Title: Non-invasive versus invasive blood pressure measurement in the morbidly obese parturient (BMI ≥ 40 kg/m^2) with severe preeclampsia: A comparison of direct arterial blood pressure measurements with readings obtained using either large cylindrical, radial cylindrical, or novel conical bariatric upper arm blood pressure cuffs.

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Aim: To compare agreement of invasive blood pressure measurements with non-invasive blood pressure measurements measured with a conical blood pressure, radial cuff, and large standard upper arm rectangular cuff in morbidly obese severely hypertensive (systolic blood pressure > 160 mmHg) parturients.

Background and Significance: A morbidly obese [Body Mass Index (BMI) ≥ 40 kg/m^2] pregnant woman is at singular risk for all the complications of pregnancy, most notably preeclampsia (PE) [1, 2]. Furthermore a woman who is already chronically hypertensive is quite likely to develop superimposed PE [3, 4]. Uncontrolled systolic hypertension in pregnancy prompts placental abruption, hemorrhagic stroke, and systolic or diastolic heart failure. Mhyre rightly asserts that: "Systolic blood pressure …above 160 mm Hg constitutes a hypertensive crisis in a pregnant woman and requires urgent treatment to minimize risk for cerebral hemorrhage" [5]. The American College of Obstetrics and Gynecology Task Force on Hypertension in Pregnancy also now recommends the use of antihypertensive therapy for persistent severe maternal hypertension (SBP at or above 160 mm Hg) [6]. Accurate blood pressure measurement is therefore a prerequisite to controlling dangerously high SBP to enable labor and delivery to be conducted safely in association with PE. An algorithm has been implanted on Vanderbilt Labor and Delivery, using SMFM guidelines, to guide treatment of these severe range blood pressures[20]. Precise SBP measurement is also a precondition for clinically testing hypotheses concerning the existence of druggable targets that will allow prolongation of pregnancy in the face of severe PE and /or intra-uterine growth restriction (IUGR) remote from term [7, 8].

Hypertensive hemorrhagic stroke is the most common cause of maternal death related to preeclampsia [5]. Upper arm SBPs measured with a standard rectangular cylindrical cuff exceeding 160 mm Hg are not infrequently seen in severe preeclampsia. During general anesthesia for cesarean section direct arterial SBPs well in excess of 160 mm Hg have been recorded during both laryngeal intubation and extubation [9, 10]. SBPs this high place the preeclamptic parturient at serious risk for hemorrhagic stroke [5]. We hypothesize that measurement of noninvasive blood pressure (NIBP) in morbidly obese patients (BMI ≥ 40) with large upper arm circumferences

adds a further margin of under-reading error when compared with direct arterial, invasive blood pressure (IBP) recording, thus compounding the risk of maternal stroke.

Oscillometric NIBP measurement is the customary standard blood pressure monitoring method most often used in the labor suite and obstetric operating room today. For this purpose a rectangular, cylindrical blood pressure (BP) cuff placed on the upper arm is connected to an oscillometric blood pressure device. Yet inaccuracies related to the fact that oscillometric NIBP devices under-read high SBP relative to IBP measurements have been recognized as a potential source of maternal morbidity for years [11]. A decade ago Martin et al. highlighted the importance of treating SBP rather than diastolic blood pressure (DAP) to avoid stroke in severe preeclampsia and eclampsia, concluding that: "A paradigm shift is needed toward considering antihypertensive therapy for severely preeclamptic and eclamptic patients when systolic blood pressure reaches or exceeds 150-160 mm Hg." [12].

In non-pregnant patients a recent retrospective analysis of data obtained from a cohort of more than 15,000 men and women showed that systolic, mean, and diastolic upper arm blood pressures measured non-invasively with rectangular, cylindrical blood pressure cuffs that fell within the normal range correlated relatively well with direct IBP recordings obtained via a radial artery catheter, the latter method currently representing the "gold standard" for clinical BP determination [13]. However, outside the normal ranges NIBP tended to under read at higher pressures but paradoxically, over read at lower blood pressures. Cross over points for SBP, MAP and DAP agreement between NIBP and IBP were noted to be 111, 95 and 80 mm Hg respectively. Similar disparities between NIBP and IBP recordings in hyperacute stroke patients have been documented [14]. A recent systematic review of the subject under scrutiny here confirms the relative inaccuracy of current NIBP methods when compared to IBP recording [15].

Rectangular, cylindrical BP cuffs have been noted to overestimate SBP relative to troncho-conical cuffs in morbidly obese (mean body mass index 41.4 ± SEM 0.7) men and women (group 4) by as much as 9.7 mm Hg , most notably in those subjects with shorter upper arm lengths [16]. The incidence of hypertension among this group of morbidly obese patients was purported to be 54.6% using the cylindrical cuff, but was found to be only 40.0% using the conical cuff ($p < 0.001$). Thus 15% of subjects who appeared hypertensive with the cylindrical cuff were actually normotensive. In contrast, in a limited study of "severely" obese male and female subjects (n = 16) NIBPs measured on the upper arm with both cylindrical and conical cuffs, and on the forearm with cylindrical cuffs were noted to be little different from corresponding radial artery catheter pressures [17].

With regard to pregnancy, Langenegger et al. compared both manual ausculatory and automated oscillometric NIBP to direct arterial IBP when monitoring acute severe hypertension in 23 preeclamptic patients (gestational ages 22 - 40 weeks; BMI 19 - 45) [18]. Mean oscillometric SBP (148 ± 18 mm Hg) and manual auscultatory readings (152 ± 15) were on average 24 ± 17 and 20 ± 15 mm Hg respectively lower than the direct arterial SBP recordings (172 ± 11 mm Hg). To

the best of our knowledge, no such comparisons have yet been made in a cohort of morbidly obese (BMI ≥ 40) pregnant women manifesting severe hypertension.

The conical Ultracheck Curve (reusable or single use) BP cuff (Statcorp Medical, Jacksonville, Florida, U.S.A.) is advertised (Sharn Anesthesia Inc., Tampa, Florida, U.S.A.) as: "A Breakthrough Solution for Accurate Bariatric Blood Pressure Readings. We intend to compare IBP readings obtained from morbidly obese, severely hypertensive (SBP > 160 mm Hg) parturients with NIBP consecutively measured with new innovative conical Ultracheck Curve BP cuffs and large standard upper arm rectangular cylindrical as well as radial BP cuffs.

Methods: Twenty-five morbidly obese (BMI ≥40 kg/m^2) severely hypertensive (SBP > 160 mm Hg) parturients with clinically indicated radial artery lines already in situ or who agree to placement of an arterial line after a thorough explanation of limited complications related to arterial line insertion will be recruited to the study. Both IRB approval and the patients' written informed consent for the study will be obtained. The following measurements (left and right arm) will be made and recorded with the patient lying in a 15º left lateral tilt position, arms by their side and forearms pronated:

1) Proximal upper arm circumference - just below the axilla.
2) Distal upper arm circumference - 0.5 cm above antecubital fossa.
3) Upper arm length - axilla to the antecubital fossa.
4) Blood pressure cuff size

For comparative purposes BP will be measured and documented sequentially and in random order (computer generated random numbers table). NIBPs will be recorded using either an upper arm large adult [American Heart Association (AHA): 16-36 cm.] cylindrical BP cuff, a radial cuff, or an UltraCheck Curve bariatric BP cuff. The BP cuffs will be linked to an Oscillometric BP recording device (Philips M1574A). There will be an initial set of readings on admission, and subsequent sets of readings before a medication administration on the Vanderbilt Management Guideline for Acute Hypertension Algorithm. A set of readings will also be attained at decision for ICU transfer or cesarean section. SBP, MAP and DAP will be recorded from each cuff site (3 cuffs total) and then repeated after swapping the cuffs over to the opposite arm . Direct invasive arterial pressure readings will be charted simultaneously for comparative purposes.

The primary outcome of this investigation will be to compare the agreement of NIBP and SBPmeasurements relative to IBP SBP recordings. Secondary outcomes will be: To compare the agreement of MAP and DAP NIBP recordings with IBP levels; to compare agreement of the SBP, MAP and DAP NIBP measurements obtained with cylindrical upper arm and radial BP cuffs with those recorded using conical BP cuffs.

Agreement between devices (NIBP vs IBP and NIBP cylindrical (upper and radial) versus conical BP cuffs) will be determined. The relationship between upper arm circumference minus distal arm circumference and upper arm cylindrical pressure and intra-arterial SBP difference

will be defined as well. The same relationship between upper arm minus distal arm circumference and conical cuff and intra-arterial SBP recordings differences will also be assessed.

Main Inclusion Criteria:
Written, signed and dated informed consent
≥ 18 years of age
Morbidly obese (BMI ≥ 40 kg/m^2) severely hypertensive (SBP > 160 mm Hg) parturients with clinically indicated radial artery lines already in situ or who agree to placement of an arterial line after a thorough explanation of limited complications related to arterial line insertion will be recruited to the study
Gestational age greater than or equal to 24 weeks
Parturients admitted for induction of labor

Exclusion Criteria:
Parturients admitted in labor

Statistical Plan:
Bland-Altman plots will be used to look at agreement of NIBP (SBP, MAP and DAP) and IBP. Regression analyses will examine the relationship between upper and lower forearm circumference measurements and difference between NIBP (SBP, MAP and DAP) cylindrical and radial cuffs versus conical (obesity) BP cuffs.

Based on the 2012 report from South Africa[17] we estimate that 25 patients will initially need to be investigated. A difference of 10 mm Hg (SBP, MAP and DAP) will be considered clinically significant.

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