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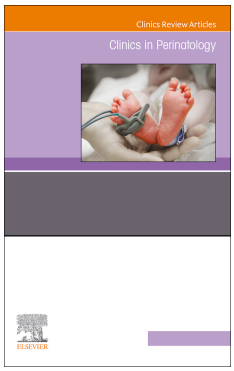

Neonatal Blood Pressure Standards: What's "normal"?

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PII: S0095-5108(20)30060-9

DOI: https://doi.org/10.1016/j.clp.2020.05.008

Reference: CLP 1176

To appear in: *CLINICS IN PERINATOLOGY*

Please cite this article as: Batton B, Neonatal Blood Pressure Standards: What's "normal"?, *CLINICS IN PERINATOLOGY* (2020), doi: https://doi.org/10.1016/j.clp.2020.05.008.

Neonatal Blood Pressure Standards: What's "normal"?

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Disclosure Statement: No commercial or financial conflicts of interest or any funding sources to disclose

SYNOPSIS

Blood pressure (BP) is routinely measured in newborn infants. Published BP nomograms demonstrate a rise in BP following delivery in healthy infants at all gestational ages (GA) and evidence that BP values are higher with increasing birth weight and GA. However, the complex physiology that occurs in newborn infants and range of BP values observed at all GA make it difficult to identify "normal" BP for a specific infant at a specific time under specific conditions. As such, complete hemodynamic assessment should include the physical examination, perinatal history, other vital signs, and laboratory values in addition to BP values.

KEY WORDS

blood pressure, cuff, neonate, nomogram, normal values

KEY POINTS

- Blood pressure increases spontaneously with increasing postnatal age, birth weight, and gestational age at birth
- For infants born at all gestational ages, a wide range in blood pressure values is observed for each postnatal hour over the first postnatal week
- The range of blood pressure values observed and complex physiological changes which occur after birth make it difficult to identify a "normal" blood pressure for an individual newborn infant under specific conditions.
- Blood pressure should not be sole criteria used to assess a newborn infant's hemodynamic status.

INTRODUCTION

Measurement of the arterial blood pressure (BP) in neonates was introduced more than 60 years ago.[1,2] In subsequent decades, various techniques for arterial BP measurement were developed[3-5] and numerous tables of observed BP values for neonates across a broad range of gestational ages at birth (GA) and postnatal ages have been published.[6-19] While observed BP data is widely available, attempts to describe "normal" BP for neonates – particularly preterm infants – has been challenging. This is partly due to the various techniques utilized to measure BP, rapidly changing physiology in the immediate postnatal period as the neonate adapts to the extra-uterine environment, the presence of factors which can impact BP values in the neonatal period, and difficulties defining "normal" values in an inherently abnormal patient population such as preterm infants in a neonatal intensive care unit (NICU).[20,21]

The intent of this review is to: 1) describe the strengths and limitations of the two most common techniques used for measuring arterial BP in the neonate (non-invasive oscillometry and continuous BP monitoring through an umbilical arterial catheter [UAC]); 2) discuss antenatal and postnatal factors which can impact BP values and; 3) provide data regarding observed BP values for several different neonatal populations. Discussion and review of BP values for infants beyond the neonatal period can be found elsewhere.[22,23]

METHODS FOR BLOOD PRESSURE MEASUREMENT

Intra-arterial blood pressure measurements

Invasive BP monitoring requires arterial access. In neonates, this is most commonly obtained by inserting an appropriately sized arterial catheter into an umbilical artery. Less commonly, the radial, posterior tibial, or femoral arteries are cannulated. The tip of the umbilical arterial catheter (UAC) should be positioned in the thoracic descending aorta between the sixth and tenth ribs on x-ray.[3-5] Blood pressure measurements are then obtained using a disposable pressure transducer placed at the infant's mid-chest level which is connected to the UAC and then calibrated. Invasive monitoring is considered the "gold standard" method of neonatal BP measurement as it can provide continuous intra-arterial BP values, is the most reliable and accurate method of BP measurement, and allows for prompt assessment of BP following therapeutic interventions intended to improve hemodynamic status.[3-5] Arterial access is typically reserved for the most critically ill patients in the NICU due to difficulties obtaining access, technical issues related to invasive monitoring, and the risk of known complications. Technical issues include frequent re-positioning in order to maintain the pressure transducer at the level of the right atrium, the presence of air bubbles which can interfere with BP measurement, dampening of the waveform for various reasons, and the need to calibrate the system four to six times per day. Known complications include tissue ischemia distal to the catheter, bleeding, central line associated infection, thromboembolic events, and catheter migration to the pleural or pericardial space.[3-5,24]

Non-invasive blood pressure measurements

Oscillometric devices for BP measurement include a cuff and monitor to detect the amplitude of pulsations within the artery. The cuff is inflated above the systolic BP. As the cuff gradually deflates, the maximal amplitude of the arterial pulsation is determined to be the mean arterial BP.[25] Using computer generated algorithms specific to each device manufacturer, systolic and diastolic BP values are then calculated. Oscillometric BP measurements should be obtained by placing an appropriate size cuff around the infant's right bicep with the cuff bladder overlying the brachial artery. The cuff bladder width should be ~40% of the arm circumference (AC) at a point midway between the olecranon and the acromion, and the bladder length should cover 80 to 100% of the circumference of the arm at that point (Figure 1). A variety of BP cuff sizes are available which can be used to obtain BP values from any extremity. However, non-invasive BP values obtained from the right arm are considered optimal as they best reflect BP in the ascending aorta.[4,26] Since systolic and diastolic BP are calculated based on device specific algorithms, values can vary significantly.[4,5]

Intra-arterial versus non-invasive blood pressure measurements

Significant differences in BP values obtained by intra-arterial versus oscillometric methods have been reported.[27-31] These differences may represent true differences in the BP value obtained or may be related to patient selection, device or algorithm utilized, or slight differences in the postnatal age at the time of study. In extremely preterm infants, non-invasive values tend to be higher, but this is not a universal observation.[27-30] Since intra-arterial BP values are considered

the "gold-standard",[3,4,26] such values should generally be accepted when there is a discrepancy between invasive and non-invasive measurements. Arterial access and continuous BP monitoring should be considered in any patient with hemodynamic instability and a concerning BP.[3-5]

FACTORS AFFECTING BLOOD PRESSURE VALUES

Antenatal factors affecting neonatal blood pressure measurements

The impact of a wide range of antenatal treatments and conditions on neonatal BP values has been investigated, including medications, demographics, maternal conditions, perinatal factors, and fetal conditions (Table 1).[32-57] Studies to date have been limited by the presence of confounding variables, small samples sizes, differential timing between the antenatal treatment or condition and the GA at birth, and study design. Preterm infants born to mothers who received antenatal corticosteroids appear to have higher BP values in the immediate postnatal period and a decreased likelihood of receiving therapies for low BP.[36,42,43,47,49] Umbilical cord milking or delayed cord clamping seem to have similar effects on increasing BP as compared to immediate cord clamping.[47,54,55] For many other antenatal conditions and therapies, conclusions with strong supporting evidence are lacking due to confounding factors influencing the relationship between the antenatal variable and postnatal BP measurements.

Postnatal factors affecting neonatal blood pressure measurements

The evolving complex physiological changes that occur in the immediate postnatal period, potential presence of disease states, differences in infant characteristics, and the range of medical care provided make it difficult to define "normal" BP values for a specific infant at a specific time under specific circumstances. Blood pressure nomograms have been developed for infants

based on the GA at birth, postnatal age (in hours or days), and birth weight as studies over the last 40 years have provided strong data that observed BP values increase as each of these variables increases.[6-19] However, a wide range in BP values has been reported for infants of all postnatal ages, GA, and birth weights with significant overlap across these three variables such that identifying "normal", "expected", or "acceptable" BP is challenging. This is partly due to variability in the method used to obtain BP values (invasive versus non-invasive), patient heterogeneity, and a lack of clarity regarding the presence of antenatal and postnatal factors (Table 2) impacting BP values in the patient population investigated.[58-85] Studies rarely provide information regarding factors such as the circumstances at delivery, presence of medical conditions or disease states, or circumstances at the time of BP measurement (e.g. time of day, position, state of arousal) when publishing figures with observed systolic, diastolic, and mean arterial BP values.[6-19] The commonly proposed threshold for therapeutic intervention for low BP of a mean arterial BP (in mmHg) numerically equivalent to an infant's GA (in weeks) is not physiologically based, had little evidence supporting it when proposed nearly 30 years ago, commonly occurs in the immediate postnatal period for most extremely preterm infants, and is not associated with improved infant outcomes.[66,80,86-88] Other proposed thresholds such as a mean BP less than 30mmHg again also have little supporting evidence upon which to base this recommendation.

OBSERVED BLOOD PRESSURE VALUES FOR NEONATES

The range of observed BP values reported in the first 24 hours for extremely preterm infants born $23^{0/7}$ – $26^{6/7}$ weeks GA in the immediate postnatal period are provided (Figures 2 and 3). For

preterm infants born ≤28 weeks GA, population estimates of BP values over the first 80 hours after birth (Figure 4) and over the first postnatal month (Figure 5, Panel A) are also presented.

Observed systolic, diastolic, and mean BP values over the first postnatal week for moderately preterm infants are also presented in Figure 5 (Panels B and C). Figure 6 provides GA based neonatal BP values beyond the first postnatal week for preterm infants born 28 – 36 weeks GA.

Observed BP values for infants born at term over the first four days after birth are provided in Figure 7. The data in Figure 8 reports estimated BP values after two weeks of age in infants from 26 to 44 weeks post conceptual age.

SUMMARY

Many factors impact BP in the neonatal period, including antenatal care and conditions, evolving changes in physiology following birth, and postnatal variables such that “normal” BP values for an individual newborn infant at a specific time under specific conditions are difficult to define. While a wide range of BP values are observed for infants following delivery at all GA, there is a strong body of literature dating back >40 years which demonstrates that systolic, diastolic, and mean BP values increase spontaneously over at least the first week after birth for infants of any GA. A BP that fails to increase or decreases over time is cause for concern and warrants further clinical investigation. Blood pressure values outside the range of commonly observed values such as those above the 90th percentile or below the 10th percentile for commonly cited reference ranges (Figures 2 – 8) may be a sign of underlying pathology, but are not universally indicative

of a disease state as they frequently occur in infants at all gestational ages who clinically appear well. As with any vital sign measurement, assessment of BP values should be done conscientiously (Figure 9) and considered in context with the entire clinical picture, including the perinatal history, infant's size and age, available laboratory data, and the physical examination.

Best Practices

What is the current practice for neonatal blood pressure measurement?

What changes in current practice are likely to improve outcomes?

- Assessment of a newborn infant's blood pressure should incorporate his/her postnatal age, birth weight, and gestational age at birth.
- The range of blood pressure values observed varies significantly (figures 2 – 8).
- Multiple antenatal, perinatal, and postnatal factors can influence blood pressure in newborn infants (tables 1 and 2).
- Multiple factors should be considered when assessing blood pressure in a neonate.

Clinical Algorithm: see Figure 8

Major Recommendations

- A wide range of BP values are observed for infants following delivery at all gestational ages (2A)
- Systolic, diastolic, and mean BP values increase spontaneously with increasing birth weight, gestational age at birth, and postnatal age (2A)
- Blood pressure values outside the range of commonly observed values such as those above the 90^{th} percentile or below the 10^{th} percentile for commonly cited reference ranges are not universally indicative of a disease state as they frequently occur in infants who clinically appear well (2A)
- Assessment of blood pressure values should be considered in context with the entire clinical picture, including the perinatal history, infant's size and age, available laboratory data, and the physical examination (2C)

Bibliographic Source(s): see references 3, 11 – 21, 26 – 30, 84, 87

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FIGURE LEGENDS

Figure 1: Blood pressure cuff placement for neonates.

Figure 2: Systolic (A), diastolic (B), and mean (C) arterial blood pressure curves over the first 24 hours for extremely preterm infants born at $23^{0/7}$ – $26^{6/7}$ weeks gestation (n = 367).

Figure 3: Gestational age (GA) specific changes in the systolic (a), diastolic (b) and mean (c) arterial blood pressure 50th percentile curves over the first 24 hours for infants born at $23^{0/7}$ – $26^{6/7}$ weeks GA (n = 367).

Figure 4: Population estimate of blood pressure (BP) values for extremely preterm infants born ≤28 weeks gestation by postnatal age in hours. Dashed lines represent the BP estimate, solid line represents the boundaries of the 95% confidence interval. Orange: systolic BP; blue: mean arterial BP; green: diastolic BP.

Figure 5: Figure 5: Increase in systolic (a), diastolic (b), and mean (c) arterial blood pressure during the first month of life in groups of infants classified by estimated gestational age: ≤28 weeks (squares), 29–32 weeks (triangles), 33–36 weeks (circles), and ≥ 37 weeks (stars).

Figure 6: Gestational age (GA) specific normative blood pressure (BP) trends for preterm infants over the first 28 postnatal days; (A) BP for infants born at 28 to 29 weeks GA; (B) BP for infants born at 30 to 31 weeks GA; (C) BP for infants born at 32 to 33 weeks GA; (D) BP for infants

born at 34 to 36 weeks GA. Boxes delineate 10th and 90th percentiles, with vertical black marks delineating range.

Figure 7: Systolic, mean, and diastolic blood pressure values obtained from healthy term neonates (n=406) in the newborn nursery.

Figure 8: Estimated blood pressure values after two weeks of age in infants from 26 to 44 weeks post conceptual age.

Figure 9: Algorithm for neonatal blood pressure assessment.

TABLES

Table 1: Antenatal factors affecting neonatal blood pressure measurements

Table 1: Antenatal factors affecting neonatal blood pressure measurements	
Category	**Reference #**
Medications	
General anesthesia	49
Corticosteroids	36, 42, 43, 47
Magnesium sulfate	37,48
Maternal conditions	
Smoking	34, 35, 40

Advanced maternal age	38, 44
Chorioamnionitis	39, 43, 45
Hypertension	32, 33, 38, 50
Perinatal factors	
Mode of delivery	34, 41, 46
Delayed umbilical cord clamping	47, 54, 55
Fetal conditions	
Intrauterine growth restriction	51 – 53
Breech presentation	44
Twin twin transfusion syndrome	56, 57

Table 2: Postnatal factors other than gestational age, birth weight, and postnatal age which can affect neonatal blood pressure measurements

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Category	**Reference #**
Patient variables	
Race / ethnicity	44, 59, 61, 65
Gender	59, 60, 64
Multiple gestation	9, 68

Small for gestational age	71, 74
Circadian rhythm / sleep	60, 73
Medical conditions	
Patent ductus arteriosus	83
Anesthesia	84
Sepsis	86
Hypovolemia	86
Perinatal distress/acidosis/ low Apgar score	59
Cardiac disease, congenital heart disease	66, 86
Bronchopulmonary dysplasia	62, 63
Care interventions	
Pacifier use	67, 76
Hands-on care	69
Infant position (prone versus supine)	58, 77
Enteral feeding	59, 67, 72
Caffeine	85
Blood transfusions	17, 81, 86
Therapies for low blood pressure: Isotonic fluid boluses	 17, 81

Dopamine	17, 78, 79, 81, 82
Dobutamine	78, 81, 82
Epinephrine	81, 86
Corticosteroids	79 – 81

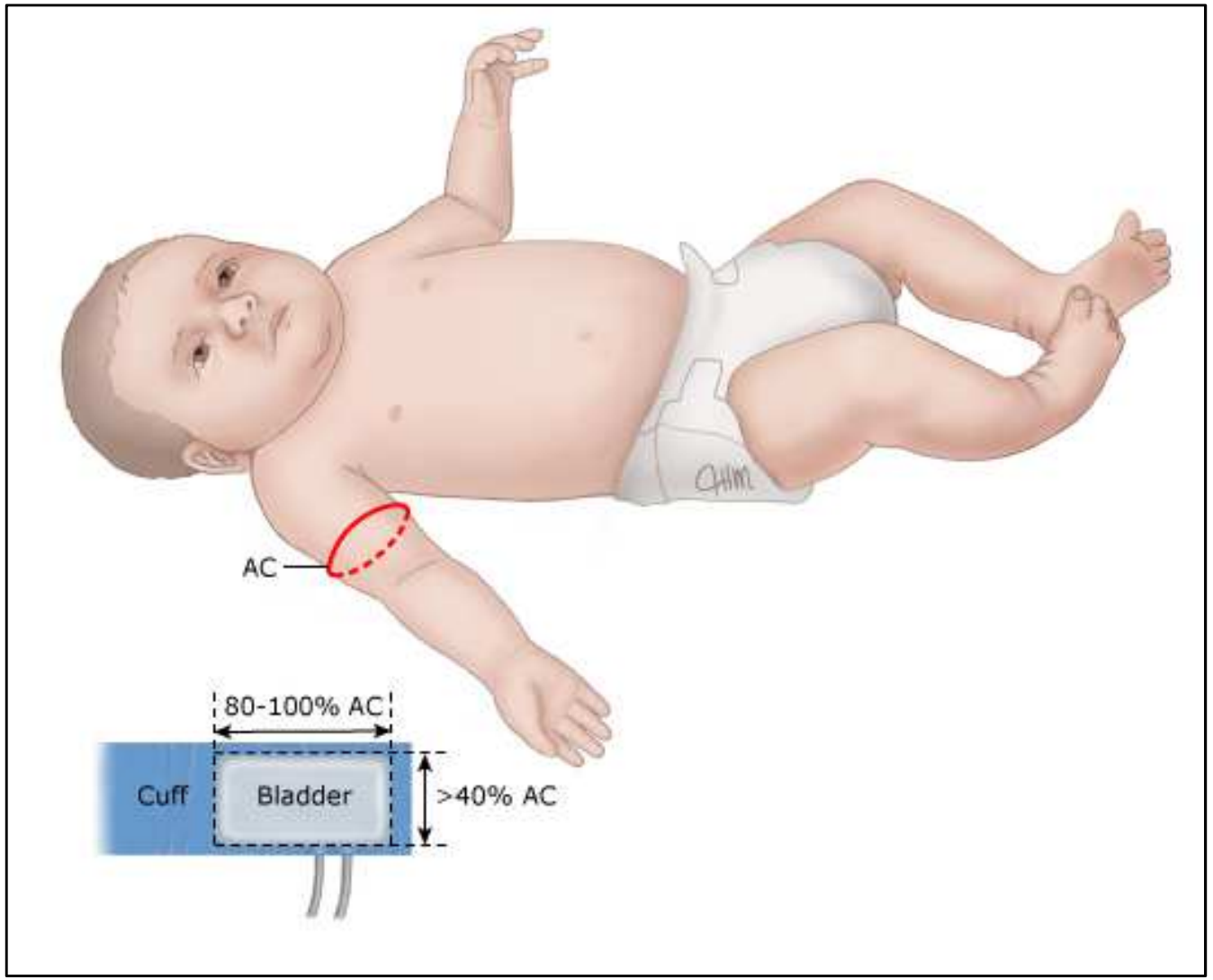

Figure 1: Blood pressure cuff placement for neonates. From Flynn JT. Etiology, clinical features, and diagnosis of neonatal hypertension. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on September 26, 2019); with permission

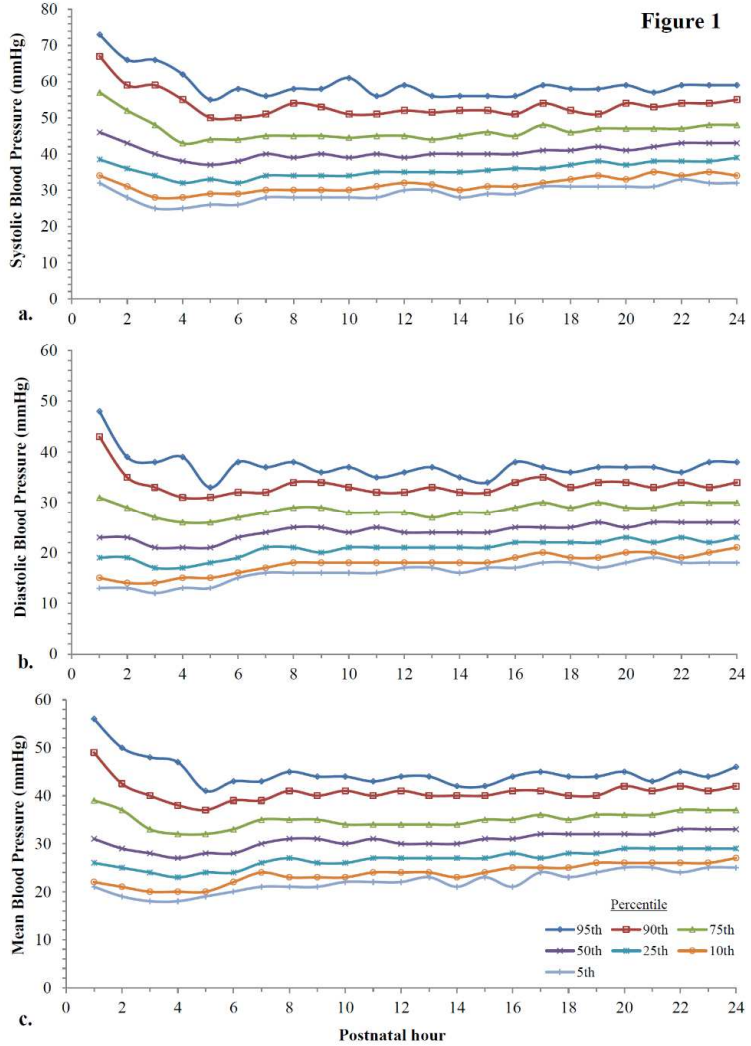

Figure 2: Systolic (A), diastolic (B), and mean (C) arterial blood pressure curves over the first 24 hours for extremely preterm infants born at $23^{0/7}$ – $26^{6/7}$ weeks gestation (n = 367). From Batton B, Li L, Das D, et al. Evolving blood pressure dynamics for extremely preterm infants. *J Perinatol* 2014; 34:301; with permission.

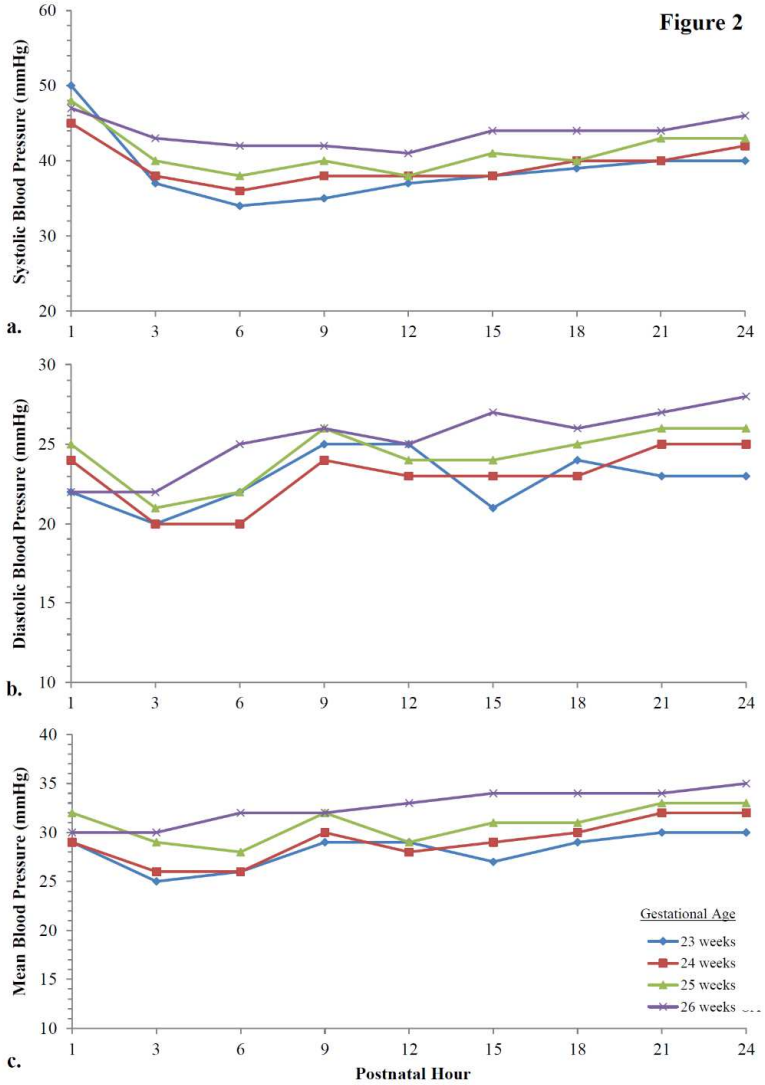

Figure 3: Gestational age (GA) specific changes in the systolic (a), diastolic (b) and mean (c) arterial blood pressure 50th percentile curves over the first 24 hours for infants born at $23^{0/7}$ – $26^{6/7}$ weeks GA (n = 367). From Batton B, Li L, Das D, et al. Evolving blood pressure dynamics for extremely preterm infants. *J Perinatol* 2014; 34:301; with permission.

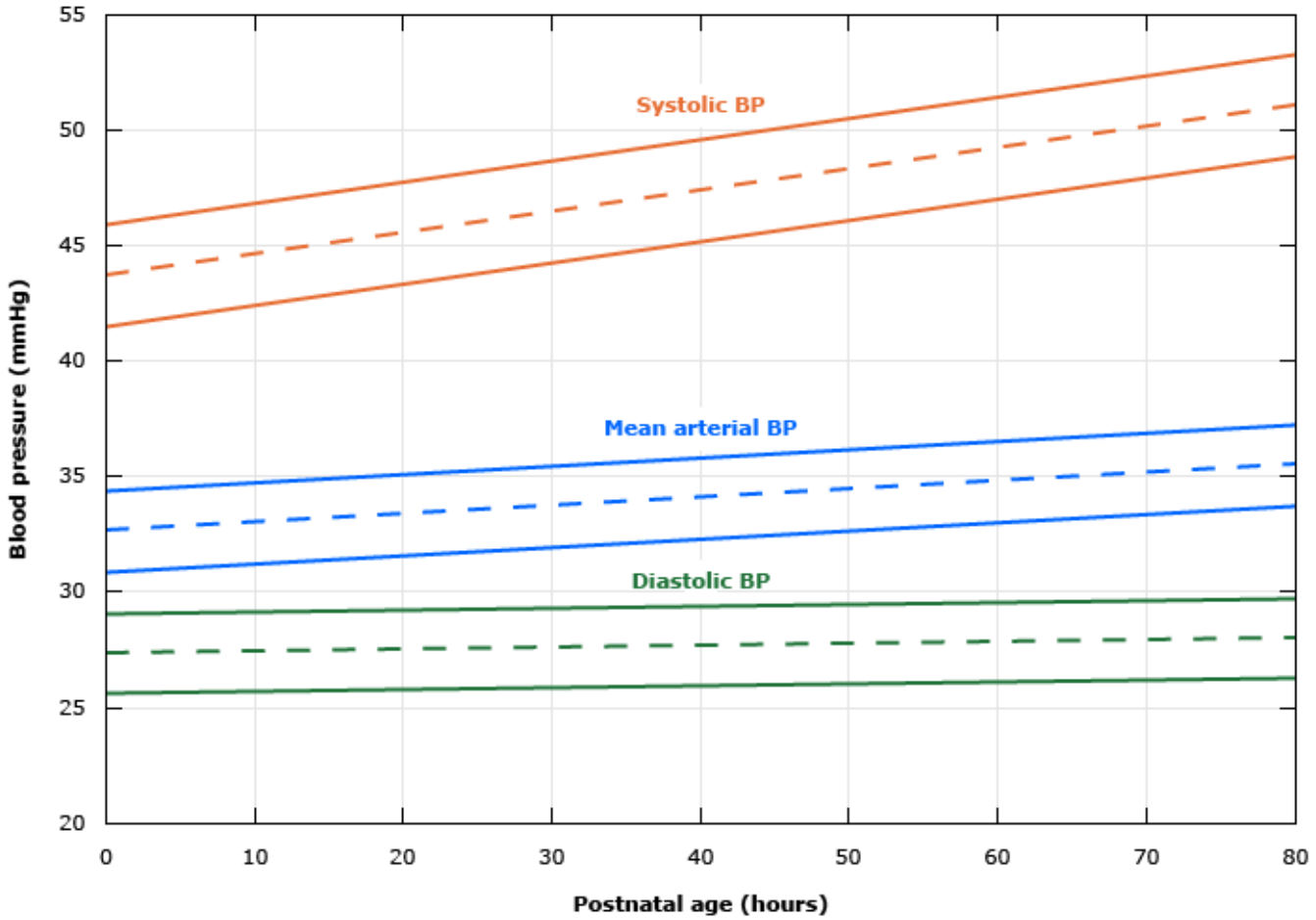

Figure 4: Population estimate of blood pressure (BP) values for extremely preterm infants born ≤28 weeks gestation by postnatal age in hours. Dashed lines represent the BP estimate, solid line represents the boundaries of the 95% confidence interval. Orange: systolic BP; blue: mean arterial BP; green: diastolic BP. From Vesoulis ZA, El Ters NM, Wallendorf M, Mathur AM. Empirical estimation of the normative blood pressure in infants <28 weeks gestation using a massive data approach. *J Perinatol* 2016; 36:291; with permission.

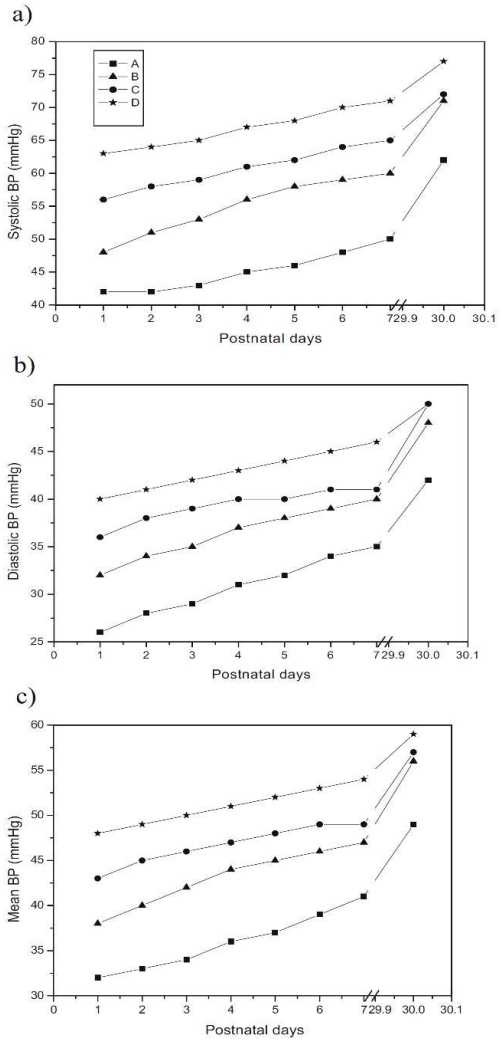

Figure 5: Increase in systolic (a), diastolic (b), and mean (c) arterial blood pressure during the first month of life in groups of infants classified by estimated gestational age: ≤28 weeks (squares), 29–32 weeks (triangles), 33–36 weeks (circles), and ≥ 37 weeks (stars). From Pejovic B, et al. Blood pressure in non-critically ill preterm and full-term neonates. *Pediatr Nephro* 2007; 22: 249-57; with permission.

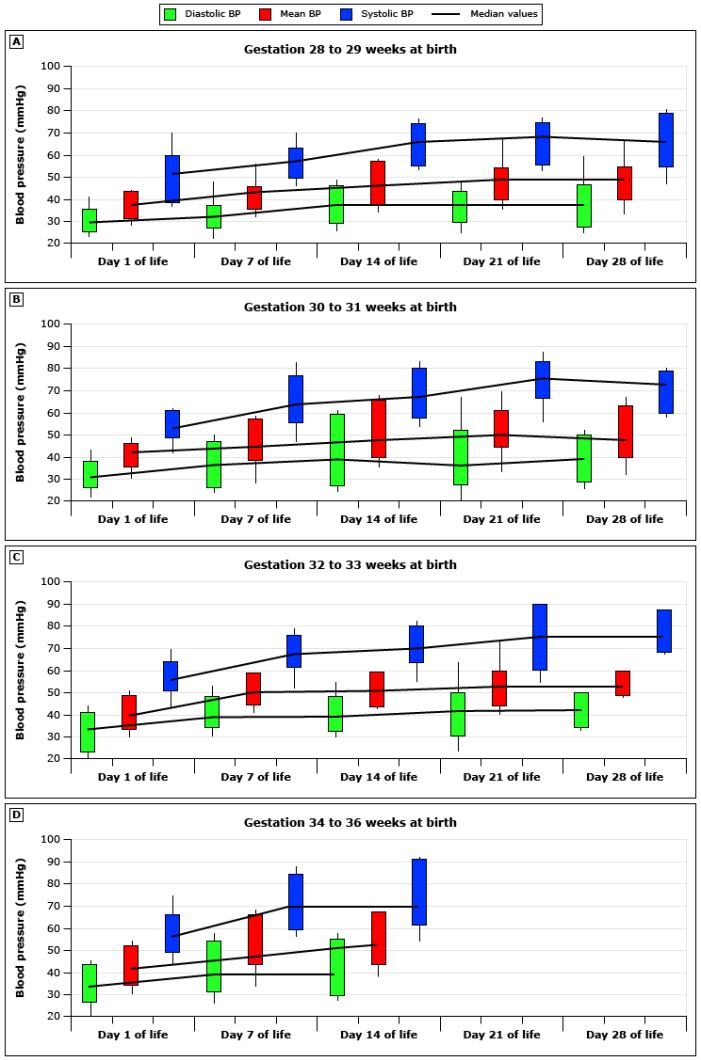

Figure 6: Gestational age (GA) specific normative blood pressure (BP) trends for preterm infants over the first 28 postnatal days; (A) BP for infants born at 28 to 29 weeks GA; (B) BP for infants born at 30 to 31 weeks GA; (C) BP for infants born at 32 to 33 weeks GA; (D) BP for infants born at 34 to 36 weeks GA. Boxes delineate 10th and 90th percentiles, with vertical black marks delineating range. From Kent A, Meskell S, Falk MC, Shadbolt B. Normative blood pressure data in non-ventilated premature neonates from 28-36 weeks gestation. *Pediatr Nephro* 2009; 241:141; with permission.

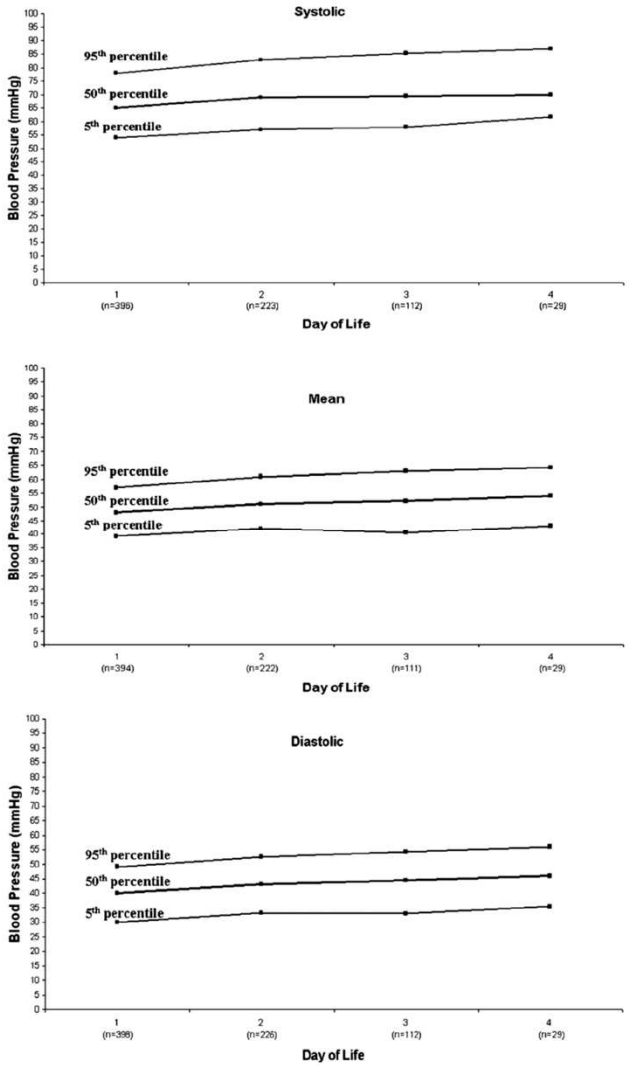

Figure 7: Systolic, mean, and diastolic blood pressure values obtained from healthy term neonates (n=406) in the newborn nursery. From Kent A. Normative blood pressure data in the early neonatal period. *Pediatr Nephro* 2007; 22: 1335-41; with permission.

Post-conceptual age	50th percentile	95th percentile	99th percentile
44 weeks			
SBP	88	105	110
DBP	50	68	73
MAP	**63**	**80**	**85**
42 weeks			
SBP	85	98	102
DBP	50	65	70
MAP	**62**	**76**	**81**
40 weeks			
SBP	80	95	100
DBP	50	65	70
MAP	**60**	**75**	**80**
38 weeks			
SBP	77	92	97
DBP	50	65	70
MAP	**59**	**74**	**79**
36 weeks			
SBP	72	87	92
DBP	50	65	70
MAP	**57**	**72**	**77**
34 weeks			
SBP	70	85	90
DBP	40	55	60
MAP	**50**	**65**	**70**
32 weeks			
SBP	68	83	88
DBP	40	55	60
MAP	**49**	**64**	**69**
30 weeks			
SBP	65	80	85
DBP	40	55	60
MAP	**48**	**63**	**68**
28 weeks			
SBP	60	75	80
DBP	38	50	54
MAP	**45**	**58**	**63**
26 weeks			
SBP	55	72	77
DBP	30	50	56
MAP	**38**	**57**	**63**

Figure 8: Estimated blood pressure values after two weeks of age in infants from 26 to 44 weeks post conceptual age. From Dione J. Erratum to: Hypertension in infancy: diagnosis, management and outcome. *Pediatr Nephro* 2012; 27:159–160; with permission.

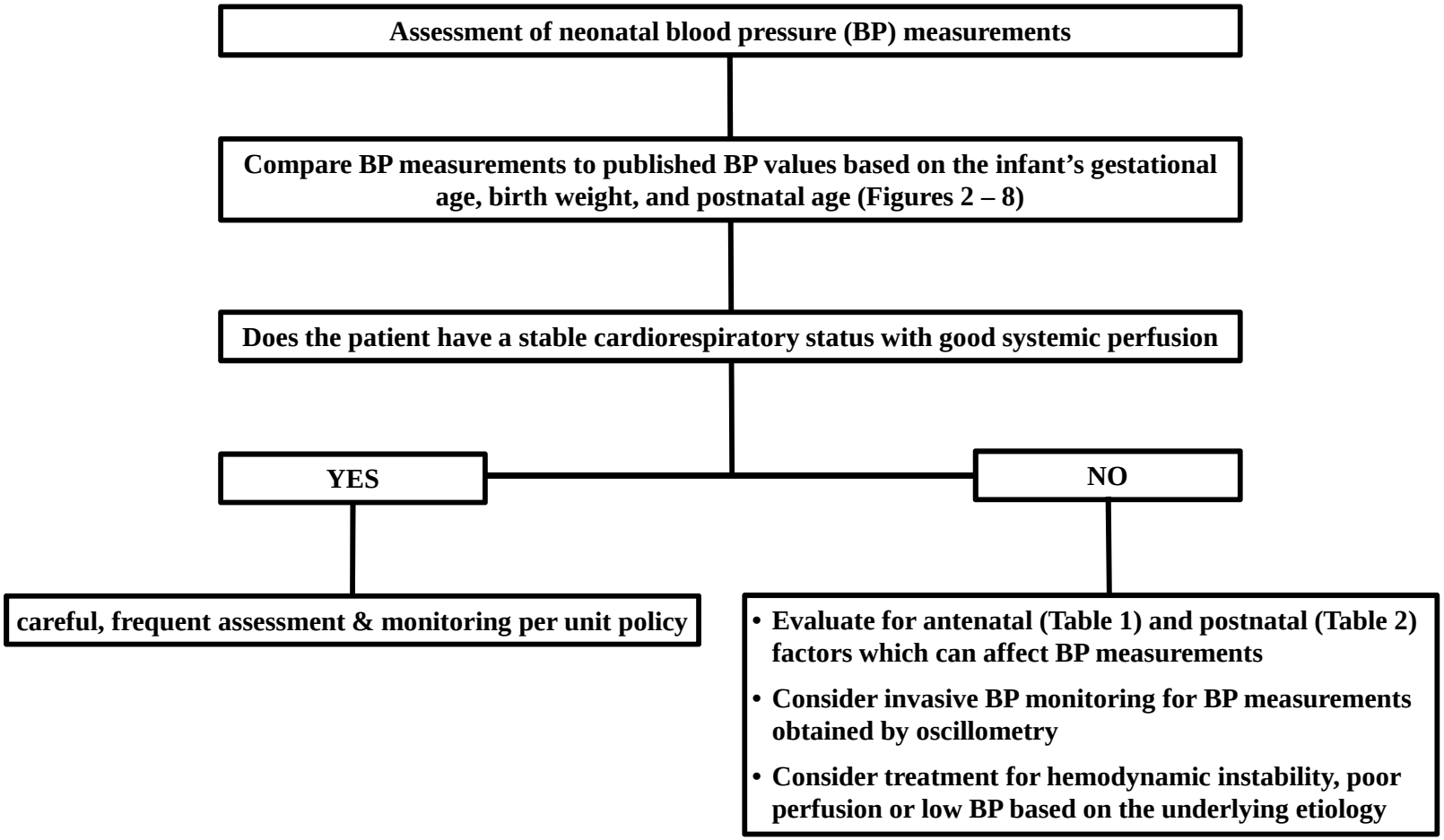

Figure 9: Algorithm for neonatal blood pressure assessment.