9.5

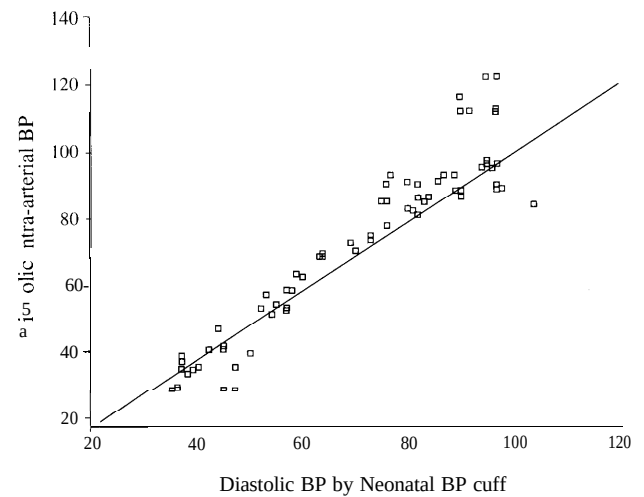
BP: blood pressure; IABP: intra-arterial blood pressure

TABLE II: LIMITS OF AGREEMENT AND RESIDUAL BIAS BETWEEN THE TWO TECHNIQUES OF MEASURING BLOOD PRESSURE

	Mean difference (bias) (mmHg)	SD (mmHg)	95% limits of agreement (mmHg)
Diastolic BP	4.0	4.3	-4.3, 12.4
Mean BP	0.3	1.2	-2, 2.5
Systolic BP	-3.5	6.1	-15.5, 8.5

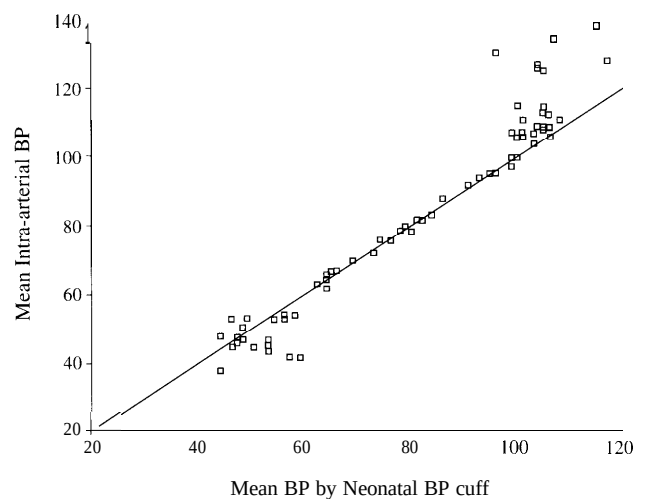
SD: standard deviation; BP: blood pressure

ing limits of agreement between methods. The plots clearly show evidence of a systematic bias, with the non-invasive method reading higher at low blood pressures and lower at high blood pressures.



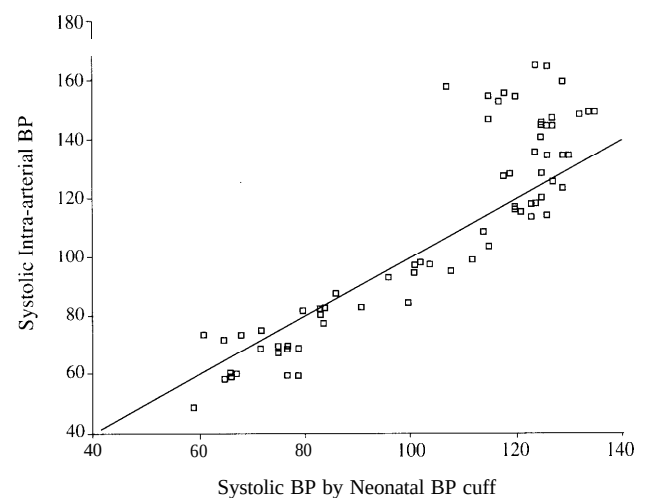
Note: Line shown is Y=X reference line, not a regression best-fit line.

Fig. 1. Scatter plot of paired diastolic blood pressure readings



Note: Line shown is Y=X reference line, not a regression best-fit line.

Fig. 2. Scatter plot of paired mean blood pressure readings.



Note: Line shown is Y=X reference line, not a regression best-fit line.

Fig. 3. Scatter plot of paired systolic blood pressure readings.

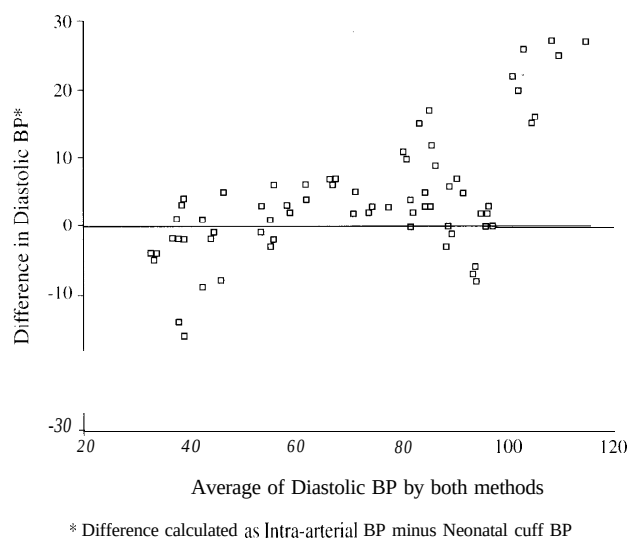


Fig. 4 Plot of difference versus mean for pawed diastolic blood pressure readings

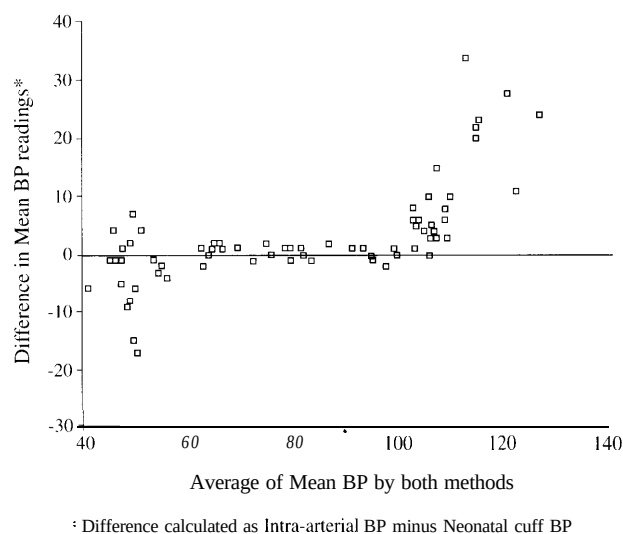


Fig. 5 Plot of difference versus mean for pawed mean blood pressure readings

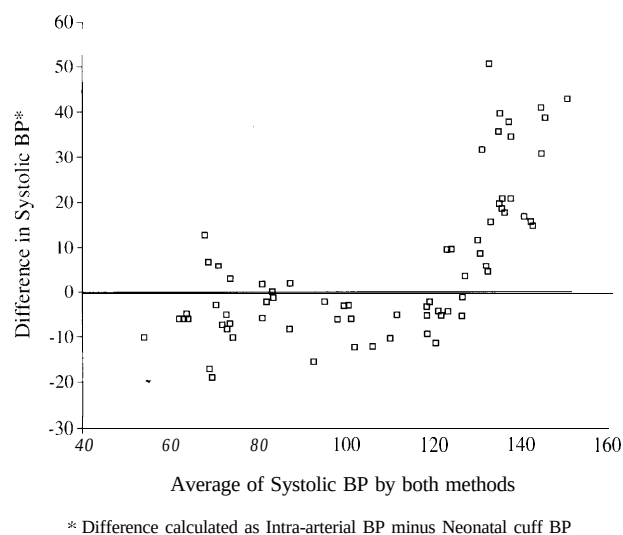


Fig. 6. Plot of difference versus mean for paired systolic blood pressure readings.

A secondary analysis was performed, restricted to pairs of blood pressure reading with mean values within the normotensive range. Limits of agreement and residual bias were calculated and are shown in Table II.

Discussion and Conclusion

The results of this study showed high correlation between measuring blood pressure by intra-arterial catheter and by means of a neonatal blood pressure cuff applied around the base of the tail in the pig. A cursory analysis would therefore suggest that the neonatal blood pressure cuff is an excellent technique for measuring blood pressure in the pig and may be used to replace intra-arterial blood pressure measurement. High correlation however does not always mean that the two techniques agree.¹⁴ Analysis by the method of Bland and Altman suggested lack of agreement in the extreme or non-physiological ends of the blood pressure spectrum. This is not unexpected. Agreement between blood pressure measured by pressure cuff and by an invasive intra-arterial system is known to deviate at pressures higher and lower than the physiological range.¹⁶

The magnitude by which results obtained using the new technique differ from that obtained from the standard technique has more relevance than statistical correlation between the results.^{14,15,17,18} If results from the new technique are likely to differ from that of the established technique by a magnitude likely to cause difficulties in interpretation of the results, then the new technique cannot replace the established technique even if the results correlate significantly. The method of Bland and Altman specifically addresses this issue.

In the normotensive range, readings obtained using the neonatal blood pressure cuff technique differs from that obtained from intra-arterial catheters by a mean of 0.3 mmHg. There is a 95% chance that the result obtained from the neonatal blood pressure cuff will fall within -2 to 2.5 mmHg of the readings obtained from the invasive technique. The range of possible differences in the two readings is small in relation to the normotensive blood pressure range (66 to 100 mmHg). This neonatal blood pressure cuff technique can therefore be confidently used to replace the invasive intra-arterial technique. In the context of research in experimental surgery, this neonatal blood pressure cuff technique would be ideal for intra-operative monitoring of blood pressure. Where repeated blood pressure monitoring is required e.g. repeated procedures (e.g. biopsies) carried out on the same animal over a period of time, this technique is superior to invasive techniques because of the ease of application and the absence of complications.

It is difficult to comment on the use of the neonatal blood pressure cuff technique to measure blood pressure under extreme conditions in this pig model. The hypertensive and hypotensive blood pressure ranges

created in this study were essentially caused by pathological conditions (and in the case of the hypotensive range - terminal conditions). The mean differences between the two techniques remained small but the suitability and relevance of this neonatal cuff technique for measuring blood pressure under such extreme conditions would depend on the aims and end points of such experiments.

The results of this study are similar to those obtained using the more expensive photo-electric flow sensor in the Yucatan mini-pig.¹⁹ The neonatal blood pressure cuff technique used in this study has many advantages. It is cheap, the blood pressure cuff is easily available and no equipment besides the normal monitoring instruments found in any experimental surgery facility is required.

In summary, this study confirmed that the simple neonatal blood pressure cuff technique developed in our institution is a good substitute for the standard invasive intra-arterial technique of monitoring blood pressure in the pig model and this is especially relevant in the intra-operative setting. Where the pig model is used in experiments designed to create extreme changes in blood pressure, the use of this technique would however not be appropriate and any readings obtained must be interpreted with caution.

REFERENCES

- Bunag R D, Butterfield J. Tail-cuff blood pressure measurement without external preheating in awake rats. *Hypertension* 1982; 4:898-903.
- Widdop R E, Li X C. A simple and rapid method for measuring tail cuff systolic pressure in conscious rats. *Clin Sci (Colch)* 1997; 93:191-4.
- Swindle M M, editor. *Swine as Models in Biomedical Research*. 1st ed. Ames: Iowa State University Press, 1992:312.
4. Calne R Y, White H J O, Yoffa D E, Magnin R R, Binns R M, Samuel J R, et al. Observation of orthotopic liver transplant in the pig. *Br Med J* 1967; 2:478-80.
5. Peacock J H, Terblanche J. Orthotopic homotransplantation of the liver in the pig. In: Read A E, editor. *The Liver*. London: Butterworth, 1967:333-6.
6. Goto S. Orthotopic liver transplantation in miniature pigs: some technical considerations in recipient. *Nippon Geka Gakkai Zasshi* 1988; 89:215-26.
7. Chow P K H, Jeyaraj I, Tan S Y, Fook Cheong S, Soo K C. Serial ultrasound-guided percutaneous liver biopsy in a partial hepatectomy porcine model: A new technique in the study of liver regeneration. *J Surg Res* 1997; 70:134-7.
8. Kahn D, van Hoorn-Hickman R, Terblanche J. Liver blood flow after partial hepatectomy in the pig. *J Surg Res* 1984; 37:290-4.
9. Kahn D, Hichman R, Terblanche J. Partial hepatectomy and liver regeneration in pigs-The response to different resection sizes. *J Surg Res* 1988; 45:176-80.
10. Drougas J G, Barnard S E, Wright J K, Lopez R R, Stokes K A, Williams I E, et al. A model for the extended studies of hepatic haemodynamics and metabolism in swine. *Lab Anim Sci* 1996; 46:648-55.
11. Ayuse T, Brienza N, Revelly J P, Boitnott K, Robotham J L. Role of nitric oxide in porcine liver circulation under normal and endotoxaemic conditions. *J Appl Physiol* 1995; 78:1319-29.
12. Lindner K H, Ahnefeld F W, Bowdler I M. Cardiopulmonary resuscitation with interposed abdominal compression after asphyxial or fibrillatory cardiac arrest in pigs. *Anesthesiology* 1990; 72:675-81.
13. Howard-Jones N. A CIOMS ethical code for animal experimentation. *WHO Chronicle* 1985; 39:51-6.
14. Bland J M, Altman D G. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 307-9.
15. Bland J M, Altman D G. Comparing methods of measurement: why plotting difference against standard method is misleading. *Lancet* 1995; 346:1085-7.
16. Vater M. Monitoring during anaesthesia. In: Aitkenhead A R, Smith G, editors. *Textbook of Anaesthesia*. Avon: Churchill Livingstone, 1990:363.
17. LaMantia K R, O'Connor T, Barash I G. Comparing methods of measurement: An alternative approach. *J Anaesth* 1990; 72:781-3.
18. Murray G D, Miller R. Statistical comparison of two methods of clinical measurement. *Br J Surg* 1990; 77:385-7.
19. Cimini C M, Zambraski E J. Non-invasive blood pressure measurement in Yucatan miniature swine using tail cuff sphygmomanometry. *Lab Anim Sci* 1985; 35:412-6.