Health Care: Current Reviews
ISSN: 2375-4273

Vonck et al., Health Care Current Reviews 2017, 5:1
DOI: 10.4172/2375-4273.1000185

Research Article Open Access

Optimization of Simple Sphygmomanometric Blood Pressure Measurement in Routine Prenatal Care

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Abstract

Background: Despite reported early subclinical hypertension of women at risk, blood pressures at threshold 140/90 mm Hg are used today to guide prenatal care. We aim to investigate the most appropriate gestation-specific threshold to measure early gestational blood pressures, allowing for a simple stratification between pregnant women at low/high risk for hypertension.

Methods: Singleton pregnancies were selected at Clinic Oost-Limburg, Genk, Belgium. A standard protocol was used to measure systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) in supine and standing position, by mode of an oscillometric sphygmomanometer around 12 and 20 weeks of gestation. After delivery, outcome was categorized in normotensive or hypertensive pregnancies. In a subgroup, routine blood pressures retrieved from prenatal records were compared to standardized blood pressures. ROC analysis was used to define early gestational blood pressure thresholds with best discriminative performance for hypertension. All analyses were done in SPSS software ($\alpha \leq 0.05$).

Results: A total of 780 women were measured at 12 weeks, of which 433 pregnant women were re-evaluated around 20 weeks. At both occasions, blood pressures were significantly higher in hypertensive than in normotensive pregnancies ($p<0.0001$). Analysis showed for DBP in standing position at cut off 79 mmHg a sensitivity, specificity, positive predictive value and negative predictive value of 72%, 64%, 15,5% and 96% at 12 weeks and 86%, 69%, 20% and 98% at 20 weeks at cut off 77 mm Hg. At 20 weeks, Area under the Curve (AUC) for DBP was 83% in standing position and 80% in supine position. For routine versus standardized blood pressure measurement, AUC was 66% versus 72% at 12 weeks and 69% versus 82% at 20 weeks, respectively.

Conclusion: Simple blood pressure measurements with gestation-specific thresholds can easily be used worldwide towards improved planning of prenatal care as compared to current protocols.

Keywords: Blood pressures; Sphygmomanometer; Threshold; Hypertension; Pregnancy; Screening

Introduction

During normal pregnancy, the blood pressure decreases in the first 20 weeks and then gradually returns to preconceptional values when term approaches [1,2]. Around 6-8% of all expectant mothers will experience an aberrant blood pressure pattern leading to diverse hypertensive disorders, with maternal and neonatal mortality and morbidity such as cardiac arrest, renal failure, premature delivery, low birth weight, intra-uterine growth restrictions etc. [3,4]. Usually their blood pressure will remain stable during the first 20 weeks, where after an increase will initiate noticed in third trimester [5].

Today, a minimum of 140/90 mm Hg measured at 2 occasions, >6 h apart, is generally used as threshold to diagnose hypertension in pregnancy [6]. Hypertension already noticed at <20 weeks of gestation is labelled essential or chronic hypertension, and is considered a major risk factor for preeclampsia [7]. However, in most cases of gestational hypertension and preeclampsia, the hypertension is diagnosed at ≥ 20 weeks of gestation in women with "normal" blood pressure values earlier in pregnancy [6].

It is known that maternal cardiovascular (mal) adaptation during the first weeks of gestation plays a fundamental role in the regulation of blood pressure and the development of later hypertensive disorders [8,9]. Several studies [1,10,11] report already higher blood pressure values around 12 weeks of gestation in women who eventually develop preeclampsia, gestational or essential hypertension, compared to women who remain normotensive. Today, subclinical higher blood pressures (<140/90 mm Hg) are not considered clinically relevant. In this study, we evaluated whether early gestational diagnosis of subclinical hypertension would be helpful to identify the proportion of women destined to develop GHD, as early identification of those high risk cases could help decreasing the maternal and neonatal consequences [12].

Methods

Patients

Women with singleton pregnancies in first or second trimester, attending the obstetric ultrasound clinic (Ziekenhuis Oost-Limburg, Genk, Belgium) for their routine obstetrics scans, were invited to

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Received January 06, 2017; **Accepted** February 06, 2017; **Published** February 13, 2017

Citation: Vonck S, Oben J, Staelens AS, Lanssens D, Molenberghs G, et al. (2017) Optimization of Simple Sphygmomanometric Blood Pressure Measurement in Routine Prenatal Care. Health Care Current Reviews 5: 185. doi: 10.4172/2375-4273.1000185

participate in a prospective, observational study. Approval of the Ethical Committee was obtained before study onset (MEC ZOL, reference: 13/090U). Blood pressures were measured as part of a reported standardized non-invasive cardiovascular assessment protocol using impedance cardiography (ICG), combined ECG/Doppler sonography and bio-impedance [13-15]. Oral informed consent was obtained before inclusion. At birth, gestational outcome was defined and categorized in normotensive pregnancy (NP) or hypertensive pregnancies (HP), which included gestational hypertension (GH), preeclampsia (PE) and essential hypertension (EH). GH was diagnosed when a high blood pressure (≥ 140/90 mm Hg) was observed after midpregnancy, without proteinuria, twice measured with 6 h in between. The diagnosis of PE was determined when gestational hypertension was accompanied with *de novo* proteinuria (≥ 300 mg per 24 h). EH was defined as hypertension present before pregnancy or before 20 weeks of gestation [6]. Pregnancies diagnosed with isolated intra-uterine growth retardations (IUGR) and/or multiples were excluded from analysis as they are reported with different cardiovascular profiles [16,17]. Additionally, demographic details were recorded: maternal age (years), pregestational BMI, gestational age at assessment and at delivery, parity, cigarette usage, medication, neonatal birth weight and percentile.

Protocol

The systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) of all patients were measured and registered around 12 weeks and/or 20 weeks of gestation. The blood pressure measurements were performed as part of the Non-Invasive Continuous Cardiac Output Monitor assessment (NICCOMO, Medis Medizinische Messtechnik GmbH, Ilmenau, Germany) by use of an oscillometric sphygmomanometer at standardized time-points in a previously reported protocol [18]. Each patient performed the complete ICG examination first in supine position and afterwards in standing position. Before the first blood pressure measurement, the patient was already comfortably in supine position for 5 min. 1,5 min after supine blood pressure measurement, the patient changed position to standing. The second blood pressure measurement was taken after a rest period of 2 min in standing position (Figure 1). Blood pressures were always taken on the right arm and with an appropriate cuff width.

Statistics

Normality was checked via Shapiro-Wilk for continuous variables. Even though there is a comparison of several parameters at two different time points (12 weeks and 20 weeks), each comparison is of the two-group type. To this end, the non-parametric Mann Whitney U was used at $\alpha<0,05$ to test the null hypothesis whether the distribution of the parameter of interest, at a given time point, is identical between the two groups. For categorical variables, Chi-square test was done. Data are presented as median and interquartile ranges (IQR) or n (%). ROC analysis was used to examine the different thresholds for each blood pressure in standing and supine position and sensitivity, specificity, positive and negative predictive value for prediction of hypertension were calculated. Youdens Index was used to identify the most appropriate threshold for every blood pressure measurement. All analyses were done in SPSS (SPSS Inc., Chicago, Illinois, USA).

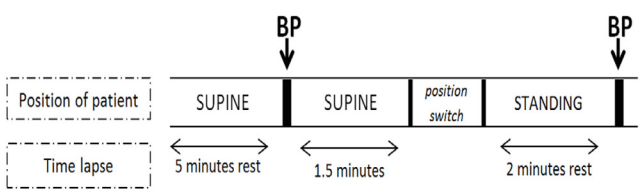

Figure 1: Graphical representation of the protocol.

Sub analysis

In a subgroup of the studied population, the standardized blood pressure values, measured as explained above, were compared to the blood pressures values at corresponding gestational age recorded in the prenatal files as part of the routine prenatal visits by the obstetrician or midwife. These latter blood pressures values were retrieved retrospectively from the patient's records. Paired t-tests at nominal level $\alpha=0.05$ and Pearson Correlations Coefficients (PCC) were calculated between blood pressures measured in the standardized conditions versus the blood pressures measured at prenatal visit. All analyses were done in SPSS (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 870 pregnant women had first trimester standardized blood pressure measurements; 433 of those women also had second trimester measurements. After birth, 716 patients were classified as normotensive and 64 as hypertensive patients at 12 weeks. At 20 weeks, 398 normotensive patients and 35 hypertensive patients were measured. A total of 90 pregnancies with isolated IUGR were excluded. The hypertensive group in first trimester included 24 women with GH (37.5%), 22 (34.5%) with PE and 18 (28%) with EH. A summary on maternal demographics is shown in Table 1. In the HP group, compared with NP, women were heavier, older and the nulliparity percentage is higher. The general use of medication is also significantly higher in the HP group, where 65% consists of blood pressure medication vs. 1.5% blood pressure medication in the NP group. Hypertensive patients delivered at an earlier gestational age and their neonates had a lower birth weight. Due to the slight differences between maternal age, pre-pregnancy BMI and nulliparity between HP and NP (Table 1), the comparisons done were supplemented with linear regression analyses, comparing groups while correcting for potential confounders. The results are identical in the sense that all group comparisons remain highly significant.

The 12 and 20 week blood pressures (SBP, DBP and MAP) of NP and HP were compared and all values were significantly higher in HP at both gestational ages (Table 2). There were conducted several comparisons here and it is therefore prudent to apply a multiple comparisons correction. However, given the highly significant nature of the test statistics and the relatively modest number of tests, an adjusted alpha level still leaves the results highly significant. Indeed, for the 12 tests reported in Table 2, the adjusted alpha level would be 0.00417; all p-values reported are well below this threshold.

ROC analysis was used to evaluate the performance of SBP, DBP or MAP in supine and standing position to predict the hypertensive cases. The most appropriate thresholds for each blood pressure were identified via the Youdens Index (Table 3). Based on the AUC and Youdens Index, the DBP in standing position around 12 weeks and 20 weeks of gestation showed the best performance (Figure 2). This represents for 12 weeks at cut off 79 mmHg a 72% sensitivity, 64% specificity, 15,5% positive predictive value and 96% negative predictive value. Similarly at 20 weeks, a cut off of 77 mmHg showed an 86% sensitivity, 69% specificity, 20% positive predictive and 98% negative predictive value. Despite a significant difference between standing and supine blood pressure ($p<0.004$), the AUC's between standing and supine do not vary so much. At 20 weeks, AUC for DBP was 83% in standing position and 80% in supine position.

	NP	HP	p-value
	(n=716)	***(n=64)***	
Characteristics at inclusion			
Maternal age, years	30 (27, 33)	31 (28, 35)	**0.029**
Gestational age at inclusion, weeks	12 w 2 d (11 w 5 d, 12 w 5 d)	12 w 2 d (11 w 4 d, 12 w 5 d)	0.557
Pre-pregnancy BMI, kg/m²	23 (21, 26)	24 (22, 28)	**0.028**
Nulliparity	341 (47.6%)	40 (62.5%)	**0.023**
Cigarette smoker	67 (9.4%)	4 (6.3%)	0.408
Chronic Hypertension	0	18 (28%)	**--**
Gestational Hypertension	0	24 (37.5%)	**--**
Preeclampsia	0	22 (34.5%)	**--**
Medication	60 (8.4%)	20 (31.3%)	**0.0001**
Outcome characteristics			
Birth weight, g	3425 (3145, 3750)	3205 (2740, 3670)	**0.001**
Birth weight, percentile	57 (35, 77)	52 (27,77)	0.39
Gestational age at delivery, weeks	39 w 5 d (38 w 5 d, 40 w 4 d)	38 w 5 d (36 w 6 d, 39 w 6 d)	**0.0001**

Data are presented as medians with interquartile ranges or n (%). Differences between NP and HP are presented as p-values

α<0,05 was considered significant

Table 1: Patient and outcome characteristics of normotensive pregnancies (NP) and hypertensive pregnancies (HP).

	12 w		20 w	
	NP	**HP**	**NP**	**HP**
SBP standing (mm Hg)	115 (108-124)	124 (116-134)	113 (105-121)	122 (114-135)
DBP standing (mm Hg)	75 (71-81)	82.5 (78-90)	73 (68-78)	82 (78-89)
MAP standing (mm Hg)	85 (81-91)	92 (88-102)	83 (78-88)	92 (87-99)
SBP supine (mm Hg)	113 (106-121)	123.5 (116-141)	110 (103-119)	122 (114-133)
DBP supine (mm Hg)	70 (66-75)	75 (71-85)	68 (64-73)	77 (71-84)
MAP supine (mm Hg)	80 (75-85)	86.5 (82-96)	78 (73-83)	86 (81-95)

Data are presented as medians with interquartile ranges. All comparisons were done using Mann Whitney U test

P-values are <0,0001

Table 2: Median+IQR for standardized SBP, DBP and MAP in supine and standing position at 12 weeks and 20 weeks.

IQR: Interquartile Range; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; NP: Normotensive Pregnancies; HP: Hypertensive Pregnancies.

	AUC (95% CI)	Threshold	Sensitivity	Specificity	FPR
12 WEEKS					
SBP standing	0.696 (0.631-0.762)	122 mm Hg	0.61	0.69	0.31
DBP standing	0.744 (0.68-0.808)	79 mm Hg	0.72	0.64	0.36
MAP standing	0.744 (0.683-0.805)	87 mm Hg	0.81	0.56	0.44
SBP supine	0.726(0.659-0.793)	116 mm Hg	0.76	0.60	0.40
DBP supine	0.739(0.678-0.799)	71 mm Hg	0.81	0.54	0.46
MAP supine	0.744 (0.681-0.806)	83 mm Hg	0.73	0.64	0.36
20 WEEKS					
SBP standing	0.712 (0.624-0.799)	111 mm Hg	0.89	0.44	0.56
DBP standing	0.829 (0.765-0.893)	77 mm Hg	0.86	0.69	0.31
MAP standing	0.805 (0.732-0.877)	86 mm Hg	0.89	0.61	0.39
SBP supine	0.731 (0.644-0.819)	118 mm Hg	0.69	0.71	0.29
DBP supine	0.798 (0.724-0.871)	71 mm Hg	0.80	0.63	0.37
MAP supine	0.810 (0.739-0.880)	81 mm Hg	0.83	0.66	0.34

Table 3: Detection performance of blood pressures. Sensitivity, specificity and FPR of each blood pressure, when using the most appropriate threshold indicated by ROC analysis and Youdens Index at 12 weeks and 20 weeks.

AUC: Area under the Curve; FPR: False-Positive Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure

The sub analysis in 262 (33.6%) first trimester and 141 (32.6%) second trimester pregnancies showed a significant, but weak correlation between standardized DBP (stDBP) and routine DBP (rDBP) (12w: PCC=0.425, p<0.0001; 20 w: PCC=0.429, p<0.0001). Paired t-test comparison revealed significant differences between stDBP and rDBP at 12 weeks (76 ± 7 mm Hg vs. 71 ± 9 mm Hg resp., p<0.0001) and 20

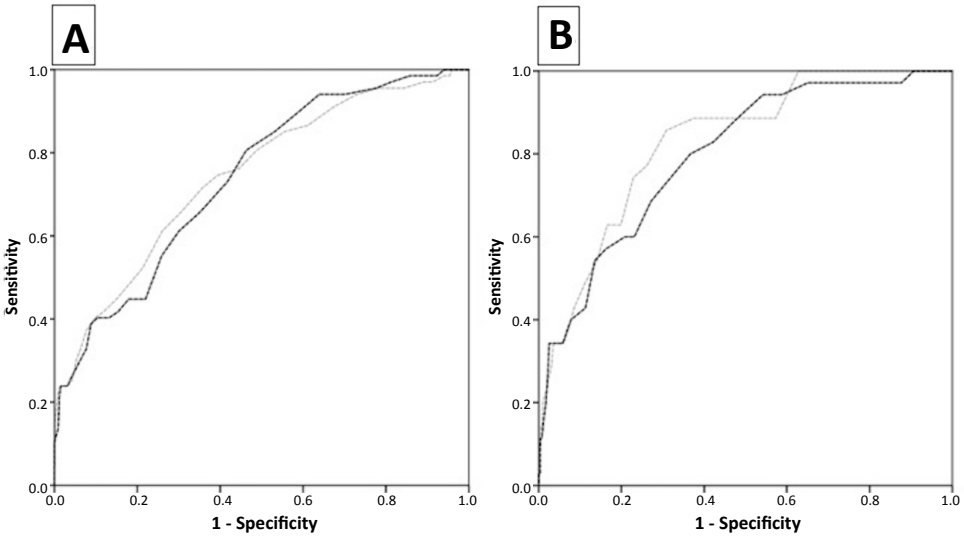

Figure 2: A: DBP ROC curves at 12 weeks, where grey indicates DBP standing (AUC: 0.744) and black indicates DBP supine (AUC: 0.739). **B**: DBP ROC curves at 20 weeks, where grey indicates DBP standing (AUC: 0.829) and black indicates DBP supine (AUC: 0.798). DBP: Diastolic Blood Pressure; ROC: Receiver Operating Characteristic; AUC: Area Under the Curve

weeks (73 ± 7 mmHg vs. 69 ± 8 mm Hg resp., p<0.0001) of gestation. AUC of routine versus standardized BP measurement was 66% versus 72% at 12 weeks and 69% versus 82% at 20 weeks, respectively.

Discussion

This study illustrates the potential of simple sphygmomanometric blood pressure measurements in early pregnancy for diagnosing subclinical hypertension. In our study, a standardized measurement of DBP in standing position showed the best performance with threshold 79 mm Hg at 12 weeks and 77 mm Hg at 20 weeks. These observations suggest that the general threshold of 140/90 mm Hg should be adjusted in function of the gestational age, as the use of a lower threshold improves the early predictability of hypertension in pregnancy. Our findings are relevant to all prenatal care workers because (rudimentary) early gestational screening for hypertensive disease becomes universally available worldwide using a very simple and already generally applied technique of sphygmomanometric blood pressure measurement, without the need for other technologies or expensive devices.

The strength of this study is the rigid standardized protocol for measuring the blood pressures and the amount of inclusions. All women gave birth in the same hospital, where data on gestational, maternal and neonatal outcome were traceable in the hospital records. Our study population is however not yet large enough to adjust the general used threshold of 140/90 mm Hg in clinic. The FPR presented in this paper can be lowered with implementation of other clinical or physical parameters to the screening process, but the lower thresholds can already serve as first discriminant tool seen the NPV is 96% at 12 weeks. With this accuracy, the focus lies not completely on detecting the hypertensive cases (as PPV is 15-20%), but more on eliminating the healthy cases with more certainty.

Subclinical higher blood pressures (<140/90 mm Hg) in the first half of pregnancy are reported as a first sign of hypertension [1,19]. Our data are in line with this. Hypertensive disorders during pregnancy result from maternal cardiovascular maladaptation, initiated during the first weeks of gestation. Normally a physiological cascade is initiated by the fall of the peripheral vascular resistance, whereby heart rate and cardiac output increase. This vasodilatation lowers the blood pressures, because the cardiac output incline is not sufficient to prevent a blood pressure fall. Systolic as well as diastolic blood pressure keeps decreasing until 24 weeks. The peripheral vascular resistance is shown to be higher in future hypertensive patients and do not experience a blood pressure fall [20].

Based on our results, a DBP above 79 mm Hg at 12 weeks or above 77 mm Hg at 20 weeks identifies 2-3 times more patients at risk than the currently used threshold of 90 mm Hg in the first and second trimester. We have at 12 weeks a 72% sensitivity and 64% specificity, but this improves when measuring at 20 weeks again: 86% sensitivity and 69% specificity. This suggests that the current obstetric practice may benefit from changing the currently used 'gold standard of blood pressure measurement' by using different and gestation specific cut off values, a suggestion which has already be postulated by Hermida et al. [21]. This may be useful to all clinics where technologies to screen for gestational hypertensive disease are not available and potentially to those women considered for initiating preventive medications such as low-dose aspirin [22,23] or calcium [24]. Another opportunity could be the implementation of home blood pressure monitoring devices as follow up method, which - when used under standardized conditions- may offer valuable information without the need for increasing the number of prenatal visits or the risk of unnecessary medication intervention [25,26]. One study by Penny et al. on ambulatory automated blood pressure monitoring showed that a cut off of 135/85 mm Hg had a better positive predictive value than 140/90 mm Hg [27]. Also Gallery et al. identified lower 'at risk' blood pressure values at 17-20 weeks: the risks for hypertension were higher with blood pressure values above 110/75 mm Hg sitting or 100/65 mm Hg lying in left lateral position [1]. The latter group also observed that the fall in systolic and diastolic blood pressure from preconception to midgestation was larger in the normotensive than the hypertensive group, which is completely in line with the physiology or mentioned above [1].

Our data also emphasizes the relevance of posture: standing blood pressure values were significantly higher than the supine values. The heart is required to pump more blood to the brain and needs therefore

a higher pressure. As mentioned above in the study of Gallery, cut off values depend on how the patients are positioned and thus it is important to interpret the observations relative to position specific thresholds too [1]. Applied on our study, based on AUC's, we noticed a slightly better predictive outcome with standing blood pressures instead of supine blood pressures. There is however some inconsistency concerning the influence of position on the blood pressure: lower supine blood pressures are reported as compared to sitting [1,28,29], but also higher values have been observed [30] as well as no differences at all [31,32]. These conflicting results may relate to different populations or other methods of measurement.

This paper emphasizes the importance of a standard protocol, as the reliability of blood pressure measurements in routine care seems rather low [33]. Values obtained under standardized, calm conditions in a consequent position are more informative than those obtained as a routine clinical activity. Already in the 90s, some authors discussed that identification of high risk patients is better with an automated blood pressure protocol instead of a conventional measurement in the antenatal clinic. The clinical readings are influenced by inaccuracy due to observer bias, presence of the doctor (white coat hypertension), device bias etc. [27,34,35]. Benedetto et al. promotes a 24 h blood pressure monitoring to estimate the risk. Aside the fact that Benedetto et al. also suggests lower blood pressure thresholds based on his results, it is easier to perform only a short protocol on each patient in clinic instead of a 24 h protocol [19]. Since blood pressure values are the main indicator of hypertension, doctors and midwives should pay more attention to the measurement technique and to opting for the best performing protocol which is gestation-specific, position-specific, population-specific and possibly clinic-specific depending on the used method [1,36-38]. Reports mention that 45% of the obstetricians never use an appropriate cuff [39] or 66% report the blood pressure to the nearest 5 mm Hg, which automatically leads to over or under estimation [40]. Routine antenatal visits are troubled with fast and non-standardized blood pressure measurement in patients who had to sit in the waiting room for minutes to hours or were rushed because of an appointment delay [37,38]. This scenario is to be prevented with a standardized protocol, where the measurement of taking the blood pressure is a real moment. Ciccone et al. showed improved clinical outcome of patients suffering from cardiovascular diseases, diabetes or heart failure due to the active clinical implementation of health care managers (specially trained nurses) as compared to a doctor visit alone [41]. Parallel to this study, midwives could be an added value in the disease management for gestational hypertensive disorders.

From the data presented in this paper, we conclude that a simple blood pressure measurement, if measured in a standardized way, can already be very valuable to classify the complete patient population into high vs. low risk at their first prenatal visit. This might be an important starting point for a universal screening tool, certainly for patients in their first pregnancy. Applying a threshold of 79 mm Hg at 12 weeks or 76 mm Hg at 20 weeks gives us at least a ≥ 96% negative predictive value, which is helpful to exclude hypertensive disorders early in pregnancy, leaving a "high" risk group requiring a somewhat closer observation or advanced screenings tests with multi-marker algorithms.

Acknowledgement

The first author of this work is funded by a Ph.D. grant of the Agency for Innovation by Science and Technology (IWT) in Brussels, Belgium and all authors are part of the Limburg Clinical Research Project (LCRP) at Hasselt University, Belgium. We also want to thank Dr. Petra Nijst for her input on the paper.

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