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RESEARCH

Observation of the pulse oximeter trace to estimate systolic blood pressure during spinal anaesthesia for Caesarean section: the effect of body mass index

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Background: The estimation of systolic blood pressure by disappearance and reappearance of the pulse oximeter trace during cuff inflation and deflation was compared with non-invasive blood pressure (NIBP) measurement, across the range of body mass index (BMI), during spinal anaesthesia for Caesarean section.
Methods: Seventy-five parturients were recruited, with BMI of < 30 (Group 1), 30–40 (Group 2), and > 40 kg/m² ((morbidly obese, Group 3). A non-invasive blood pressure monitor was used with the pulse oximeter probe on the ipsilateral arm. Estimations were done before induction and 5 min after induction of spinal anaesthesia, during cuff inflation and deflation. Bland and Altman analysis was performed and the concordance correlation coefficient (r) estimated.
Results: For estimation of systolic blood pressure during cuff inflation under spinal anaesthesia in Groups 1, 2 and 3: r = 0.57, 0.74 and 0.91; bias = –0.4, –2.9 and 0.8 mmHg, and limits of agreement = –27.7 to 26.9, –27.7 to 21.9, and –15.9 to 17.5 mmHg respectively. The mean (SD) time saved by estimation during inflation compared with measurement in Groups 1, 2 and 3 was 22.8 (13.2) s, 30.0 (11.6) s and 33.0 (15.6) s respectively. In Group 3, the percentage error was ± 13% of mean systolic blood pressure.
Conclusions: Estimation of systolic blood pressure during cuff inflation under spinal anaesthesia in the morbidly obese is more precise than in lower BMI parturients. Time to estimation is relevantly shorter than measurement. This could improve patient safety by rapid and accurate identification of hypotension in these high-risk patients. This estimation method is associated with limits of agreement that may be clinically significant even in morbidly obese patients, and should not be considered a replacement for subsequent NIBP measurement.

Keywords: body mass index, Caesarean section, pulse oximeter trace, spinal anaesthesia, systolic blood pressure

Introduction

Spinal hypotension in obstetrics is commonly associated with maternal nausea and vomiting and impaired uteroplacental perfusion. Hypotension is mainly due to a marked decrease in systemic vascular resistance induced by sudden sympathetic blockade.[1]

The latest UK Confidential Enquiry into maternal deaths published in 2014, MBRRACE-UK: Saving Lives, Improving Mothers' Care, showed that of the maternal deaths reported over 22% of women were overweight and 27% obese. The report also highlighted the increasing prevalence of obesity amongst the pregnant population.[2–3] Hence, the obstetric anaesthetist is encountering the challenge of a rising number of obese parturients presenting for Caesarean section (CS).[4] In South Africa, the preferred anaesthetic technique for emergency or elective Caesarean section is single-shot spinal anaesthesia (SA), since there is limited capacity to perform epidural or combined spinal epidural anaesthesia in resource-limited areas. Spinal hypotension demands prompt recognition and timely intervention with fluids and vasopressors, and this may be more difficult in morbidly obese patients (body mass index BMI > 40 kg/m²).

The standard method of blood pressure (BP) monitoring is with an automated non-invasive blood pressure (NIBP) device, which utilises the oscillometric measuring method. To improve response time, an alternative method to obtain an indication of the patient's systolic blood pressure (SBP) is to observe the **d**isappearance (DOT) or **r**eappearance (ROT) **o**f the pulse oximetry **t**race during BP cuff inflation and deflation respectively.

One previous study in women with a normal body mass index (BMI), undergoing SA for CS, included an assessment of blood pressure by disappearance of the pulse oximeter trace. The investigators showed poor accuracy and precision.[5]

The accuracy, precision and the rapidity of the estimate are all important. Regarding accuracy and precision, our clinical observation has been that the rate of increase of pressure in the cuff is more gradual in the high body mass patients, where a larger, higher volume cuff is required for accurate blood pressure measurement. This could make the accurate and precise visual estimation of blood pressure using DOT/ROT easier in obese patients than in low body mass patients, where the escalation of pressure is more rapid. As regards response time, NIBP readings often take longer in obese patients, and it is important to establish the time taken for the estimation of blood pressure, as well as the time saved by doing the visual estimate, across the physiological range of body mass indices. It was therefore decided to study the effect of the larger cuff required in patients with a raised body mass index on the accuracy and precision of estimation of SBP by disappearance/reappearance of the pulse oximeter trace (DOT/ROT) with cuff inflation during SA for

Caesarean section. We also investigated the time taken to achieve this estimate and the time taken for the NIBP measurement.

The main concordance analysis was an agreement comparison (bias and limits of agreement) between DOT/ROT and NIBP, across the full BMI range (normal to morbidly obese). The most clinically relevant estimation of SBP was during inflation of the cuff after induction of SA. Further analysis included a comparison of the time to measurement of DOT/ROT and NIBP, in the BMI range.

Our hypothesis was that estimation of blood pressure by observation of the disappearance of the pulse oximeter trace is more accurate and precise in morbidly obese patients, who require a larger blood pressure cuff. Also, this method could save a clinically relevant amount of time when compared with NIBP measurement. Accurate and early detection of SBP could improve the safety of spinal anaesthesia in morbidly obese patients.

Methods

Approval for the study was obtained from the Health Sciences Faculty Human Research Ethics Committee of the University of Cape Town (UCT). This prospective observational study was performed at the Groote Schuur Hospital Maternity Centre and Mowbray Maternity Hospital, Cape Town, South Africa. Written informed consent was obtained from all participants in the ward at the time of recruitment to the study.

Recruitment was stratified by three BMI groups (1: < 30 kg/m^2, 2: 30–40 kg/m^2 and 3: > 40 kg/m^2) to ensure that the agreement analysis would be possible across the entire BMI spectrum, as well as within each BMI stratum. Therefore, 25 patients requiring elective or emergency Caesarean section were recruited in each stratum to complete the study sample size of 75.

Inclusion criteria were age > 18 years, ASA Class 1 to 3 and gestation > 36 completed weeks. Exclusion criteria were pre-existing hypertension, pre-eclampsia or eclampsia, treatment with drugs that are known to affect blood pressure, any respiratory disease affecting arterial oxygen saturation, any condition causing impaired circulation to the hands, and multiple pregnancy. In the case of failed spinal anaesthesia, the recruited subject would be withdrawn from the study.

The same DASH® 3000 monitor (GE Healthcare, Amersham, UK) was used for all measurements for the study. An appropriately sized blood pressure (BP) cuff for non-invasive SBP measurements was applied to patients in all groups, following American Heart Association guidelines.[6] (Adult cuff 27.5–36.5 cm and Large Adult cuff 35.5–46 cm [UNIMED Medical Supplies Inc., Shenzhen, China]). Cuffs were applied snugly, allowing only enough room for one finger to be slipped between the cuff and the skin surface. The BP cuff and the pulse oximeter probe were applied to the arm and index finger on the ipsilateral side. The BP cuff was positioned at the level of the heart.

An intravenous catheter was placed. For all NIBP measurements, patients were placed supine on the operating table with 15° left lateral tilt, using an obstetric wedge. The first two NIBP readings for the study were taken 1 min apart, immediately before the induction of SA, using the dedicated DASH monitor. During these first measurements for the study the investigator observed the dynamic pressure readings of the NIBP machine as the cuff inflated, recording the SBP at the point when the pulse oximeter waveform disappeared (Pre-SA inflation [DOT]). The time taken for this estimation and the actual NIBP measurement were noted. For this purpose, a stop watch was used, started at the time when cuff inflation was initiated. With the second measurement, the investigator observed the dynamic pressure readings of the NIBP machine as the cuff deflated, recording the SBP at the point when the pulse oximeter waveform reappeared (Pre-SA deflation [ROT]). Once again, the time taken for this estimation and the actual NIBP measurement were noted.

SA was induced with the patient in the sitting position, using 2.0 ml hyperbaric 0.5% bupivacaine plus 10 µg fentanyl, with co-loading of crystalloid 15 ml/kg. All patients, after induction of SA, were positioned supine on the operating table, with 15° left lateral tilt using an obstetric wedge. The attending anaesthetist took non-invasive blood pressure measurements as per usual practice using the dedicated operating theatre monitor, using the cuff that was employed for the study, every minute until delivery. Five minutes post-induction of SA, a further two NIBP readings were taken for the study, 1 min apart, using the dedicated DASH monitor, employing the same methodology as the pre-SA readings (Post-SA inflation [DOT], and Post-SA deflation [ROT]). For all readings, the investigator was blinded to the NIBP measurements of systolic, diastolic and mean BP, which were recorded by the attending anaesthetist. This was done by placing an opaque rectangular cover over the blood pressure display panel of the DASH monitor. The same investigator took all the measurements, to eliminate inter-observer variability. The investigator was aware of the body habitus of the patient.

Prevention and management of hypotension were at the discretion of the attending anaesthetist. The usual practice is administration of a bolus of 50–100 µg of phenylephrine or 5–10 mg ephedrine.

Statistical methods

Sample size

The limits of agreement are calculated using the standard deviation of the difference between estimated and measured blood pressure. To assess whether the variability in the difference in estimated and measured blood pressure is associated with BMI, a test for a significant negative correlation can be used to confirm a decline in variability with increasing BMI. The correlation is calculated between the absolute value of the difference in blood pressure and BMI. A pilot study suggested a moderate negative correlation. For a sample size of 75 parturients, equally distributed over the BMI target range through stratification, the Fisher's z test will have 90% power to detect a correlation coefficient of –0.40 at a 5% significance level.

Analysis

Descriptive statistics of the demographic and anthropometric variables were compiled, as well as for the blood pressure by estimation and measurement (mean and standard deviation) during inflation of the cuff (DOT) and deflation (ROT), pre- and post-SA, and by BMI group. The main agreement analysis was a Bland and Altman comparison of DOT or ROT and NIBP measurements. The concordance correlation coefficient of Lin was also estimated. Plots of the limits of agreement were constructed. For the estimation and measurement of clinical interest, namely SBP post-SA inflation, the association of BMI with the bias, and the variability of the difference, were investigated. For evaluating the association of the bias with BMI, the correlation between the difference in estimated and

measured blood pressure and BMI was determined (Spearman correlation coefficient). For assessing the association between the variability of the difference between estimated and measured blood pressure and BMI, the correlation between the absolute value of the difference and BMI was calculated and tested (Spearman correlation coefficient). The F-test for the equality of the estimated and measured means and variance is also reported for the study overall and for the BMI strata, and non-significance indicates concordance.

Results

Three groups of 25 women were studied as defined in the Methods section. The pooled demographic and anthropometric results of the 75 participants are provided in Table 1. Table 2 gives the measured systolic blood pressure values (mean [SD], mmHg) per measurement time, in the three BMI categories and overall. There was a significant positive correlation between pre-SA measured systolic blood pressure and BMI (Spearman $r = 0.63$, $p < 0.001$).

The mean (SD) time (seconds [s]) required for the estimation of the pre-SA SBP during inflation was 7.9 (1.3) s, 12.2 (3.8) s and 19.2 (3.9) s in Groups 1, 2, and 3 respectively. The mean (SD) time required for measurement of the SBP, was 31.1 (5.7) s, 35.8 (6.7) s and 43.0 (7.1) s in the three groups respectively. In the pre-SA period, the mean (SD) time saved by estimation during the inflation period (i.e. time for measured SBP minus time for estimated SBP during inflation) was approximately 24 s, and 7 s during the deflation period. The mean (SD) time saved in Groups 1, 2 and 3 was 23.3 (5.7) s, 23.5 (5.4) s and 23.7 (5.4) s respectively. The mean (SD) time required for estimation of the SBP during inflation after induction of SA, was 7.5 (1.1) s, 11.8 (3.8) s and 16.8 (4.2) s in Groups 1, 2 and 3 respectively. The mean (SD) time required for measurement of post-SA SBP during inflation in Groups 1, 2 and 3 was 30.3 (13.1) s, 41.3 (10.2) s and 49.8 (14.6) s respectively. In the post-SA period, mean time saved by estimating SBP during inflation was approximately 28.5 s, compared with 9 s during deflation. The time saved in Groups 1, 2 and 3 was 22.8 (13.2) s, 30.0 (11.6) s and 33.0 (15.6) s respectively.

Table 3 summarises the concordance correlation coefficient *r*, the bias and the limits of agreement of the differences between measured and estimated SBP overall, and by BMI group, during inflation and deflation of the cuff. Concerning the clinically most relevant estimation in terms of time saved and treatment of hypotension, namely SBP during inflation post-SA: for DOT post-SA, the F-test for equality of means and variances are non-significant, indicating acceptable concordance for the study overall ($p = 0.59$), and within the three BMI strata. For Group 1, $r = 0.57$, bias = –0.4, limits of agreement = –27.7 to 26.9 mm Hg. For Group 2, $r = 0.74$, bias = –2.9, limits of agreement = –27.7 to 21.9 mmHg. For Group 3, $r = 0.91$, bias = 0.8, limits of agreement = –15.9 to 17.5 mmHg.

Table 1: Patient demographic details (***n*** = 75)

Variable	Minimum	P25[b]	P50[b]	P75[b]	Maximum
BMI (kg/m²)[a]	22	28.5	35.6	42.3	59.2
Arm circumference (cm)	24.8	28	32.5	39.1	49
Height (m)	1.45	1.56	1.6	1.64	1.74
Weight (kg)	56	70	90	112	150
Age (years)	18	26	30	33	40

[a]BMI = body mass index.
[b]P25, P50, P75 = 25th, 50th and 75th percentiles, respectively.

Table 2: Systolic blood pressure measurements during each study time period, in the three BMI categories and overall

BMI (kg/m²)	Time of NIBP measurement	*n*	Mean SBP	SD
< 30 kg/m²	Pre-SA inflation	25	122.7	12.3
	Pre-SA deflation	25	118.0	10.6
	Post SA inflation	25	110.5	15.3
	Post-SA deflation	25	109.9	10.8
30–40 kg/m²	Pre-SA inflation	25	130.4	13.2
	Pre-SA deflation	25	128.2	11.6
	Post SA inflation	25	110.4	18.7
	Post-SA deflation	25	110.0	15.8
> 40 kg/m²	Pre-SA inflation	25	147.4	12.2
	Pre-SA deflation	25	142.6	14.3
	Post SA inflation	25	122.9	20.2
	Post-SA deflation	25	120.8	18.9
Overall	Pre-SA inflation	75	133.5	16.2
	Pre-SA deflation	75	129.6	15.8
	Post SA inflation	75	114.6	18.9
	Post-SA deflation	75	113.6	16.1

Notes: BMI = body mass index; SBP = systolic blood pressure (mmHg); SD = standard deviation.

Figure 1 is a combined Bland and Altman plot showing the bias as well as the limits of agreement of the differences between measured and estimated SBP values for post-SA inflation (DOT), in the three BMI groups. Also depicted are the overall limits of agreement not taking BMI into account. Overall the bias was not associated with BMI (Spearman $r = 0.09$, $p = 0.43$), whereas the variability in the difference was negatively associated with BMI (Spearman $r = –0.29$, $p = 0.01$), indicating a significant reduction in variability between estimated and measured blood pressure with increasing BMI.

There were no missing values in the study. There were two cases where initial blood pressure measurements post-SA could not be obtained due to acute hypotension. These measurements were repeated after treatment of the hypotension.

Discussion

This prospective observational study showed that estimation of the SBP during cuff inflation post-SA (DOT) is more accurate and precise in morbidly obese parturients undergoing CS under SA, compared with parturients with lower BMI status. The negative association between the variability of the difference and BMI was statistically significant and thus the hypothesis of better precision of the DOT method in morbidly obese parturients was confirmed. This inverse association is directly reflected in the narrower limits of agreement in the parturients with BMI over 40 kg/m². The estimation of SBP by the DOT method also reduces the delay associated with formal NIBP measurement in this group, by a clinically relevant period when compared with ROT. The results probably reflect the inflation characteristics of the larger cuff required for accuracy in patients with a raised BMI.

Using the DOT method in morbidly obese parturients, the limits of agreement indicate that the percentage error will be ± 13% of the average SBP observed in this group (122 mm Hg). In these high BMI parturients, the error is ± 16 mm Hg compared with ± 27 mm Hg in parturients with normal BMI. Mean (SD) time

Table 3: Concordance, bias and limits of agreement of the differences between measured and estimated SBP overall, and by BMI group, during cuff inflation (DOT) and deflation (ROT)

Overall					
Period	**Timing of estimate**	**Concordance correlation coefficient *r* (95% CI)**	**Bias (SD) mmHg**	**95% limits of agreement (mmHg)**	**F-test for equal means and variances *p*-value**
Pre-SA[a]	Inflation	0.73 (0.63–0.84)	−0.9 (11.4)	−23.2 to 21.4	0.51
Pre-SA	Deflation	0.90 (0.85–0.94)	−2.7 (7.3)	−17.0 to 11.6	< 0.01
Post-SAb	Inflation	0.79 (0.71–0.88)	−0.8 (11.9)	−24.1 to 22.4	0.59
Post-SA	Deflation	0.87 (0.81–0.92)	1.7 (8.9)	−15.8 to 19.2	< 0.01
Group 1: BMI < 30 kg/m²					
Period	**Timing of estimate**	**Concordance correlation coefficient *r* (95% CI)**	**Bias (SD) mmHg**	**95% limits of agreement (mmHg)**	**F-test for equal means and variances *p*-value**
Pre-SA	Inflation	0.53 (0.26–0.80)	−5.2 (12.6)	−29.9 to 19.6	0.09
Pre-SA	Deflation	0.78 (0.64–0.93)	−3.3 (7.1)	−17.3 to 10.6	0.03
Post-SA	Inflation	0.57 (0.29–0.84)	−0.4 (13.9)	−27.7 to 26.9	0.95
Post-SA	Deflation	0.68 (0.48–0.88)	3.3 (9.7)	−15.7 to 22.2	0.06
Group 2: BMI: 30–40 kg/m²					
Period	**Timing of estimate**	**Concordance correlation coefficient r (95% CI)**	**Bias (SD) mmHg**	**95% limits of agreement (mmHg)**	**F-test for equal means and variances *p*-value**
Pre-SA	Inflation	0.73 (0.54–0.92)	−3 (9.5)	−21.6 to 15.5	0.31
Pre-SA	Deflation	0.79 (0.66–0.92)	−1 (9.2)	−19.1 to 17.0	0.01
Post-SA	Inflation	0.74 (0.55–0.92)	−2.9 (12.7)	−27.7 to 21.9	0.41
Post-SA	Deflation	0.90 (0.82–0.97)	0 (8)	−15.7 to 15.7	0.09
Group 3: BMI > 40 kg/m²					
Period	**Timing of estimate**	**Concordance correlation coefficient r (95% CI)**	**Bias (SD) mmHg**	**95% limits of agreement (mmHg)**	**F-test for equal means and variances *p*-value**
Pre-SA	Inflation	0.69 (0.49–0.88)	5.5 (9.2)	−12.6 to 23.5	0.02
Pre-SA	Deflation	0.91 (0.85–0.98)	−3.8 (4.9)	−13.4 to 5.8	< 0.01
Post-SA	Inflation	0.91 (0.84–0.98)	0.8 (8.5)	−15.9 to 17.5	0.89
Post-SA	Deflation	0.90 (0.82–0.97)	1.7 (9.1)	−16.0 to 19.5	0.22

[a]Pre-SA = 5 min before induction of spinal anaesthesia.
[b]Post-SA = 5 min after induction of spinal anaesthesia.

saved by estimating the SBP by this method was 33 (15.6) s, which has greater clinical relevance in high BMI parturients with regard to the longer measurement time required of 49.8 (14.6) s.

Concerning the most clinically relevant estimation, namely SBP during inflation (DOT) post-SA, we found a small bias between measured and estimated SBP in morbidly obese women,

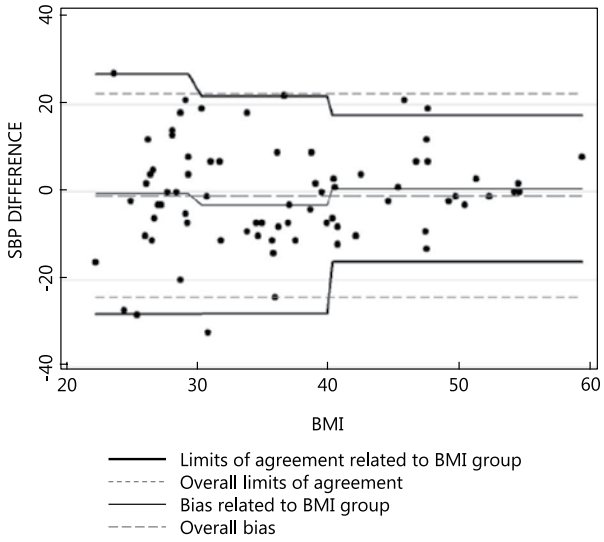

Figure 1: Bias and limits of agreement between estimated blood pressure during cuff inflation (DOT), and measured systolic blood pressure, post spinal anaesthesia in the three BMI groups, and overall.

excellent concordance and acceptable limits of agreement. By contrast, women with normal BMI showed poor concordance and broader limits of agreement.

The oximeter method to estimate BP has a few limitations. Only SBP can be obtained. Also, estimation of SBP using the oximeter can be subject to observer variation and differing results between the various NIBP devices. Each NIBP device has minor variations in the algorithms used to calculate SBP and DBP, and in speeds of inflation and deflation, so our results might not be entirely reproducible with all other devices.[6–8] We used the DASH® 3000 monitor, which is in common use globally. We observed that cuff inflation was more rapid than deflation, especially in the normal compared with the large adult cuff. This device takes its measurement during deflation, which explains the slower rate of deflation compared with inflation, as well as the more accurate and precise estimation of SBP across the BMI range during deflation (see Table 2). This is also in keeping with the finding that the disappearance of the trace during inflation occurs at a higher percentage of the baseline blood flow than during reappearance of the trace during deflation.[9] However, the delay associated with NIBP measurement is only marginally longer than estimation during cuff deflation. Therefore, it was important that acceptable accuracy and precision were associated with SBP estimation during cuff *inflation* in Group 3 where the delay in obtaining SBP is considerably less than using NIBP measurement.

Several studies have been performed using the pulse oximeter trace to estimate SBP.[10–17] However, most of these studies assessed the degree of correlation between the different methods[10–12,14,15] and, as Bland and Altman have pointed out, the more relevant comparison should involve the establishment of the limits of agreement.[18] Most also used a manual BP cuff, which allowed control of the rate of inflation and deflation of the cuff, resulting in moderately accurate results with good correlation.[10–12,16,17] However, in obstetric anaesthesia practice, an NIBP device is used for automated regular and frequent determinations.

A limited number of studies have utilised Bland–Altman analysis.[5,13,16,17] A study done by Chawla *et al.* evaluated the use of pulse oximetry to accurately monitor systolic blood pressure in 100 healthy volunteers. Using the oximetry method, they estimated arterial blood pressure at the disappearance of the waveform during manual blood pressure cuff inflation, at the reappearance of the waveform during manual cuff deflation, and by averaging the two estimations (BP_{AV}). By using Bland–Altman analysis, they found good agreement between the BP_{AV} of oximetry-based SBP estimates and blood pressure measured by auscultation or a non-invasive oscillometric device. In nearly 95% of cases, the differences between BP_{AV} and conventional methods were likely to be within ± 14 mm Hg.[13] Using an average of two SBP estimations as in this study is time-consuming, and eliminates the advantage of an earlier response time attained in our study.

Only one previous study in an obstetric population during SA has used Bland–Altman analysis to investigate observation of the oximeter trace to estimate SBP. Sabharwal *et al.* used radial artery palpation and observation of the oximeter trace during inflation and deflation, to estimate the SBP in 20 healthy volunteers and 20 parturients undergoing SA for CS. The study found that both methods had poor accuracy and low precision for estimating the SBP recorded by the NIBP device. Both methods underestimated SBP by an average of 10–20 mm Hg, except for pulse oximetry during cuff inflation, which overestimated SBP by a mean of 20–30 mm Hg. Mean (SD) BMI was 23.6 (4.0) kg/m^2 in the volunteers and 23.0 (4.0) kg/m^2 in the parturients, so the effect of BMI was not considered.[5] The very low BMI of the patients in this study could have contributed to very rapid cycling of the blood pressure cuff, and the greater bias shown than in our study. No studies could be found examining the influence of BMI on accuracy and precision.

As in the Sabharwal investigation, we did not study the influence that intravenous fluids or vasopressors might have on blood pressure determination but followed routine clinical practice. We also did not record heart rate, which may have had an effect on our estimations. In our study, heart rates ranged from 70 to 100 beats per minute. Our aim was also not to compare the accuracy of the DOT method to the intra-arterial pressure, but to evaluate its accuracy in estimating the SBP measurement, as this is the standard monitoring used intraoperatively. It can be especially useful in patients with very low blood pressure, for whom oscillometric measurements might be unobtainable, as was found in two instances in our study.

We documented which Caesarean sections were elective and which were urgent. No patients with foetal distress (category 1) were included. There was thus adequate time for informed consent and adherence to the protocol in every case. We did not specifically examine the difference between elective and urgent cases. Only 33% of patients were urgent and the study was not powered to distinguish between the outcomes in elective versus urgent cases.

In conclusion, the DOT method for post-SA estimation of SBP during CS in morbidly obese patients appears to be more precise than in lower BMI patients. The DOT technique is also associated with less delay in obtaining SBP in obese patients than with measurement using the NIBP device, and this may ensure an earlier response time for the recognition of hypotension. Thus, the use of the DOT method could improve safety during SA for CS

in morbidly obese patients. However, this method is associated with limits of agreement that may be clinically significant even in morbidly obese patients, and therefore should be used as a supplement and not be considered a replacement for NIBP measurements during spinal anaesthesia for Caesarean section.

Competing interests – The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this paper.

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