The comparison of non-invasive blood pressure monitoring with brachial intra-arterial blood pressure monitoring in patients with severe pre-eclampsia

By

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Declaration

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Abstract

The comparison of non-invasive blood pressure monitoring with brachial intra-arterial blood pressure monitoring in patients with severe pre-eclampsia

Principal investigator: Dr Samier Jacobs

Principal promoter: Dr Eduard Langenegger

OBJECTIVE: The aim of this study was to compare the accuracy of non-invasive brachial blood pressure measurements, using automated and manual devices, to invasive brachial intra-arterial blood pressure measurements in patients with pre-eclampsia, during acute severe hypertension.

STUDY DESIGN: A prospective descriptive cross sectional study was conducted in the Obstetrics Critical Care Unit (OCCU) of Tygerberg Hospital. Pre-eclamptic patients with acute severe hypertension, who required the placement of brachial intra-arterial lines due to failed radial intra-arterial line placement, were included in the study. Both automated oscillometric and blinded manual aneroid sphygmomanometric blood pressures were recorded during hypertensive peaks and after stabilization of BP using intravenous Labetalol or Nepresol. These two non-invasive methods of blood pressure measurements were compared to brachial intra-arterial blood pressure measurements.

RESULTS:

There was weak correlation between manual and intra-arterial SBP (r = 0.27, p = 0.048) for SBP≥160mmHg. The calculated mean difference between manual SBP compared to the intra-arterial SBP in this group was -23.19mmHg (+/- 19.40). There was moderate correlation between automated and intra-arterial SBP (r = 0.69, p < 0.05). The calculated mean difference between automated SBP compared to the intra-arterial SBP in this group was -16.85mmHg (+/- 11.58).

CONCLUSION:

This study of pre-eclamptic women demonstrated that both non-invasive methods of BP measurement were inaccurate measures of the true systolic intra-arterial BP and significantly underestimated SBP≥160mmHg when compared to brachial intra-arterial

measurements. The SBP was also underestimated, to a lesser degree, for mild moderate hypertension.

This study also demonstrated that direct invasive BP monitoring using the brachial artery is a safe method for accurate haemodynamic monitoring.

We recommend the use of intra-arterial BP monitoring in pre-eclamptic women with acute severe hypertension. Radial arterial cannulation should be used as the first option and the brachial artery should be used if the first option fails.

Opsomming

Die vergelyking van nie dringende bloeddruk monitering met bragiale intra-arteriele bloeddruk monitering in pasiente met erge pre-eklampsie

Primêre Navorser: Dr Samier Jacobs
Primêre Promotor: Dr Eduard Langenegger

DOELWIT: Die doel van hierdie studie was om die akuraatheid van nie indringende bragiale bloeddruk metings, wat met outomatiese en manuele aparate geneem is, te vergelyk met bragiale intra-arteriele bloeddruk metings gedurend akute erge hipertensie in pasiente met pre-eklampsie,

STUDIE ONTWERP: 'n Prospektiewe beskrywende dwarssnit studie was in die Obstetriese Kritiese Sorg Eenheid (OCCU) van Tygerberg Hospitaal uit gevoer. Pre-eklamptiese pasiente met akute erge hipertensie, wat bragiale intra-arteriele lyne nodig gehad het, as gevolg van gefaalde radiale intra-arteriele lyn plasing, was in hierdie studie ingesluit. Beide outomatiese ossilometriese en geblinde aneroide sfigmomanometriese bloeddrukke, tydens hipertensiewe pieke en na stabilisering van bloeddrukke met binneaarse Labetalol of Nepresol, was aangeteken, Die twee nie indringende metodes van bloeddruk meting was met bragiale intra-arteriele bloeddruk metings vergelyk.

RESULTATE:
Daar was 'n swak korrelasie tussen manuele en intra-arteriele sistoliese bloedrukke SBP ($r = 0.27$, p = 0.048) vir SBP≥160mmHg. Die berekende gemiddelde verskil tussen manuele SBP en intra-arteriele SBP was -23.19mmHg (+/- 19.40) in hierdie groep. Daar was 'n matige korrelasie tussen outomatiese en intra-arteriele SBP ($r = 0.69$, p < 0.05). Die berekende gemiddelde verskil tussen outomaties SBP vergelyk met intra-arteriele SBP was -16.85mmHg (+/- 11.58) in hierdie groep.

GEVOLGTREKKING:
Hierdie studie van pre-eklamptiese vrouens, het getoon dat beide nie indringende metodes van bloeddruk meting, nie akurate metings van ware sistoliese intra-arteriele bloeddruk is nie, en SBP≥160mmHg word aansienlik onderskat wanneer dit

met bragiale intra-arteriele metings vergelyk word. Die SBP was ook tot 'n minder mate onderskat vir matige hipertensie.

Die studie het ook getoon dat die direkte bragiale intra-arteriele metode van bloeddruk monitering, 'n veilige metode van hemodinamiese monitering is.

Ons beveel die gebruik van intra-arteriele bloeddruk monitering aan, in pre-eklamptiese vrouens met akute erge hipertensie. Radiale arteriele kanulasie moet gebruik word as die eerste opsie en die bragiale arterie moet gebruik word as die eerste opsie faal.

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List of Abbreviations

AHA	American Heart Association
ASSHP	Australasian Society for the Study of Hypertension in Pregnancy
BMI	Body mass index
BP	Blood pressure
DBP	Diastolic blood pressure
GCS	Glascow coma scale
HELLP	Haemolysis, elevated liver enzymes and low platelets
NCCEDM	National Committee for the Confidential Enquiries into Maternal Deaths
NIBP	Non-invasive blood pressure
NICE	National Institute for Health and Care Excellence in the UK
OCCU	Obstetric Critical Care Unit
PGWC	Provincial Government of the Western Cape
SBP	Systolic blood pressure

Introduction

The incidence of pre-eclampsia, ranges from 3 to 9% of all pregnancies worldwide. It is a pregnancy–specific multisystem disorder characterised by diffuse vascular endothelial dysfunction. It is associated with significant maternal and perinatal morbidity and mortality. Pre-eclampsia and eclampsia account for 10 – 15% of maternal deaths globally. The commonest causes of death in pre-eclamptic patients are intracranial haemorrhage, multi-organ failure and respiratory failure.[1,2,3,4,5,6,7]

In the latest Saving Mothers' Report (2008-2010), there was an increase in maternal deaths from 3595 to 4867 in South Africa since the previous triennial report (2005-2007). The number of reported cases of maternal deaths mainly increased due to an increase in the number of non pregnancy related infections (indirect obstetric deaths) and obstetric haemorrhage (direct obstetric deaths). Hypertension in pregnancy was the 3rd highest cause of maternal mortality, accounting for 14% of all maternal deaths. 61% of these deaths were deemed to be preventable. 50% of all women who died from hypertension in pregnancy were younger than 25 years of age. Cerebral complications were the final cause of death in half of the women with complications of hypertension. Intracranial haemorrhage accounted for 23% of the maternal deaths due to hypertensive disease in pregnancy. A key recommendation in the Saving Mothers' Report was to aggressively control high blood pressure, especially persistent severe SBP, in the ante-, peri- and immediate postpartum periods.[1,8,9]

In the US, pre-eclampsia is the 3rd leading cause of maternal mortality[7]. In the Eight Report of Confidential Enquiry into deaths in the UK, it was shown that 9 of the 22 pre-eclamptic maternal deaths were due to intracranial haemorrhage. Inadequate treatment of severe systolic hypertension in these patients was attributed to these deaths. According to the NICE guidelines, recommendations in the UK are to institute urgent anti-hypertensive management for pre-eclamptic patients with SBP≥150-160mmHg.[10] Martin et al, also demonstrated the importance of SBP control in a case series investigating stroke in 28 patients with pre-eclampsia and eclampsia. Immediately prior to the stroke, 100% of the patients had SBP≥155mmHg and 95.8% of the patients had SBP≥160mmHg. Only 12.5% of the patients had DBP≥110mmHg prior to stroke.[11] Bushnell et al, in a review article further re-iterated the importance of prompt treatment of severe SBP to reduce the incidence of intracranial haemorrhage

in pre-eclamptic patients.[12] A similar relationship was noted in a study by Lindenstrom looking at SBP and stroke in non-pregnant patients.[13]

In the 1950s, Nelson did not include SBP in the definition of pre-eclampsia. He described pre-eclampsia as a condition with a DBP≥90mmHg on 2 occasions after 26 weeks gestation.[14] The publication by McGillivray in 1988 also excluded SBP in the definition of hypertension in pregnancy because only DBP was deemed to be of diagnostic or prognostic value.[15] Recent evidence indicates the greater importance of SBP and its association with intracranial haemorrhage, but not undermining the importance of DBP.[11,12,13,16,17,18]

The measurement of MAP is complicated and is not as simple as a peak and trough measurements for SBP and DBP. Blood pressure monitors use specific algorithms to calculate MAP. Basically, MAP is the area under an arterial pressure in the cardiac cycle divided by the beat period over a number of consecutive heartbeats. Narrow arterial waveforms have lower MAPs and the converse is true for wider waveforms.[19]

According to ACOG, in 2011, SBP≥160mmHg and DBP≥110mmHg in pre-eclampsia is classified as a hypertensive crisis, but no MAP value is indicated.[18] However, Sibai in 2007, stated that a MAP≥125mmHg is an indicator of severe pre-eclampsia and requires anti-hypertensive therapy.[20] In 2008, Walsh and Baxi also stated that the most commonly used cut-off for severe pre-eclampsia is a MAP≥125mmHg.[21] Arulkumaran in 2013, stated that MAP≥145mmHg increases the risk of haemorrhagic stroke due to loss of cerebral autoregulation.[22] According to the same author, SBP<140-150mmHg and DBP<80-90mmHg should be targeted using anti-hypertensive therapy to minimise the stroke risk.

The gold standard for BP monitoring is invasive intra-arterial monitoring which gives accurate beat to beat information. A 5-10mmHg difference is expected and acceptable when intra-arterial BP measurements are compared to non-invasive BP measuring methods with resultant higher SBP.[23,24,25]

In 1733, Reverend Hales was the first person to experiment with direct invasive BP measurements by inserting intra-arterial tubes in animals to measure BP. In 1808, Young, a scientist, first described hypertension as a disease process. In 1856, Faivre recorded human BP for the first time during a limb amputation. He used a 'Kymograph' which was a U-shaped brass pipe in an artery, connected to a

manometer. The first non-invasive BP monitoring instrument, the sphygmomanometer was developed in 1896 by an Italian physician, Riva Rocci. In 1905, Korotkoff, a Russian surgeon, measured SBP and DBP when he described sounds heard with a stethoscope over the brachial artery while deflating the Riva Rocci cuff.[25,26] The use of Korotkoff sounds is still used today in standard BP measurement. Several advances and improvements in blood pressure measurement have been made since then.

In 2009, Hager H, et al found good correlation ($r = 0.74$) for MAP measurement when comparing invasive and non-invasive BP monitoring in a study of 22 morbidly obese patients undergoing bariatric surgery. The mean error was -0.25mmHg.[27] In 2006, Araghi compared invasive radial arterial and non-invasive BP methods in critically ill overweight patients. He found that non-invasive BP methods underestimated intra-arterial BP measurements in both normo- and hypertensive patients. The differences were independent of the BMI.[24] No studies yet have compared radial and brachial arterial invasive blood pressure methods in pregnancy.

In a systematic review by Scheer in 2001, a major complication rate <1% was found in patients requiring invasive haemodynamic monitoring, which included 19617 radial, 7185 brachial, 3899 femoral and 1989 axillary artery catheterizations.[28]

In 2011, Belda demonstrated that arterial catheters were safe alternatives for advanced haemodynamic monitoring. 514 arterial catheters were placed (475 femoral, 9 axillary, 26 radial and 4 brachial). The most frequent complication was that of local haematomas at the insertion site (4.5%) and the complication of ischaemia was low (0.4%), occurring in 2 femoral arterial catheters. All complications resolved with removal of the arterial catheter or embolectomy.[29]

The accuracy of invasive blood pressure monitoring is crucial in management of the haemodynamically unstable patient. Radial and femoral arterial catheterisations are most commonly used (92%) for invasive haemodynamic monitoring. The radial artery is preferred due to the alternative blood supply to the hand from the ulnar artery, but BP measurements differ from arterial sites closer to the heart. The increase in the systolic pressure in peripheral arteries is due to pressure waves that are reflected back from the peripheral narrowed blood vessels and bifurcations. The systolic pressure is amplified by the reflected waves.[19] SBP and DBP vary throughout the body under normal conditions, but the difference between central and peripheral

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arterial pressures become more important in certain physiological and pathological states.

In a 2006 study conducted on 55 patients in an ICU, Mignini found that the aortic MAP was 3mmHg (+/- 4mmHg) higher than the radial intra-arterial MAP.[30]
In 1989, Gravlee found that radial intra-arterial SBP was 10-35mmHg higher than the aortic SBP in >50% of patients undergoing cardiopulmonary bypass. DBP and MAP were more reliable (+/- 3mmHg) in 90% and 92% of the study patients, respectively.[31]
In a study by Davies et al, in 2010, intra-arterial blood pressure was measured in the proximal aorta, subclavian, brachial and radial arteries in 12 patients undergoing coronary artery bypass surgery. He found that SBP rose progressively in the arteries which were more peripheral. The SBP was 5mmHg higher in the radial artery than brachial artery.[32]

In the early 2000's, the mercury sphygmomanometer was still regarded as the gold standard for BP measurement when used by trained health care workers.[33,34,35] This traditional method has largely been replaced by newer auscultatory and oscillometric BP measuring methods. This non-invasive method of BP measurement has proven to be inaccurate when compared to intra-arterial BP measuring methods. In South Africa the automated blood pressure measuring method is used widely despite its tendency to underestimate SBP.[8,9,23]

In a 2010 study of obstetric patients with pre-eclampsia, Langenegger demonstrated a poor correlation between the automated and manual SBP measurements when compared to radial intra-arterial SBP measurements ($r = 0.34$, $p < 0.01$; $r = 0.41$, $p < 0.01$) respectively. The calculated mean differences for manual and automated methods were 20mmHg ± 15 and 24mmHg ± 17 respectively. In his study, the automated SBP and manual SBP underestimated the intra-arterial SBP by as much as 52mmHg and 68mmHg, respectively. He found no significant statistical difference when the mean automated and manual DBP were compared to the mean intra-arterial DBP. The study also demonstrated that the automated and manual methods of SBP measurements were not very accurate in detecting SBP≥160mmHg spikes (sensitivities of 23% and 44% respectively).[36]

In 1997, Penny compared intra-arterial monitoring with 3 non-invasive BP measuring techniques in pre-eclamptic women. A calculated mean difference of 15-18mmHg was found when the automated SBP was compared to the intra-arterial SBP.

Conventional sphygmomanometry also underestimated the SBP, but overestimated the DBP.[8]

In 1999, Natarajan compared auscultatory (QuietTrak) and oscillometric (SpaceLabs 90207) blood pressure monitors in the setting of pre-eclampsia. The automated devices underestimated the SBP (25mmHg and 19mmHg, respectively) and MAP (20mmHg and 7mmHg, respectively) when compared with mercury sphygmomanometry and intra-arterial BP measurements. The author concluded that neither monitor should be relied upon clinically in patients with pre-eclampsia.[23]

In 2001, Pomini compared manual and automated (Dinamap) methods of BP measurement in normotensive pregnant women collecting 490 readings and found that the automated method underestimated SBP by 10mmHg in 22% of the readings.[37]

In 2003, Bur found that the oscillometric BP measurements had low accuracy and the measurements were consistently lower than direct MAP measurements in critically ill patients.[38]

It is evident from the findings of the Saving Mothers Report (2008-2010) that hypertension (14%) in pregnancy is still an important cause of maternal mortality in South Africa. A large proportion of young women, especially teenagers, continue to die due to pre-eclampsia and eclampsia. Both DBP≥110mmHg and SBP≥160mmHg are independent risk factors for intracranial haemorrhage, especially with low platelets. There is, thus, a serious need for improved haemodynamic management in pre-eclampsia.[18,39] Recommendations from the NCCEDM are to ensure basic monitoring equipment, such as baumanometers, are available in all obstetric institutions.[9] As previously mentioned, manual and automated BP measuring equipment are currently used widely throughout South Africa.[8,9,23] Unfortunately, the infrastructure does not exist to offer direct invasive BP facilities at all levels of health care. Therefore, it is essential that the next best method for accurate BP assessment be used at the primary and secondary level health facilities. Langenegger concluded in his study in pre-eclamptic patients with acute severe hypertension, that both the automated and manual methods of blood pressure measurements were not accurate measures of the true systolic intra-arterial blood pressure. He further recommended the use of manual aneroid sphygmomanometry, but only if intra-arterial methods were not available.[36]

Another recommendation of NCCEDM was to introduce 'Early Warning Charts' intended to identify patients who need initiation of treatment early enough to reduce morbidity. Despite the use of Early Warning Charts, some acute severe hypertensive episodes would still be missed if the non-invasive BP measuring methods continue to underestimate the SBP, as found in the previous studies.[9]

The Obstetric Critical Care Unit (OCCU) is managed by a team of experienced doctors and nurses under strict supervision by the head of OCCU. Strict admission protocols are followed prior to admission into the 4 bed unit and arterial lines are placed in all patients admitted for management of persistent severe hypertension. Automated and manual BP measuring methods are the current methods of BP measurement used in the general labour ward. If SBP and DBP measurements are persistently high despite anti-hypertensive therapy (oral nifedipine or intravenous labetalol boluses) in the labour ward, the critical care doctor evaluates the patient and facilitates the admission to the OCCU. Due to the deficiencies of the non-invasive BP measurement methods used in the general labour ward, some acute severe hypertensive episodes will be missed.[34] It increases the likelihood of SBP≥160mmHg being missed in pre-eclamptic patients and increases the risk of intracranial haemorrhages.[11,12,13]

The study by Langenegger has been the only study comparing invasive and non-invasive blood pressure monitoring in the same patients with severe pre-eclampsia, during a hypertensive blood pressure peak.[36] There is a scarcity of studies comparing intra-arterial and non-invasive BP monitoring in patients with pre-eclampsia.

The aim of this study is to test the hypothesis that non-invasive BP monitoring, using manual and automated devices, is not an accurate measure of BP when compared to brachial intra-arterial BP monitoring in patients with severe pre-eclampsia.

Methods

The study was conducted in the Obstetrics Critical Care Unit (OCCU) at Tygerberg Hospital. The University of Stellenbosch Research Ethics Committee approved the study protocol. The approval reference number is N08/10/308.

15 pre-eclamptic patients with acute severe hypertension who required invasive blood pressure monitoring, were recruited for the study during the period April 2012 and August 2013.

The patients were under no obligation to participate in the study and were required to give written informed consent. Patients were given the choice, unconditionally, to opt out of the study at any time. All the patients fulfilled the criteria for the diagnosis of pre-eclampsia (as indicated below) and had persistent SBP≥160mmHg and/or DBP≥110mmHg using the automated method in the labour ward. Patients who had severe pre-eclampsia, who could not be accommodated in the OCCU and those with depressed GCS were not included in the study.

Pre-eclamptic patients with acute severe hypertension who required OCCU admission and who had brachial intra-arterial lines were asked to participate in the study. Brachial arterial lines were placed when the radial arterial insertion failed, or the brachial pulsation was better than the radial arterial pulsation, or if the radial area was obscured by a haematoma. Participation in the study did not alter or compromise patient care or management in any way. Patients who fulfilled the above-mentioned inclusion criteria were recruited by the doctors working in the OCCU.

Pre-eclampsia was defined as the onset of hypertension with significant proteinuria after 20 weeks gestation.[15,40] Hypertension was defined as SBP≥140mmHg and/or DBP≥90mmHg on 2 or more occasions at least 4 to 6hrs apart.[41] Acute severe hypertension was defined as either SBP≥160mmHg or DBP≥110mmHg.[11,42]
Significant proteinuria is defined as 2+ proteinuria on urine dipstix,, or urine protein excretion of 0.3g/24hrs.[41]

OCCU doctors used the 20 gauge Vygon Seldinger technique arterial cannulae to insert brachial arterial lines under sterile conditions. The cannulae were connected to disposable tubing system, which delivered a constant infusion of heparinized 0.9%

saline, delivered at a rate of 2–4 ml/h to prevent occlusion of the cannulae by thrombi. Before each data collection, a rapid flush test was performed to remove bubbles from the system and reduce errors in readings due to over-damping. The transducer was placed at the phlebostatic axis, located at the 4th intercostal space and halfway between the anterior and posterior chest. Zeroing was performed by opening the transducer to atmospheric pressure and electronically zeroing the system, prior to collection of readings.

The Nihon Kohden BSM – 4113K oscillometric BP monitor was used to record the automated BP readings and intra-arterial BP readings in our study patients. The manual BP was obtained using the Welch Allyn Maxi Stabil 3 aneroid sphygmomanometer, which was A grade and validated to the British Hypertension Society protocol.[43] All equipment were calibrated and serviced on a regular basis.

During every hypertensive BP peak on the invasive intra-arterial BP monitor, the automated BP and a blinded manual BP was documented. BP readings were also recorded after stabilization of the BP with labetalol or nepresol to SBP≤160mmHg and DBP≤110mmHg. More than 1 set of readings per patient were obtained.

The manual BP was a blinded reading obtained by either OCCU nursing staff or medical doctors. The BP monitor was covered with a screen, so that the nursing staff or medical doctor measuring and recording the manual BP would be blinded from true intra-arterial and automated BP measurements.

Manual blood pressures were measured on the non dominant arm, when possible, with the patient semi-recumbent in the left lateral position or at least 30 degree tilt. The upper arm of the patient was positioned horizontally at the level of the heart, as recommended by the Australasian Society for the Study of Hypertension in Pregnancy (ASSHP) and the AHA. The middle of the cuff on the upper arm was placed level with the right atrium, at the midpoint of the sternum.[36,40]

The height, weight, body mass index and the arm circumference at mid-arm level were documented for each patient to ensure selection of the correct cuff size.[44] A cuff size of 15 by 33cm was used when the mid arm circumference exceeded 33cm, as recommended in Western Cape Provincial Guidelines.[25,35,40,41] When measuring the manual BP, Korotkoff phase V was documented as the DBP. Korotkoff phase IV was

used when phase V approached zero.[19,41,45,46] The bell-shaped head of the stethoscope was used to optimize detection of low frequency Korotkoff sound.[19]

The patient characteristics and BP readings were recorded on the data capture sheets by the OCCU staff.

There were no studies identified that used brachial intra-arterial BP monitoring in pre-eclamptic patients. It was therefore not possible to use data from previous studies to calculate sample size. In a previous study done in the OCCU, using radial intra-arterial BP monitoring in pre-eclamptic patients, a mean difference of 10mmHg was used when comparing intra-arterial SBP with automated and manual SBP. The calculated mean differences for the manual and automated methods were 20mmHg ± 15 and 24mmHg ± 17 respectively. After consultation with the statistician, a decision was made to analyse data after 50 readings in each group in our study, to determine if the sample size would be sufficient to detect a 10mmHg mean difference using a power of 80 and confidence interval of 95%.

STATISTICA 11.0 statistics and analytics software package was used to analyse the study data. All values are expressed as the mean ± standard deviation. A paired Student's t test was used to compare the mean differences between intra-arterial, automated and manual BP measurements. A p value of < 0.05 was considered statistically significant. The comparison between the 3 BP measurement methods for SBP, DBP and MAP were represented in scatter plots. Bland and Altman plots were used to determine bias and agreement between the various methods of BP measurement

Outcomes

The primary outcome of this study was:

1. To determine the accuracy of the automated and manual SBP when compared to the brachial intra-arterial SBP for SBP≥160mmHg

The secondary outcomes were as follow:

2. To determine the accuracy of the automated and manual SBP when compared to the brachial intra-arterial SBP for SBP≥140mmHg <160mmHg

3. To determine the accuracy of automated and manual DBP, when compared to the brachial intra-arterial DBP for DBP≥110mmHg

4. To determine the accuracy of the MAP of the automated and manual blood pressures, when compared to the brachial intra-arterial MAP for MAP≥125mmHg

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Results

Table 1. Patient characteristics with means and ranges

	Mean	Median	Range
Age (yrs)	28	30	(21-36)
Gravidity	2	2	(1-5)
Parity	1	1	(0-5)
Gestation (wks)	29	27	(21-41)
Weight (Kg)	82	80	(53-115)
Length (cm)	159	160	(150-170)
Body Mass Index (Kg/m²)	31	31	(21-43)
Systolic BP (mmHg)*	168.9	160	(152-201)
Diastolic BP (mmHg)*	102.6	100	(87-120)

*Initial intra-arterial systolic and diastolic blood pressure at recruitment

Table 2 Racial Distribution of patients expressed as a percentage

	Patients (*n*)	Percentage (*%*)
Black	13	86.7
Coloured	2	13.3
White	0	0
Other	0	0

Table 3 Patient characteristics expressed as a percentage

	Patients (*n*)	Percentage (*%*)
Primigravida	4	26.7
Multiparous	11	73.3
Antepartum	8	53
Postpartum	7	47
New paternity	7	46.7
Previous pre-eclampsia	5	33
Chronic hypertension	0	0
HIV positive	5	33
Smokers	1	6.6

Table 4 Complications of Pre-eclampsia

	Patients (*n*)	Percentage (*%*)
HELLP syndrome	6	40
Renal dysfunction†	4	26.6
Pulmonary oedema	2	13.3
Eclampsia	1	6.6

† Renal risk, injury and acute renal failure were included[22]

129 blood pressure readings for each BP measuring modality were collected between April 2012 and August 2013.

53 readings were for SBP≥160mmHg, 76 readings for SBP≥140mmHg and <160mmHg, and 15 readings for DBP≥110mmHg with SBP≥160mmHg. In addition, 35 readings had MAP≥125 of which 6 MAP readings were >145mmHg.

15 patients with median age of 30 years (range 21 – 36years) were recruited for the study. The median gestational age of the study patients was 27 weeks (range 21 – 41 weeks)[table 1]. The mean gravidity and parity were 2 (range 1 – 5) and 1 (range 0 - 5), respectively. The mean BMI was 31 (21-41). 53% of the patients were antenatal recruits and 26.7% were primigravidas. All patients required intravenous antihypertensive therapy for BP control and they all had significant proteinuria (>2+ proteinuria or >0.3g proteinuria per 24hrs).

The most frequent complication of pre-eclampsia encountered was HELLP Syndrome which occurred in 40% of the patients. Other complications included pulmonary oedema, renal dysfunction and eclampsia. Fortunately, no patients suffered from intracranial haemorrhage.

Group of intra-arterial SBP≥160mmHg

A moderate correlation was demonstrated when comparing automated SBP to manual SBP measurements in the intra-arterial SBP≥160mmHg group. r = 0.55 (p < 0.05). The mean automated SBP was 156.04mmHg +/- 14.96 compared to the mean manual SBP of 149.70 mmHg +/- 17.56. The calculated mean difference was 6.34mmHg +/- 15.52. (Fig. 1)

A weak correlation was demonstrated when comparing manual SBP to intra-arterial SBP measurements in this group. The correlation coefficient for SBP was r = 0.27 (p = 0.048). The mean intra-arterial SBP was 172.89mmHg +/- 14.32. The calculated mean difference was -23.19mmHg +/- 19.40. (Fig.2)

There was a positive bias of 0.15mmHg for intra-arterial SBP measurements. 2 of the 53 readings exceeded the upper limit of agreement. (Fig. 3)

A moderate correlation was demonstrated when automated SBP was compared to intra-arterial SBP measurements in this group. $r = 0.69$ ($p < 0.05$). The calculated mean difference was -16.85mmHg +/- 11.58. (Fig. 4)

Positive bias of 0.1mmHg was demonstrated for the intra-arterial method. Only 2 outliers beyond the limits of agreement were found. (Fig. 5)

Figure 1 Scatterplot of Automated against Manual SBP for SBP≥160mmHg

Scatterplot of Manual against Auto

Figure 2 Scatterplot of Intra-arterial against Manual SBP for SBP≥160mmHg
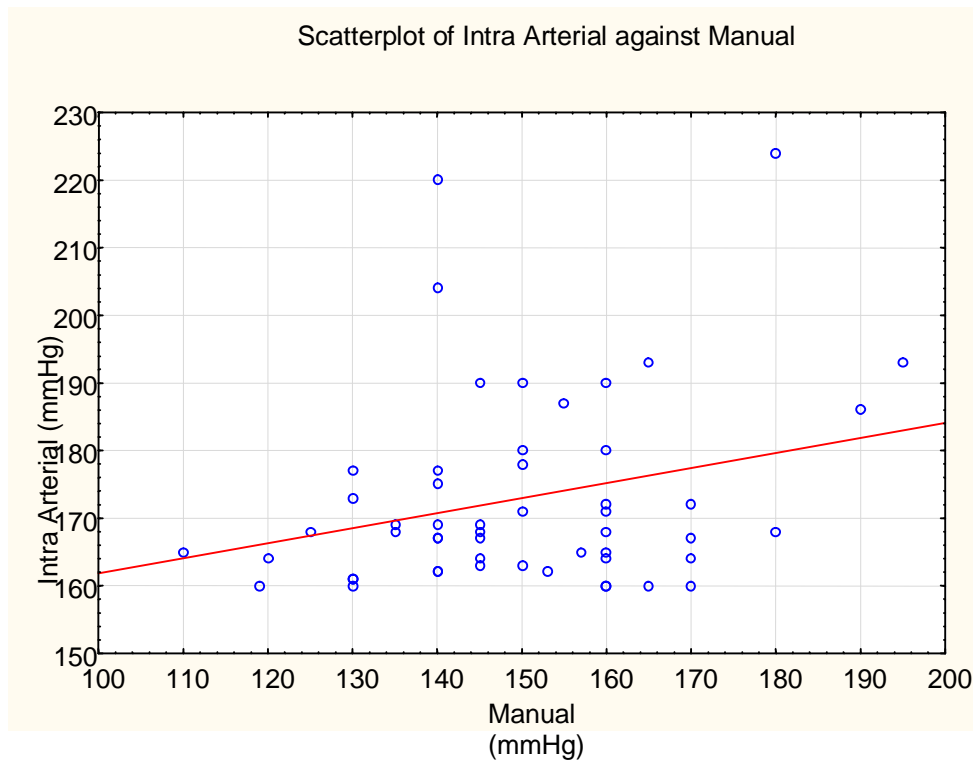
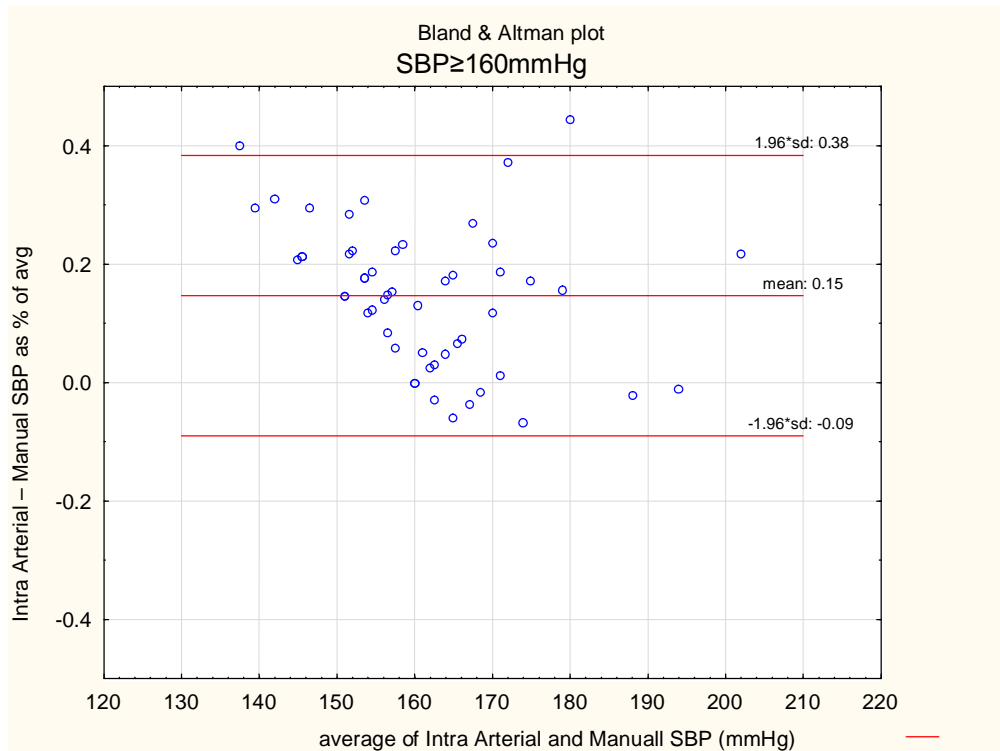**Figure 3 Bland + Altman Plot of Intra-arterial and Manual SBP for SBP≥160mmHg**

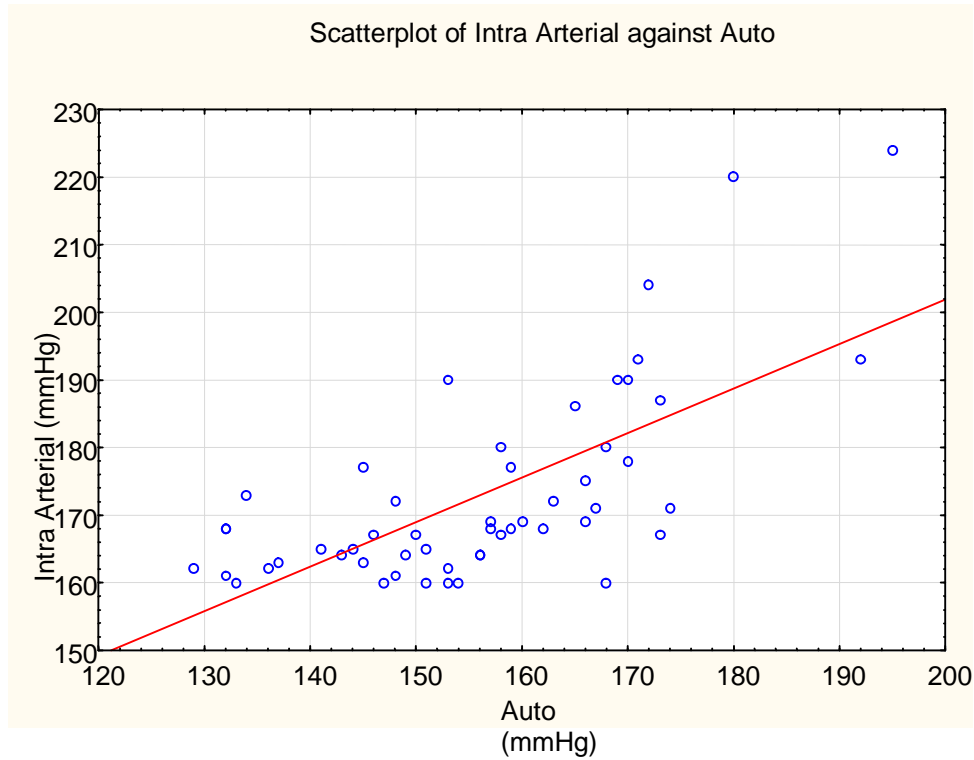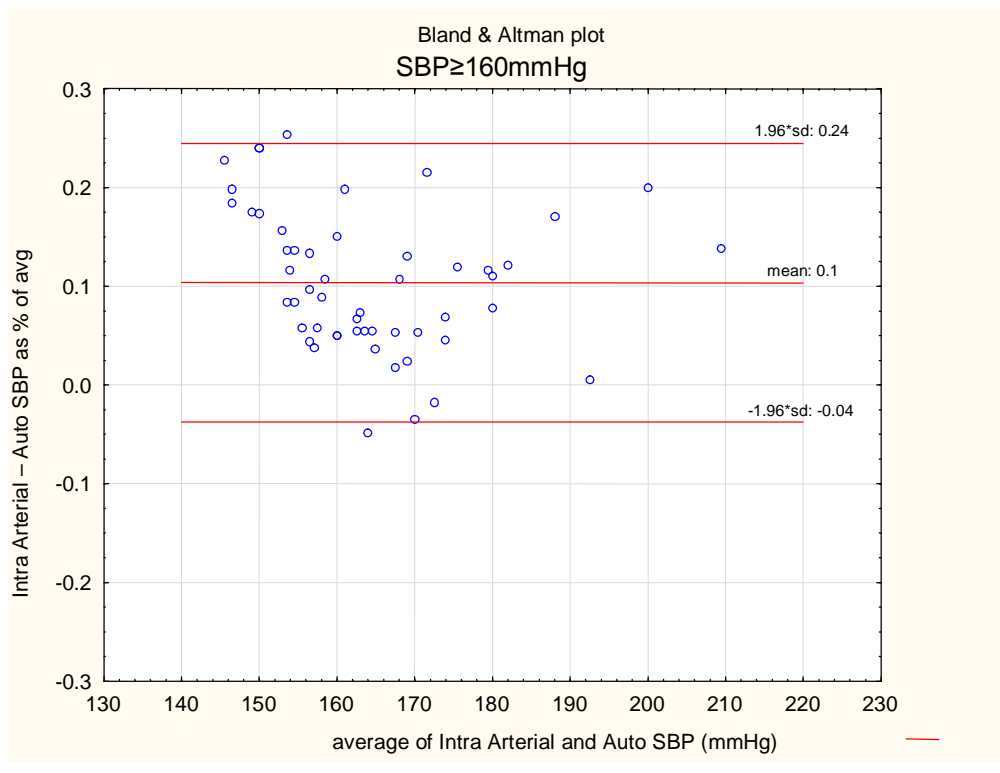**Figure 4 Scatterplot of Intra-arterial against Automated SBP for SBP≥160mmHg**

Scatterplot of Intra Arterial against Auto

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Figure 5 Bland and Altman Plot of Automated and Intra-arterial SBP for SBP≥160mmHg

Bland & Altman plot
SBP≥160mmHg

Group of intra-arterial SBP≥140mmHg and <160mmHg

A moderate correlation was demonstrated when comparing automated SBP to manual SBP measurements in the intra-arterial SBP≥140mmHg and <160mmHg group. $r = 0.43$ (p < 0.05). The mean automated SBP was 139.33mmHg +/- 12.17 compared to the mean Manual SBP of 137.57mmHg +/- 15.78. The calculated mean difference was 1.76mmHg +/- 15.21. (Fig. 6)

A weak correlation was demonstrated when comparing manual SBP to intra-arterial SBP measurements in this group. The correlation coefficient for SBP was $r = 0.24$ (p = 0.04). The mean intra-arterial SBP was 150.25mmHg +/- 5.30. The calculated mean difference was -12.68mmHg +/- 15.40. (Fig. 7)

There was a positive bias of 0.09mmHg for intra-arterial SBP measurements. 3 of the 53 readings exceeded the lower limit of agreement and 1 reading exceeding the upper limit of agreement. (Fig. 8)

A very weak correlation was demonstrated when automated SBP was compared to intra-arterial SBP measurement in this group. $r = 0.14$ (p = 0.24). The finding was not statistically significant. The calculated mean difference was -10.92mmHg +/- 12.60. (Fig. 9)

Positive bias of 0.08mmHg was demonstrated for the intra-arterial method. Only 3 outliers beyond the limits of agreement were found. (Fig. 10)

Figure   6   Scatterplot   of   Automated   against   Manual   SBP   for SBP≥140<160mmHg
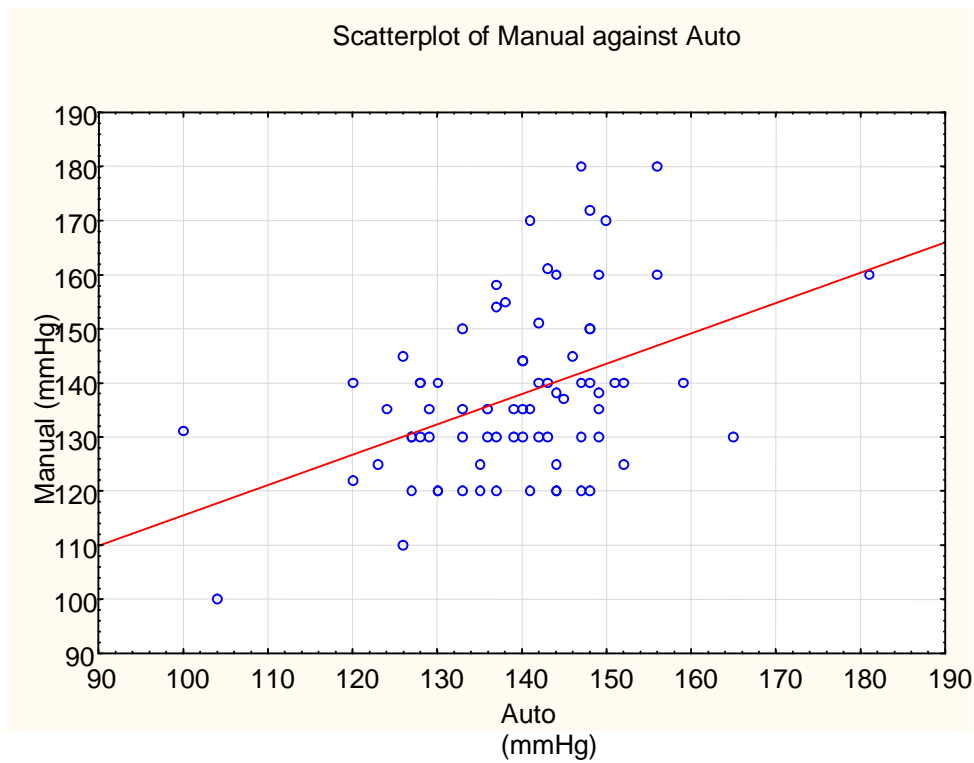

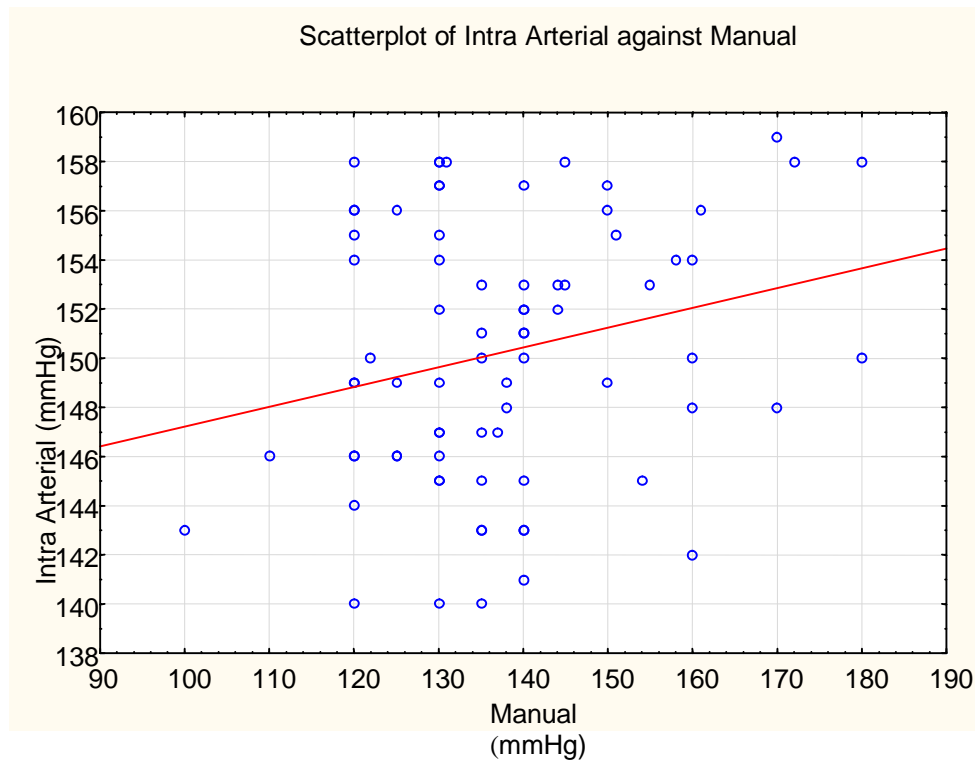**Figure 7 Scatterplot of Intra-arterial against Manual SBP for SBP≥140<160mmHg**

Figure 8 Bland + Altman Plot of Manual and Intra-arterial SBP for SBP≥140<160mmHg
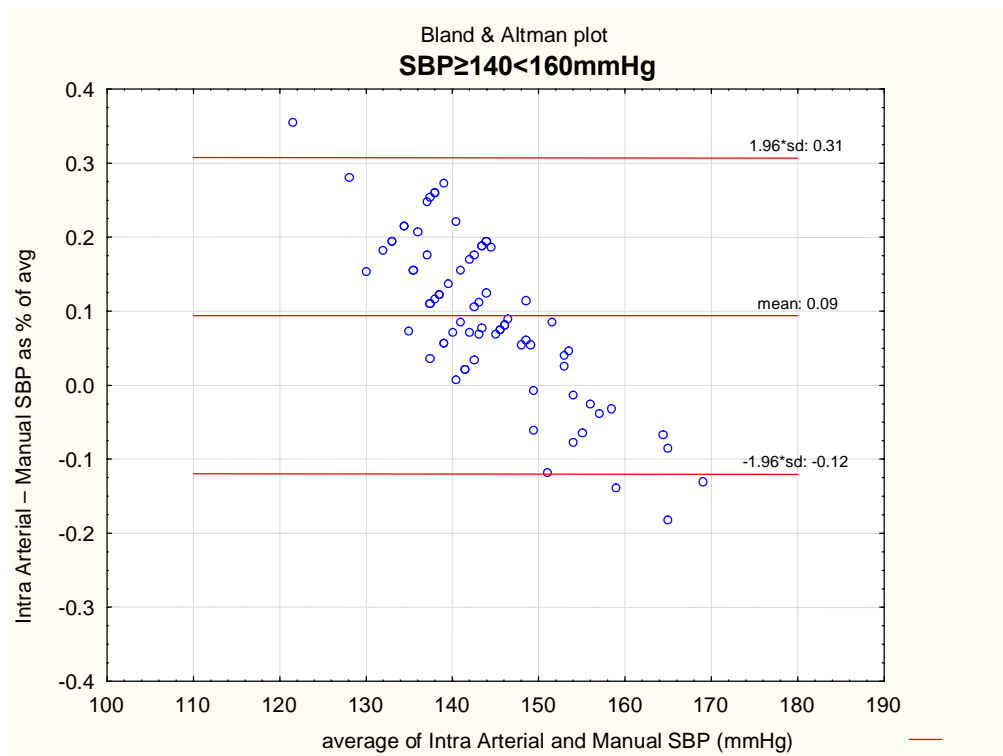

Bland & Altman plot
SBP≥140<160mmHg

Figure 9 Scatterplot of Intra-arterial against Automated SBP for SBP≥140<160mmHg
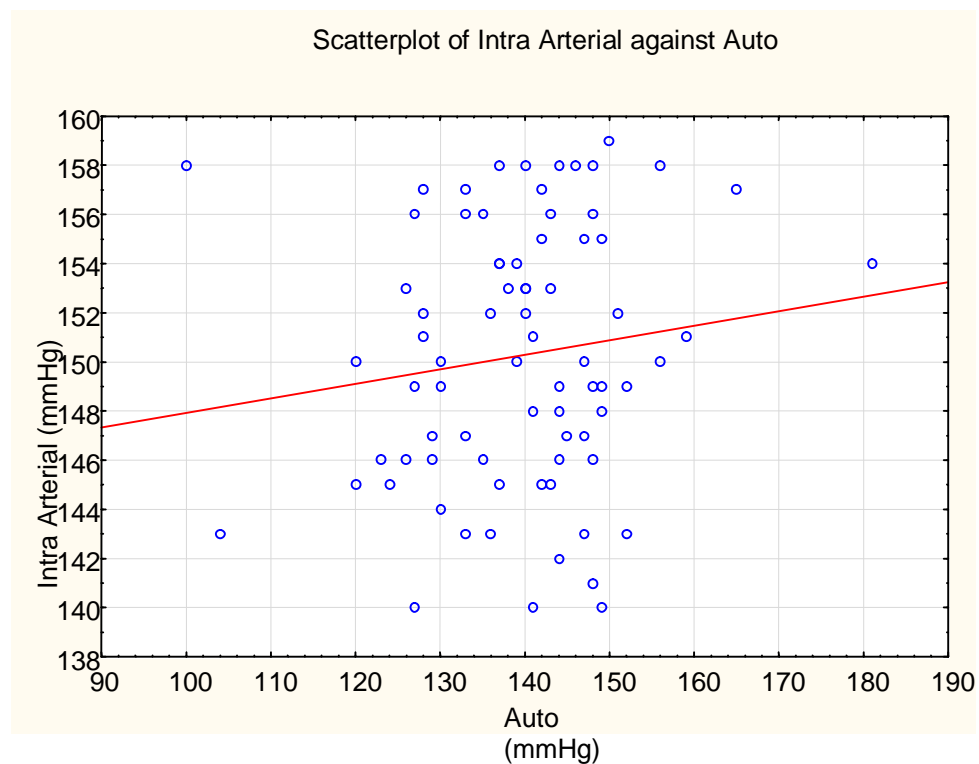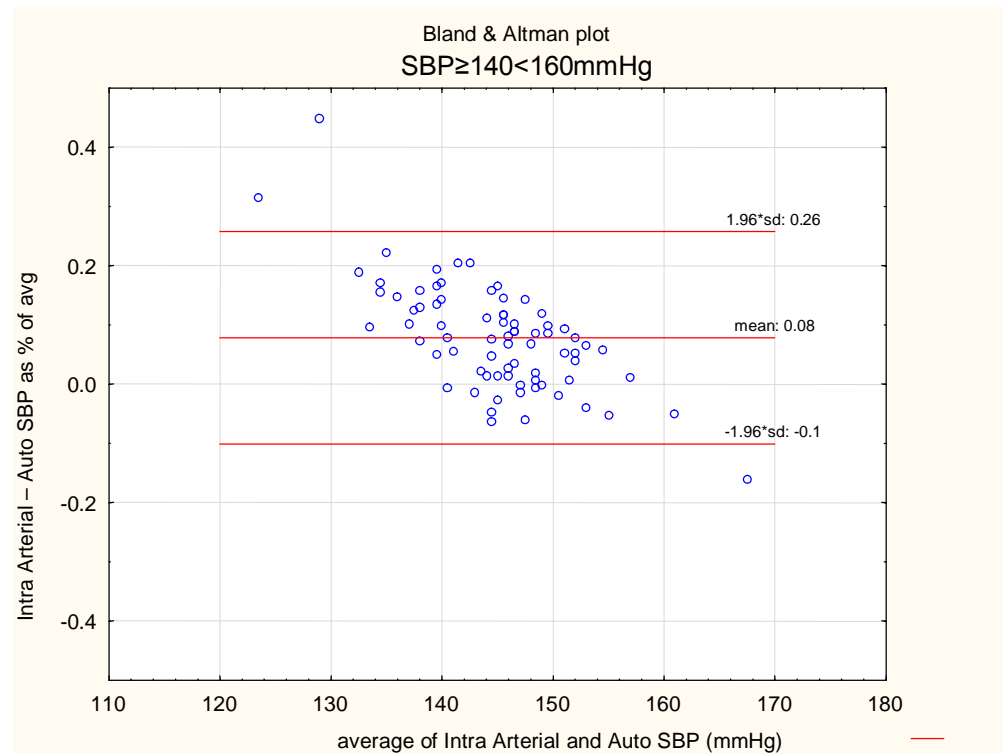

Scatterplot of Intra Arterial against Auto

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Figure 10 Bland + Altman Plot of Automated and Intra-arterial SBP for SBP≥140<160mmHg

Group of intra-arterial DBP≥110mmHg

A moderate correlation was demonstrated when comparing automated DBP to manual DBP measurements. $r = 0.59$ (p = 0.02). The mean automated DBP was 108.13mmHg +/- 6.72 compared to the mean manual DBP of 101.00mmHg +/- 11.98. The calculated mean difference was 7.13mmHg +/- 9.69. (Fig. 11)

A weak correlation was demonstrated when comparing manual DBP to intra-arterial DBP measurements. The r value for DBP was 0.38 (p = 0.16). The mean Arterial DBP was 113.53mmHg +/- 3.16. The calculated mean difference was -12.53mmHg +/- 11.17. (Fig. 12)

There was a positive bias of 0.12mmHg for intra-arterial DBP measurements. Only 1 outlier exceeded the upper limit of agreement. (Fig. 13)

A weak correlation was demonstrated when comparing automated DBP to intra-arterial DBP measurements. $r = 0.29$ (p = 0.29). The calculated mean difference was -5.4mmHg +/- 6.54. (Fig. 14)

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Positive bias of 0.05mmHg for DBP measured by the intra-arterial method was demonstrated. All readings were within the limits of agreement. (Fig. 15)

Figure 11 Scatterplot of Automated against Manual DBP≥110mmHg

Scatterplot of Manual against Auto
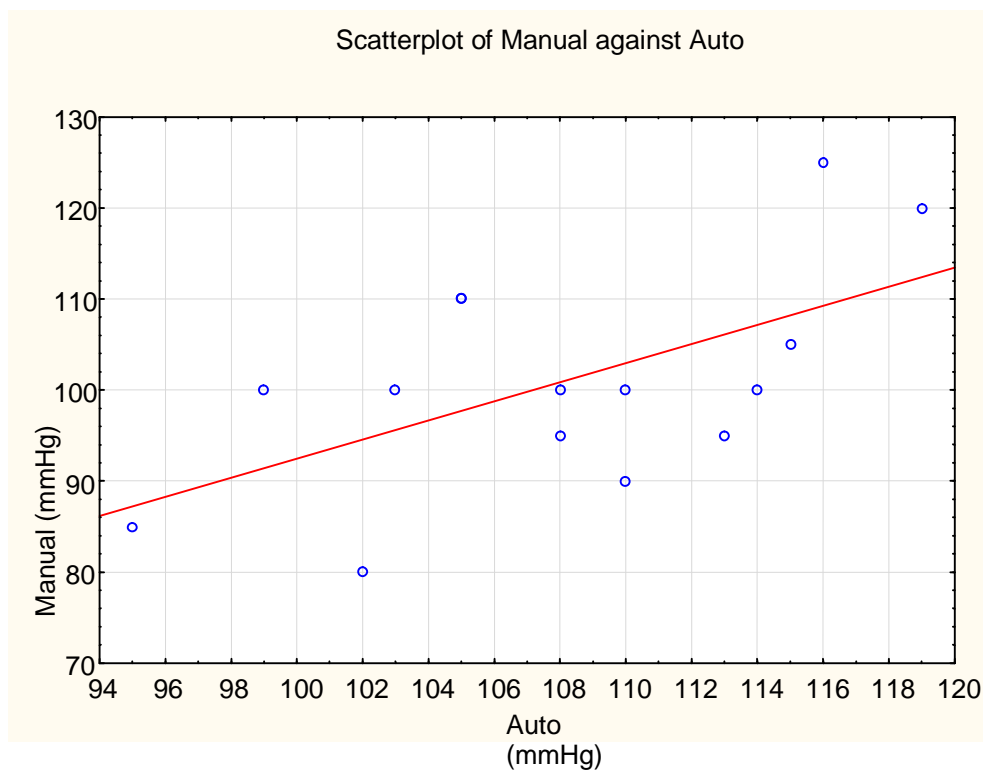
Figure 12 Scatterplot of Intra-arterial against Manual DBP≥110mmHg

Scatterplot of Intra Arterial against Manual
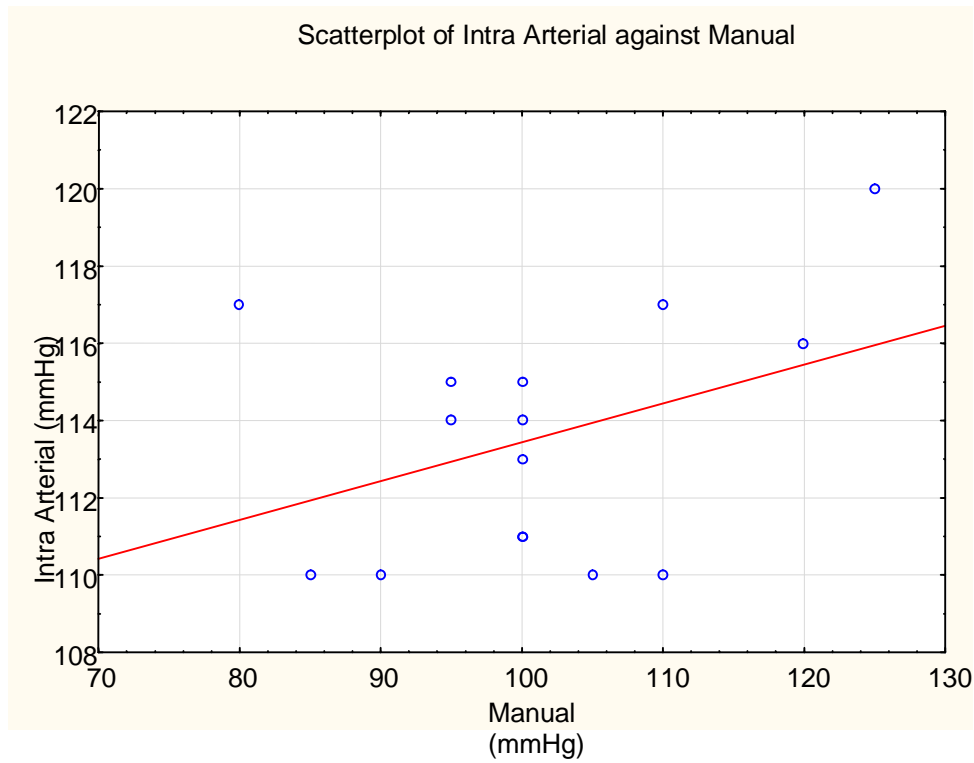
Figure 13 Bland + Altman Plot of Manual and Intra-arterial DBP≥110mmHg

Bland & Altman plot
DBP≥110mmHg

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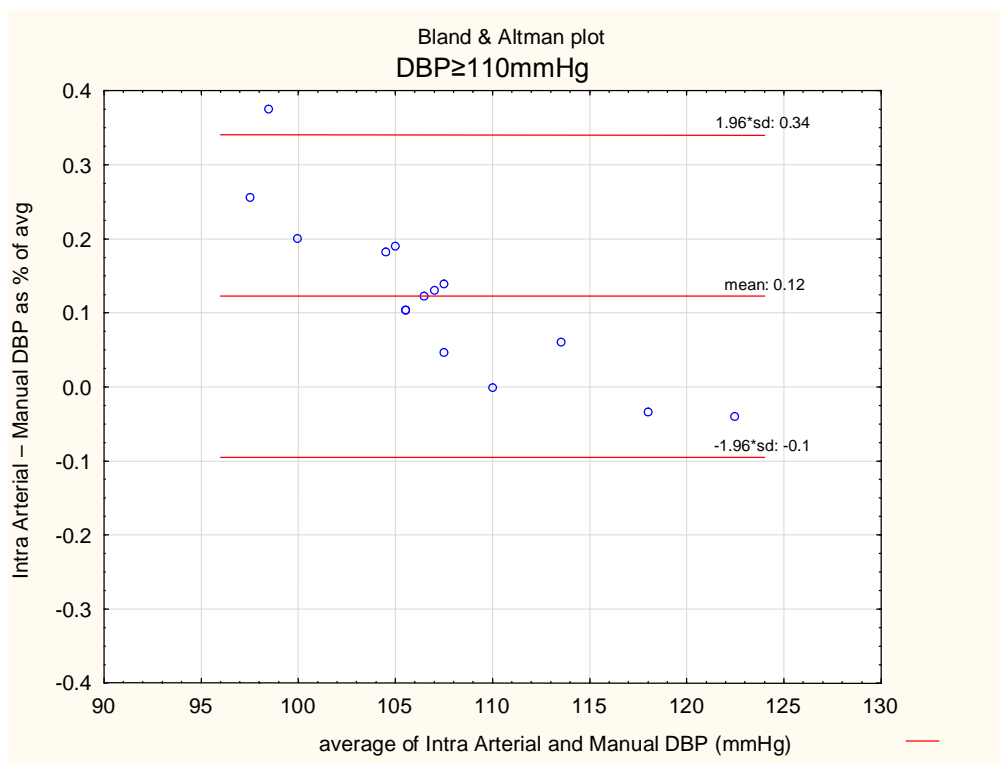
Figure 14 Scatterplot of Intra-arterial against Automated DBP≥110mmHg

Scatterplot of Intra Arterial against Auto
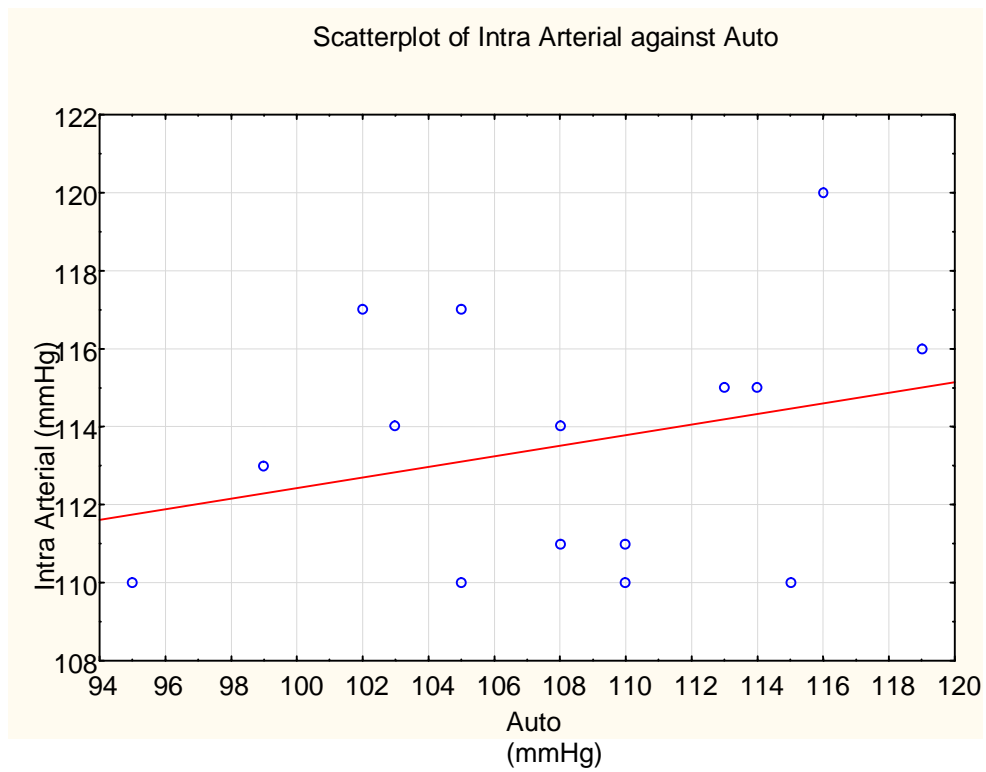
Figure 15 Bland + Altman Plot of Automated and Intra-arterial DBP≥110mmHg

Bland & Altman plot
DBP≥110mmHg

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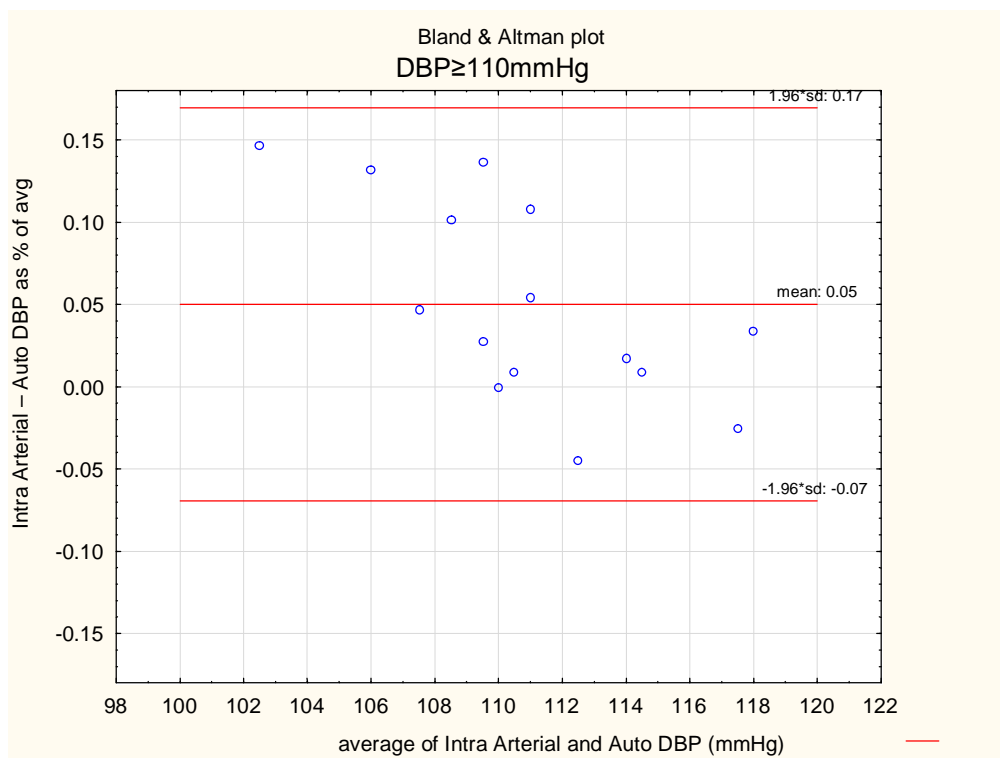
Group of intra-arterial MAP≥125mmHg

The correlation was strong when comparing automated MAP to manual MAP measurements. $r = 0.71$ (p < 0.05). The mean automated MAP was 119.06mmHg +/- 13.39 compared to the mean manual MAP of 110.20mmHg +/- 15.34. The calculated mean difference was 9.03mmHg +/- 11.08. (Fig. 16)

A moderate correlation was demonstrated when comparing manual MAP to intra-arterial MAP measurements. r = 0.53 (p < 0.05). The mean intra-arterial MAP was 135.09mmHg +/- 8.96. The calculated mean difference was -25.06mmHg +/- 13.01.(Fig. 17)

There was positive bias of 0.21mmHg for MAP measured by the intra-arterial method. 32 of the 35 readings were within the the upper and lower limits of agreement. (Fig. 18)

The scatter plots for all comparisons between manual, automated and arterial BP measurements show consistent underestimation of BP by the manual and automated readings in this group.

There was also a weak correlation when comparing automated MAP to intra-arterial MAP measurements. $r = 0.40$ (p = 0.02). The calculated mean difference was -16.03 mmHg +/- 12.79. (Fig. 19)

Positive bias of 0.13mmHg was demonstrated for MAP measurements by the intra-arterial method. Only 1 outlier exceeded the upper limit of agreement. (Fig. 20)

Figure 16 Scatterplot of Automated against Manual MAP≥125mmHg

Scatterplot of Manual against Auto
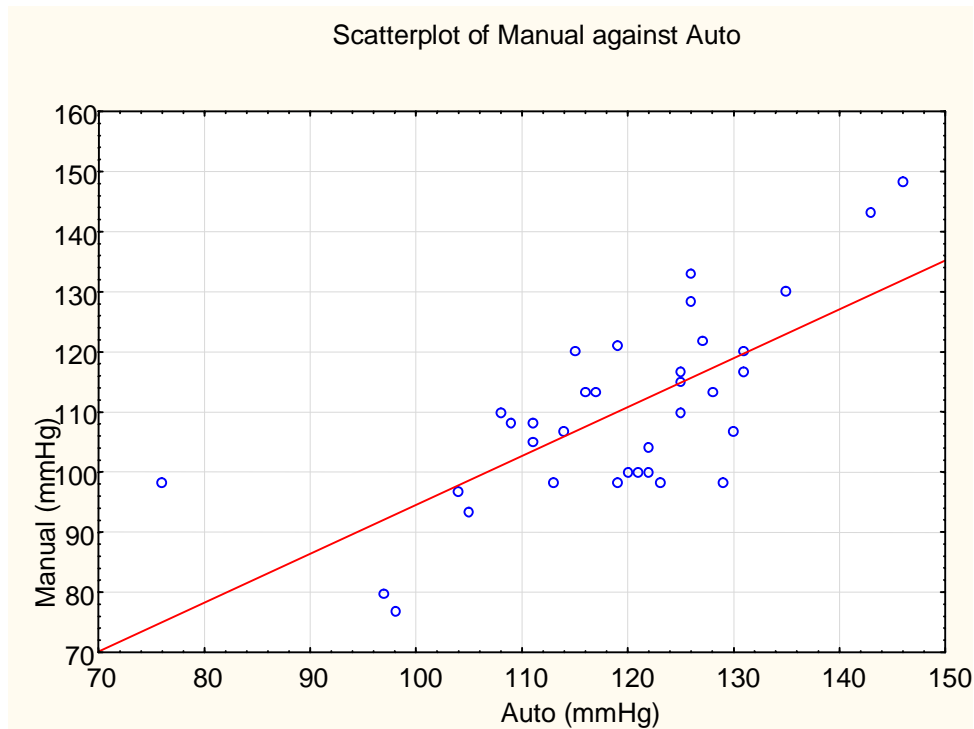
Figure 17 Scatterplot of Intra-arterial against Manual MAP≥125mmHg

Scatterplot of Intra Arterial against Manual
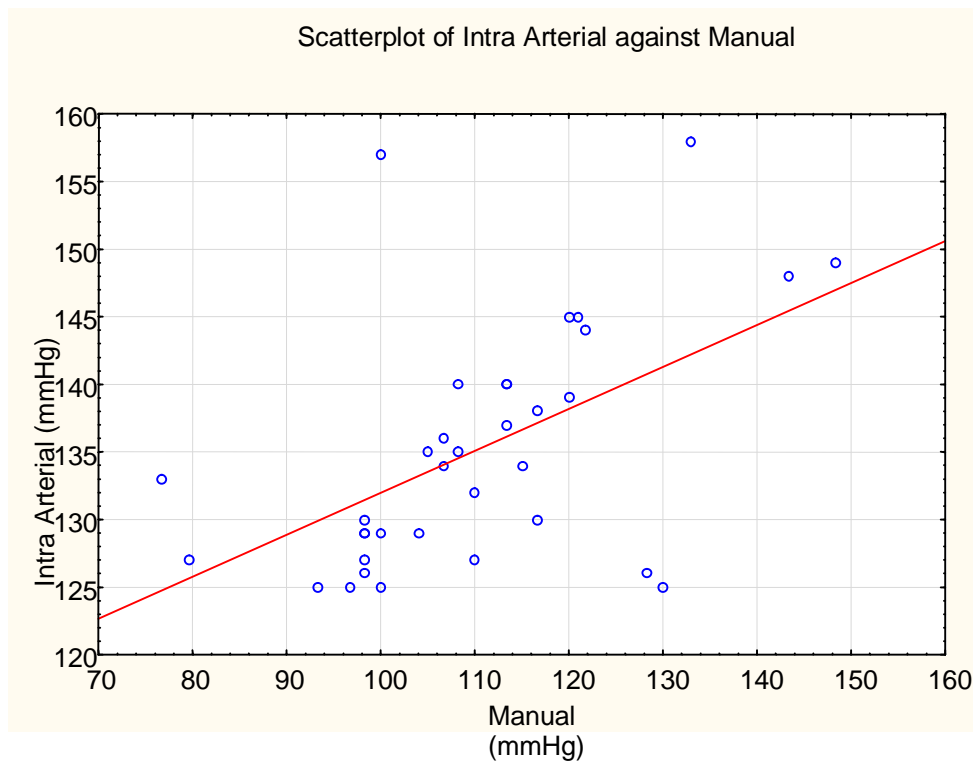
Figure 18 Bland + Altman Plot of Manual and Intra-arterial MAP≥125mmHg

Bland & Altman plot
MAP≥125mmHg
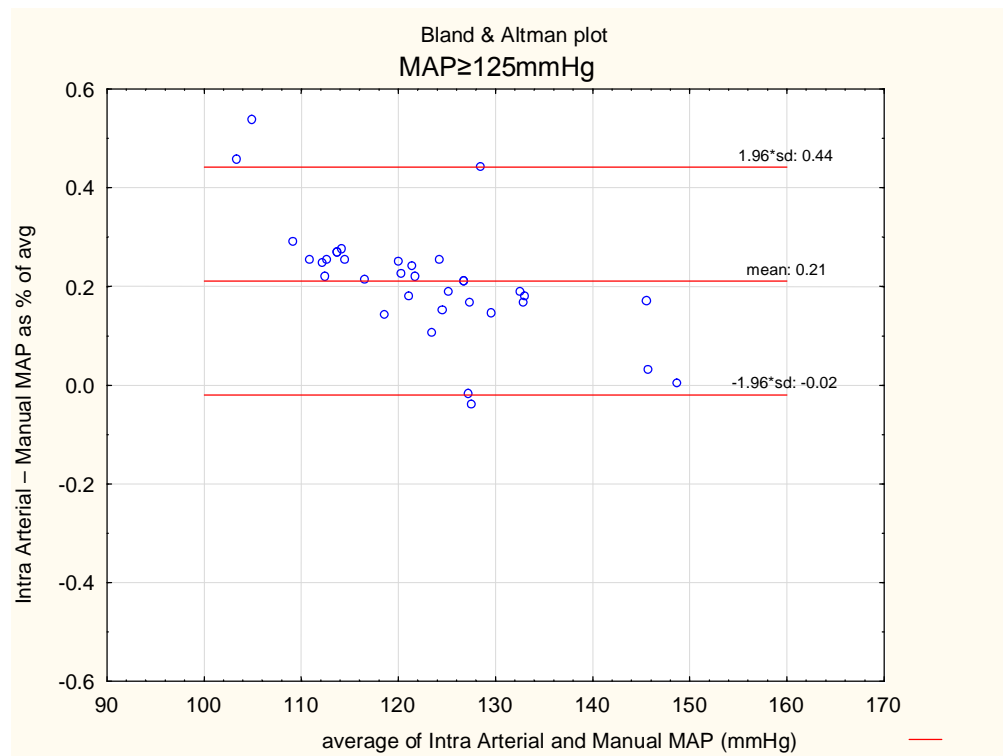
Figure 19 Scatterplot of Intra-arterial against Automated MAP≥125mmHg

Scatterplot of Intra Arterial against Auto

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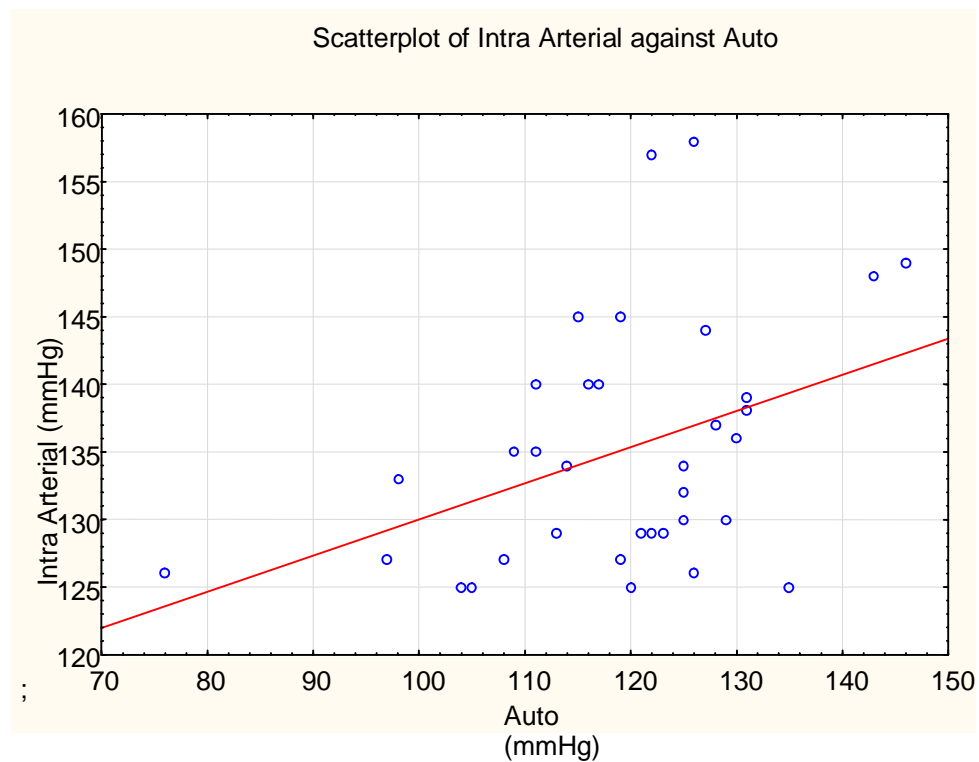
Figure 20 Bland + Altman Plot of Automated and Intra-arterial MAP≥125mmHg

Bland & Altman plot
MAP≥125mmHg
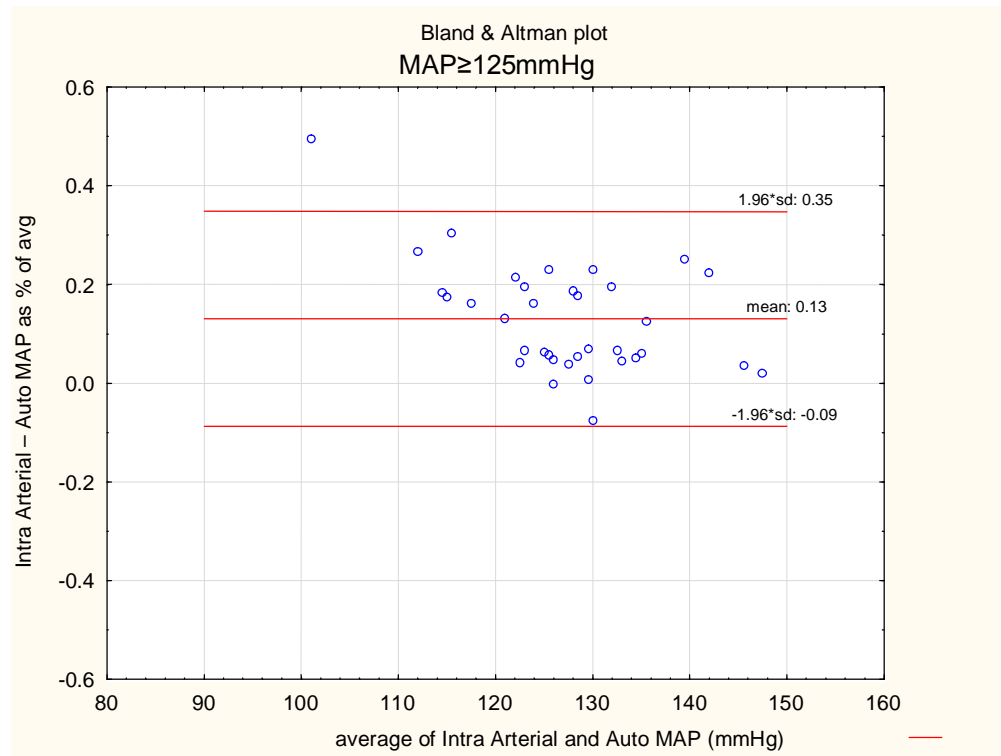
Discussion

In the recent Saving Mothers Report (2008-2010), 95% of all hypertensive deaths were due to eclampsia (51.1%), pre-eclampsia (29.3%) and its complications, accounting for just over 600 maternal deaths. Intracranial haemorrhage caused 156 hypertension related maternal deaths in South Africa during 2008-2010.[9]

In our study, we demonstrated an underestimation of BP measurements when comparing automated BP to brachial intra-arterial BP measurements. The same was true for the comparison of manual and brachial intra-arterial BP measurements. The findings were in agreement with the outcomes of an earlier study by Langenegger, who used radial intra-arterial measurements.[36]

In the SBP≥160mmHg group:

There was moderate correlation between automated SBP compared to intra-arterial SBP measurements ($r = 0.69$; $p<0.05$) which differed from the results of the study by Dalla ($r = 0.34$; $p<0.01$). The weak correlation ($r = 0.27$; $p = 0.048$) between manual SBP and intra-arterial SBP measurements did however, agree with Dalla's findings *(r = 0.41; p<0.01).*[36] The calculated mean difference when comparing mean manual SBP to mean arterial SBP was -23.19mmHg +/- 19.40. This was similar to findings by Dalla (20mmHg +/- 15) but greater than the mean difference found in Penny's study (7mmHg).[8,36] The calculated mean difference in our study when comparing mean automated SBP to mean intra-arterial SBP was lower than that for the manual SBP at -16.85mmHg +/- 11.58. This was greater in the studies by Dalla (24mmHg +/- 17) and Natarajan (19mmHg), but similar to the findings by Penny (15-18mmHg).[8,23,36] Our study showed that both manual and automated SBP, underestimated intra-arterial SBP readings. The manual method underestimated SBP by up to 56.90mmHg and the automated method by 42.75mmHg. However, our findings indicate that the automated method for BP measurement using the Nihon Kohden monitor is more accurate than the manual method when compared to the gold standard intra-arterial method. This finding is in contrast to previous studies which indicated that the manual method of SBP measurement was superior to the automated method.[8,23,36] The difference may be due the fact that in our study, invasive and non-invasive BP were measured at the same site (brachial artery), whereas in the other studies, invasive BP was measured in the radial artery. The higher BP in the radial artery compared to the brachial arterial BP may have

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contributed to the difference. The Bland and Altman plots for both manual and automated SBP compared to intra-arterial SBP demonstrated agreement between the methods of BP measurement. There was also positive bias for the brachial intra-arterial method when compared to the other 2 modalities of BP measurement, indicating that the intra-arterial method consistently measured higher SBP. Our findings illustrate that both the automated and manual methods of BP measurement are markedly inferior to the gold standard intra-arterial method for BP measurement for detecting SBP. This is still of concern because of many patients whose significant hypertension is missed because of failure to monitor BP intra-arterially and are subsequently at risk of intracranial haemorrhage.[11,12]

In the mild moderate systolic hypertension group (SBP≥140mmHg and <160mmHg): A weak correlation was demonstrated when comparing manual SBP to intra-arterial SBP (r = 0.24; p = 0.04). A very weak correlation existed when automated SBP was compared to intra-arterial SBP with r = 0.14 (p = 0.24). The calculated mean difference when comparing mean manual SBP and mean automated SBP to mean intra-arterial SBP were -12.68mmHg +/- 15.40 and -10.92mmHg +/- 12.60, respectively. This shows that the automated and manual methods of BP measurement also significantly underestimated SBP for mild moderate hypertension.

In the DBP≥110mmHg group:

The findings when studying the group with DBP≥110mmHg were similar. For this group of patients, the Bland and Altman plot displayed similar findings as seen with the SBP. There was agreement between the manual and automated methods of BP measurement when compared to intra-arterial DBP measurements. Positive bias was also demonstrated for both methods, indicating that the manual and automated methods underestimated the true DBP. There was a weak correlation between manual DBP and intra-arterial DBP (r = 0.38; p = 0.16) as well as between automated DBP and intra-arterial DBP (r = 0.29; p = 0.29). However, these findings were not statistically significant. Langenegger's study demonstrated weak positive correlation (r = 0.34 and r = 0.41 respectively; p<0.01 for both which were statistically significant. The calculated mean difference when comparing mean manual DBP to mean intra-arterial DBP was -12.53mmHg +/- 11.17, which was greater than that found by Langenegger (1mmHg +/-12; p < 0.65). The manual method underestimated DBP by up to 26mmHg which was similar to findings by Langenegger, but differed to that of Penny's study[8,36]. In those studies, the DBP was overestimated by up to 25mmHg and 6mmHg respectively, when using the manual

method compared to the intra-arterial DBP technique. The calculated mean difference when comparing mean automated DBP to mean intra-arterial DBP was -5.40mmHg +/- 6.54, which was similar to that found by Langenegger (-2mmHg +/-10, p < 0.20). The automated method underestimated DBP by up to 15mmHg. Underestimation of DBP readings using this method were similarly demonstrated by Natarajan (18mmHg) and Penny (11mmHg) but differed from Langenegger's findings (overestimation by up to 24mmHg).[8,23,36] Our findings demonstrate that some diastolic severe hypertensive readings will be missed by automated and manual BP measuring techniques. Martin concluded in his study that severe diastolic hypertension does not develop before stroke in most patients with severe preeclampsia and eclampsia.[11] However, ACOG stated that severe systolic hypertension in preeclampsia or eclampsia may be the most important predictor of cerebral haemorrhage and infarction but recommended the emergent treatment of both severe systolic (≥160mmHg) and diastolic (≥110mmHg) hypertension.[18] Hence, it remains important to identify severe diastolic hypertension and institute prompt BP control.

The criterion for entry into the study was to require an arterial line placement to monitor BP when the SBP≥160mmHg or DBP≥110mmHg. In our study, patients with significant systolic hypertension (91%) predominated. (as opposed to only 9% for diastolic hypertension). This is similar to the findings of Langenegger's study.[36] Studies by Martin and Bushnell demonstrated a strong relationship between stroke and severe systolic hypertension in pre-eclampsia.[11,12]

In the MAP≥125mmHg group:
There was moderate correlation between manual MAP when compared to intra-arterial MAP measurements. (r = 0.53; p < 0.05). There was weak correlation between automated MAP when compared to intra-arterial MAP measurements. (r = 0.40; p = 0.02). The calculated mean difference when comparing mean manual MAP to mean intra-arterial MAP was -25.06mmHg +/- 13.01, which differed to that found by Langenegger (8mmHg ±11). The calculated mean difference when comparing mean automated MAP to mean intra-arterial MAP was -16.03mmHg +/- 12.79. This too was a greater difference than found by Langenegger (5mmHg +/- 13) in his earlier study.[36] In our study, the automated and manual methods underestimated the readings obtained by the intra-arterial method for determining MAP. These findings were similar to Langenegger, Natarajan and Penny's findings which demonstrated the inferiority of these methods compared to the gold standard. In our study, the

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manual and automated methods underestimated MAP by as much as 47mmHg and 37mmHg, respectively. Natarajan demonstrated a lesser underestimation of MAP readings of up to 20mmHg when comparing automated to intra-arterial BP measurement techniques.[8,23,36]

In our study, a moderate correlation was demonstrated for SBP and DBP when automated and manual methods were compared. A strong correlation was demonstrated for MAP when automated and manual methods were compared. The calculated mean differences were small for SBP≥160mmHg (6.34mmHg +/- 15.52), SBP≥140<160mmHg (1.76mmHg +/- 15.21), DBP (7.13mmHg +/- 9.69) and MAP (9.03mmHg +/- 11.08).

Arulkumaran stated that MAP≥145mmHg increases the risk of haemorrhagic stroke due to loss of cerebral autoregulation. In this study, there were only 6 MAP readings ≥145mmHg.[22] Fortunately, no patients suffered intracranial haemorrhage in our study which is likely due to the prompt stabilization of BP with labetalol or nepresol.

In our study, the most frequent complication in pre-eclamptic patients was that of HELLP syndrome, occurring in 40% of all the patients. The 2nd most common complication was that of renal dysfunction (including acute renal failure). Only 1 patient became eclamptic and there were no intracranial haemorrhages in the study group.

In Langenegger's study which was conducted in the same setting and with the same patient profile, pulmonary oedema was the most common complication accounting for 38% of the study group.[36] In our study pulmonary oedema accounted for 13.3% of the patients. The 2nd most common complication in his study was HELLP Syndrome accounting for 30.4% of the patients. The cerebral events, which included eclampsia, posterior reversible encephalopathy syndrome (PRES), cerebral oedema, differed from our study in that it accounted 30.4% of the total study group, which included 1 patient who suffered an intracranial haemorrhage.

In 2003, Lombaard's observations of complications of pre-eclampsia in a study conducted in Gauteng province of South Africa also differed with our findings. In that study of a similar patient profile, the cerebral events accounted for 14.4 %(RR 0.52, 95% CI 0.34-0.81) and there were high rates of respiratory failure (30.8%) and cardiac failure (26%). The reason for the respiratory and cardiac failure was not

specified in that study. Differences in the complication rate could be accounted for by the small study group in this study.[47]

We adhered to the ASSHP and PGWC recommendations when obtaining manual BP readings. Korotkoff phase I (onset of sounds) was used for systolic readings and Korotkoff V (disappearance of sounds) used for systolic readings. Korotkoff V is the most accurate measure of diastolic BP.[40,41] Korotkoff IV (muffling of sounds) was occasionally used as a measure of DBP when the sounds were still audible after complete deflation of the cuff.[19,41,45,46] The bell of the stethoscope was used to improve detection of the low frequency Korotkoff sounds.[19]

This study is one of the few studies which focussed on patients with severe pre-eclampsia during a hypertensive crisis. No studies were found comparing radial and brachial intra-arterial blood pressure monitoring in pregnancy.[36]

The accuracy of invasive blood pressure monitoring is crucial in management of the haemodynamically unstable patient, but there are many pitfalls in obtaining accuracy. Invasive BP measurements are influenced by the measurement site. The SBP increases as it monitored from the aorta to the periphery, due to amplification by reflected waves. Compliance of the vessels also affects the amount of increase in pressure.[19] In a study by Mignini in 2006, conducted on 55 patients in an ICU, he found that the central MAP was 3+/- 4mmHg higher than the radial intra-arterial MAP.[30] In 1989, Gravlee found that radial intra-arterial SBP was 10-35mmHg higher than the aortic SBP in >50% of patients undergoing cardiopulmonary bypass. DBP and MAP was more reliable (+/- 3mmHg) in 90% and 92% of the study patients.[31]
In a study by Davies, in 12 patients undergoing coronary artery bypass surgery, intra-arterial BP was measured in the proximal aorta, subclavian, brachial and radial arteries. He concluded that systolic pressure rose progressively in the arteries which were more peripheral. The SBP was 5mmHg higher in the radial artery than brachial artery.[32]

In our study, we inserted brachial arterial lines which differed from Langenegger's study, which employed radial arterial lines. The hypothesis was that the systolic amplification would be less in the brachial than radial artery. We also measured invasive and non-invasive BP at the same site, the brachial artery. Hence, the brachial readings would be the more accurate available intra-arterial measure for identification of dangerous severe hypertensive spikes in order to institute prompt

emergency management. This would reduce the morbidity and mortality associated with severe hypertensive peaks in pre-eclampsia.

The patients were recruited from the OCCU which is managed by a team of experienced doctors and nurses, under strict supervision of the head of obstetric critical care unit. Strict admission protocols were followed prior to admission into the 4 bed unit and arterial lines were placed immediately when the patient had persistent severe hypertension. The OCCU doctors were experienced in placement of arterial lines. Patients with brachial intra-arterial lines were recruited if radial arterial line placement failed or was inappropriate. There was also the concern regarding the possibility of ischaemia of the limb due to thrombosis of the brachial artery which is a single feeding artery in the upper limb. However, Belda FJ demonstrated that arterial catheters were safe alternatives for advanced haemodynamic monitoring. 514 arterial catheters were placed (475 femoral, 9 axillary, 26 radial and 4 brachial). The most frequent complication was that of local haematomas at the site of insertion (4.5%) and the complication of ischaemia was only observed with femoral artery cannulations, which was very low (0.4%).[29] The major complication rate <1% was also demonstrated in the systematic review by Scheer in 2001, which include invasive haemodynamic monitoring with 19617 radial and 7185 brachial arterial catheterizations. The most common complication was the temporary occlusion of the radial artery and permanent occlusion occurred in only 4 patients (0.09%). An infected haematoma was the only serious complication observed when the brachial artery was used for invasive monitoring.[28]

Ideally, it would be interesting to compare radial and brachial arterial BP with arterial lines in the same patient to see the true difference between the 2 methods but this is unnecessary and also unethical. In our study group, there were no complications.

Observer bias is a likely limitation of our study which was also mentioned in the study by Langenegger.[36] It was clear to the staff members doing the manual blood pressure measurements that the study participants all had severe hypertension at some stage during the study but normal readings were also taken to limit observer bias; therefore, high SBP and DBP readings were expected. Thus, even though blinded to the intra-arterial BP readings, they could have provided higher readings than the actual reading.

The same automated oscillometric blood pressure monitoring system used by Langenegger was used for measuring automated BP in our study, as both studies used the same infrastructure.[36] Both studies made use of the Nihon Kohden BSM 4113K monitor which was not validated for use in pre-eclamptic subjects. This fact may have affected our automated readings but allowed for an effective comparison with the Langenegger study. Bur et al found that the oscillometric BP measurements had disturbingly low accuracy and the measurements were consistently lower than direct intra-arterial measurements in critically ill patients.[38]

Araghi compared invasive (radial intra-arterial) and non-invasive BP methods in critically ill overweight patients. He found that non-invasive BP underestimated intra-arterial BP measurements in both normo- and hypertensive patients. The underestimation of BP readings by the oscillometric automated method compared to intra-arterial method was independent of the BMI.[24] Natarajan also found underestimation of SBP and MAP readings by the oscillometric automated method of 19mmHg and 7mmHg respectively.[23] Our study showed similar findings.

In the early 2000's, the mercury sphygmomanometer was the 'gold standard' device for blood pressure measurement.[33,34,35] The current 'gold standard' for blood pressure measurement is the direct intra-arterial method. In healthy patients, the SBP is 5-10mmHg higher and DBP 5-10mmHg lower than the non-invasive methods of blood pressure monitoring. In our study, the calculated mean difference for manual and automated SBP readings were in excess of this expected difference (-23.19mmHg and -16.85mmHg respectively).[23,24,25] Our study also used the brachial arterial blood pressure measurements which are more accurate than radial arterial blood pressure measurements by 5mmHg according to Davies et al.[32]

In the high care and critical care setting, seen in level 3 and level 2 hospitals, the ideal method of blood pressure measurement is the direct intra-arterial blood pressure monitoring method. However, this is not feasible in the low resource setting with also less specialised levels of care.

Conclusion

The accuracy of BP measurement in pregnant women with pre-eclampsia is extremely important, so that severe hypertension can be identified early and treated promptly. Severe hypertension (SBP≥160mmHg, DBP≥110mmHg and MAP≥145mmHg) in pre-eclampsia is a strong predictor of intracranial haemorrhage, which was the cause of 156 hypertension-related maternal deaths in South Africa during 2008-2010. Respiratory failure and pulmonary oedema contributed to 139 and 188 maternal deaths, respectively.[9]

This study demonstrated that both the automated and manual methods of BP measurement were inaccurate measures of the true intra-arterial SBP, when managing pre-eclamptic patients with acute severe hypertension. Both methods significantly underestimated SBP≥160mmHg when compared to brachial intra-arterial measurements. The SBP was also underestimated, to a lesser degree, for mild moderate hypertension.

Intra-arterial BP monitoring is the gold standard and should be the method of choice for BP monitoring of pre-eclamptic patients with acute severe hypertension. Our study demonstrated that direct invasive BP monitoring using the brachial artery is a safe method for accurate haemodynamic monitoring. The automated oscillometric method of BP measurement was superior to the manual method in our study. It is important to note that several severe hypertensive spikes will still be missed when using the automated method, with subsequent increase in maternal morbidity and mortality.

We recommend the use of intra-arterial BP monitoring in pre-eclamptic women with acute severe hypertension. Radial arterial cannulation should be used as the first option and the brachial artery should be used if the first option fails.

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Addendums

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Data Sheet

Date: Name: G: P: GA:

Folder No: Co-Morbidity:

Time	Manual BP			Automated BP			Arterial BP				
	S	D	MAP	S	D	MAP	S	D	MAP	brach	rad

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The NIBP monitoring vs Brachial Intra-Arterial BP monitoring Pre-eclampsia Study

Name: Date:

Folder No:

DOB:

Age: Race:

Weight: Height: BMI:

Gravidity: Gestation:

Parity:

Antepartum: Postpartum:

Admission BP: Proteinuria:

Pre-eclampsia Complications:

Pulm oedema	HELLPS	Renal	Eclampsia
ICH	PRES		

Previous Pre-eclampsia:

Chronic Hypertension:

HIV Status: CD4 count:

Other Medical History:

Smoker: Alcohol:

IV Medication: MgSO4:   Labetalol:

      Nepresol: Tridil:

Oral Medication: Aldomet: Adalat XL:

      Adalat: HCTZ:

      Enalapril: Amlodipine:

      Doxazosin:

Other Anti –HPT Medication:

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM
TITLE OF THE RESEARCH PROJECT:

Comparing non-invasive blood pressure monitoring with brachial intra-arterial blood pressure monitoring in patients with severe pre-eclampsia

REFERENCE NUMBER: N08/10/308

PRINCIPAL INVESTIGATOR: Dr S Jacobs

ADDRESS: Obstetrics Critical Care Unit
 Tygerberg Hospital
 Tygerberg
  7505

CONTACT NUMBER: 021 938 5968

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Committee for Human Research at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

The study will take place in the Obstetrics Critical Care Unit at Tygerberg Hospital.

The project aims to measure and compare three different ways in which we can measure the blood pressure in patients with severe pre-eclampsia. Pre-eclampsia is when the blood pressure is raised and there is protein in the urine. When pre-eclampsia is severe, the blood pressure is very high. This is very dangerous for both the pregnant mother and her baby. For the mother, pre-eclampsia may result in the placenta separating from the uterus causing excessive bleeding, water on the lungs, kidney failure, bleeding and clotting problems, seizures, stroke and may even result in death. Complications for the baby include growth restriction, preterm birth and death. By doing this study, we will be able to determine which method is the most accurate for measuring the blood pressure. This will allow for us to better manage blood pressure, thereby preventing the above-mentioned complications.

If you have severe pre-eclampsia and are admitted to the Obstetric Critical Care Unit, we routinely measure the blood pressure with an intra-arterial line and an automated blood pressure device. An intra-arterial line is a plastic cannula, which is inserted into an artery in the fold of your arm. It is then connected via a thin plastic line to a monitor, so that we can directly measure the blood pressure. An automated blood pressure device has a blood pressure cuff attached to a small monitor. The blood pressure cuff is wrapped around the upper arm and the monitor will then automatically read your blood pressure. You may be familiar with this device, as it is often used at local clinics and pharmacies for measuring the blood pressure. This usually forms part of your routine management for blood pressure monitoring if you are admitted to the Obstetrics Critical Care Unit, whether or not you choose to participate in the study.

If you choose to participate in the study, a third method for monitoring the blood pressure will be done. This will be done each time the blood pressure is very high. Manual sphygmomanometry will be used. This means that a nurse or doctor will manually wrap a blood pressure cuff around your arm and personally listen to your blood pressure. This will be the only thing that is done in addition to your routine management whilst in the Obstetric Critical Care Unit.

All the blood pressure readings from all three methods from all the patients involved in the study will then be compared, and the most accurate method for measuring blood pressure will be determined.

No medication will be used for this study.

Why have you been invited to participate?

You have severe pre-eclampsia. As mentioned earlier, this is when the blood pressure is very high and is accompanied by protein in the urine.
You have been admitted to the Obstetric Critical Care Unit.
You already have, or require an intra-arterial line for blood pressure monitoring.
These are all the criteria that need to be fulfilled prior to being invited to participate in the study. You have been invited to participate in the study as you meet all the above-mentioned criteria that are required for inclusion into the study.

What will your responsibilities be?

There are no responsibilities that need to be fulfilled from your side.

Will you benefit from taking part in this research?

If the most accurate methods of measuring blood pressure can be established and used, it will largely improve management and reduce the complications of patients with severe pre-eclampsia. This will play an important role in

decreasing the complications of stroke and death in young women. This will be of great benefit to future patients that are diagnosed with severe pre-eclampsia.

Are there any risks involved in your taking part in this research?

There are no risks involved in you participating in this study.

If you do not agree to take part, what alternatives do you have?

You are not obliged to participate in the study and your participation is completely voluntary. If you choose not to be a participant in the study, your treatment for severe pre-eclampsia will not be affected in any way. Your blood pressure will still be routinely monitored using an automated blood pressure device.

Who will have access to your medical records?

All the information that we obtain from you, or your medical folder, will be kept strictly confidential. You will be allocated a number or a code, so your name will never be used. In this way, your identity will always be protected. In the event of your information being used in a publication or thesis, all information will be reported with anonymity. Only the principal investigator and the co-investigator will have access to your medical records.

What will happen in the unlikely event of some form injury occurring as a direct result of your taking part in this research study?

As the study only involves taking a manual blood pressure measurement in addition to your routine management in the Obstetrics High Care Unit, an injury occurring as a direct result of your participating in this research study is not likely.

Will you be paid to take part in this study and are there any costs involved?

You will not be paid to participate in the study, but your transport and meal costs will be covered if a study visit is necessary. There will be no financial costs involved for you if you do participate.

Is there any thing else that you should know or do?

You can contact Dr S Jacobs at tel. 021-938 5968 if you have any further queries or encounter any problems.

You can contact the Committee for Human Research at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.

You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I …………………………………..…………. agree to take part in a research study entitled **, "comparing non-invasive blood pressure monitoring with brachial intra-arterial blood pressure monitoring in patients with severe pre-eclampsia"**

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.

- I have had a chance to ask questions and all my questions have been adequately answered.

- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.

- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) .... on (*date*)…………..………... 2009.

....
Signature of participant   Signature of witness

Declaration by investigator

I *(name)* ………………………………………….……… declare that:

- I explained the information in this document to ……………………………..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) ....…........on (*date*) ...……………… 2012/13.

....
Signature of investigator   Signature of witness

Declaration by interpreter

I *(name)* …………………………………….……… declare that:

- I assisted the investigator (*name*) …………………………………. to explain the information in this document to (*name of participant*) …………..………………………….. using the language medium of Afrikaans/Xhosa.

- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*).................…......…………… on (*date*)………...………….. 2012/13.

....
Signature of interpreter   Signature of witness