

Evaluation of Superior Mesenteric Artery (SMA) and Celiac Artery (CA) Blood Flow Pattern in Preterm Infants and Factors Influencing the Blood Flow

Nitin Ramdas Unde^{1*}, Khaled Mahmoud El-Atawi¹, Mahmoud Saleh Elhalik² and Arif Moinuddin Faquih¹

¹Neonatal Intensive Care Unit, Latifa Women and Children Hospital, Dubai, UAE

²Head of Pediatric Department, Consultant Neonatologist, Latifa Women and Children Hospital, Dubai, UAE

*Corresponding author: Nitin Ramdas Unde, Neonatal Intensive Care Unit, Latifa Women and Children Hospital, Oud Metha Road, Al Jaddaf Dubai, UAE, Tel: +971565909700; E-mail: drnitinunde@gmail.com

Received Date: Nov 22, 2018; Accepted Date: Dec 11, 2018; Published Date: Jan 01, 2019

Copyright: © 2019 Unde NR, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: To evaluate the blood flow velocity (BFV) in superior mesenteric artery (SMA) and celiac artery (CA) in first 2 days of life in preterm (less than 32 week and less than 1 kg) and to study the influence of various factors on the blood flow velocities in the same population.

Methods: 50 preterm less than 32 week with birth weight less than 1kg was included in the prospective observation study. Assessment of SMA and CA blood flow velocities (PSV: peak systolic velocity, EDV: end diastolic velocity, TAV: time average velocity) was done twice at 24hr (20-30) and at 48hr (40-54). Blood flow indices (resistive index; RI, pulsatile index; PI) was calculated using the formula. Simultaneously data for various factors influencing the blood flow in SMA and CA was collected in the similar population.

Results: SMA BFV increases from 24hr after birth and continue to rise thereafter in first 2 days. Significant increase in SMA EDV (6.77 ± 2.38 vs 8.74 ± 4.42) and SMA PSV (37.16 ± 10.64 vs 42.72 ± 14.66) was noted postnatally. Increase in SMA TAV was also observed. CA BFV showed negative trend from 24hr after birth with reduction of all velocities (PSV, EDV and TAV). CA TAV showed significant reduction at 48hr of age compared to 24hr (28.22 ± 9.81 vs 25.00 ± 8.07). Significant PDA was associated with attenuated BFV in both the SMA and CA on both the occasions. Other factors associated with adverse blood flow velocities were blood transfusion and anemia. Trophic feeding was associated with increase blood flow velocities in both SMA and CA.

Conclusion: Postnatally increase in SMA BFV was noted in first 2 days of life indicating improved intestinal perfusion and opposite trend in CA BFV. Significant PDA was associated with abnormal blood flow velocities in both SMA and CA.

Keywords: Blood Flow Velocity (BFV); Superior Mesenteric Artery (SMA); Celiac Artery (CA); Hemodynamically Significant Patent Ductus Arteriosus (HSPDA)

Introduction

Significant physiological and functional changes takes place at various organ level including gastrointestinal system (GI) in preterm newborn after birth. Superior mesenteric artery (SMA) and celiac artery (CA) supplies the blood to most of the intestine and vital abdominal organs respectively. Feeding problems are common in immediate postnatal period due to various anatomical and functional reasons leading to complication in the form of necrotizing enterocolitis (NEC). Blood pressure, capillary refill time (CRT), blood lactate, metabolic acidosis has limited value to predict the regional organ perfusion. Recently bedside ultrasound performed by trained neonatologist proved to be highly beneficial and regional organ blood flow velocities (BFV) and perfusion can be assessed more accurately with pulse wave Doppler.

Increase in SMA blood flow velocities was documented from birth onwards during the first month of life in preterm infants [1,2] which

implies improved intestinal perfusion and maturation. Postnatal physiological changes in intestinal BFV were reported previously by few authors in term and late preterm infants [3]. Data related to physiological changes of CA BFA is limited in preterm newborns [4,5]. Various factors like cardiovascular status, neural control, humoral substances and local control determines the regional organ blood flow [6,7].

The objective of this study is to evaluate the blood flow velocity changes in major abdominal arteries (SMA and CA) in the immediate postnatal period in high risk population of preterm less than 32 week, less than 1kg and to study the various factors influencing the velocities. This data helps the clinician to understand the pattern of BFV in two major arteries in early postnatal life, which might help to reduce the feeding related problems and GI complications.

Methods

Subjects

Infants admitted to tertiary neonatal intensive care unit with GA less than 32 week and birth weight less than 1kg were enrolled for the

prospective study to evaluate the blood flow velocity in SMA and CA with simultaneous assessment of various factors influencing the blood flow pattern. Exclusion criteria were major congenital malformations, critical congenital heart disease and evidence of perinatal asphyxia requiring significant resuscitation (need of drugs).

The demographic data of study population is shown in table 1 and 2.

This study was approved by Dubai health authority (DHA) ethical committee and written informed consent was obtained from the parents before the subject enrollment.

Study design

50 infants fulfilling the inclusion criteria were included in this prospective observation study to evaluate the blood flow velocity in SMA and CA with simultaneous assessment of various factors influencing the blood flow pattern. The study population underwent bedside ultrasound twice at 24hr (20-30) and 48hr (40-54) to measure the blood flow velocities in SMA and CA. The measurements were done by single certified neonatologist trained in functional echocardiography and data for various factors influencing the blood flow velocities was collected simultaneously.

Factors studied which potentially influence the blood flow velocities

- Patent ductus arteriosus (PDA): Hemodynamically significant PDA (HsPDA) is defined as diameter ≥ 1.5 mm, ratio of left atrial to aortic root dimensions $\geq 1.5:1$, and reversal of diastolic flow in the descending aorta [8-10].
- Blood transfusion (BT): Infants receiving packed RBC transfusion as per the unit guidelines
- Anemia: Infants with hemoglobin (HB) less than 10gm%
- Presence of umbilical arterial catheter (UAC)
- Infants with proved positive blood culture sepsis
- Infants receiving trophic feeds
- Small for gestation (SGA) infants: Defined as birth weight less than 10th centile for GA

Doppler ultrasound studies

SMA and CA BFV were measured using pulsed Doppler ultrasound (vivid q GE, USA) and a 10 MHz transducer. A real-time two dimensional image and color flow mapping was used to identify the arteries. SMA was identified as the second major branch of the abdominal aorta, originating just below the CA (Figure 1). The sampling volume of the pulsed Doppler was placed 3 mm distal to the origin of the SMA and CA using a real-time two-dimensional image from a longitudinal abdominal approach. Angle correction was used when necessary.

When stable waveforms measurements were obtained, the curves were traced and the blood flow variables in each artery were calculated from at least three consecutive cardiac cycles of optimal quality. The recorded blood flow variables were: peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged mean velocity (TAV). At least two sets of measurements were taken at each time point, and the mean of these readings was used for the final analysis. The resistive index (RI): $(PSV-EDV)/PSV$. The pulsatile index (PI) : $(PSV-EDV)/TAV$.

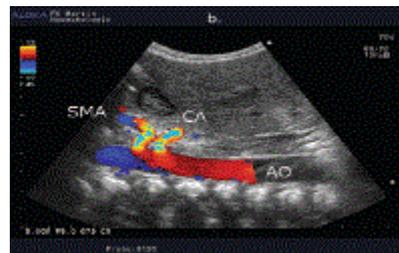


Figure 1: Doppler ultrasound view illustrating identification of the superior mesenteric artery (SMA) and celiac artery (CA) arising from the aorta (AO) in a newborn.

Statistical analysis

Blood flow velocities – PSV, EDV and TAV and indices RI and PI for SMA and CA are shown as Mean \pm SD. All the blood flow velocity variables at 24hr (20-30) and 48hr (40-54) were compared by using paired t-test. A p-value of <0.05 was considered significant. Statistical analysis were performed by using SPSS (Statistical Package for Social Sciences) version 20.0.

Results

Fifty infants were enrolled. The mean birth weight and GA of enrolled patients was 844 ± 153 gm and 27 ± 2.1 week respectively (table 1 and 2). Clinical variables that may affect the SMA and CA BFV are listed in table 1.

Variable	Value
Birth weight (gm.)	844 \pm 152
Gestational age(week)	27 \pm 2.1
Significant PDA n (%)	13(26)
Blood transfusion n (%)	8 (16)
UAC n (%)	12(24)
Trophic feeds n (%)	7/21* 14/42**
Anemia n (%)	6 (12)
Sepsis n (%)	4(8)
SGA n (%)	20(40%)
Data are the mean \pm s.d. unless otherwise indicated.	
n= number	
(*7 infants received trophic feeding at 24hr of age and ** 14 infants received trophic feed at 48hr of age)	
PDA-patent ductus arteriosus	
UAC-umbilical arterial catheter	
SGA-small for gestation	

Table 1: Demographic data and clinical variables for 50 new-born.

For each subject these variables did not change between the two scans. Postnatally, SMABFV showed rising trends with significant increase PSV (P 0.006) with simultaneous significant increase SMA EDV (P 0.001), which resulted in low RI and PI (table 3).

Variable	Distribution	Frequency
Sex	Male	26
	Female	24
GA(wk)	22-25+6	26
	26-27+6	13
	28-32	11
Birth weight(gm)	500-750	16
	751-999	34

Table 2: Demographic data.

	Variable	24hr(20-30)	48hr(40-54)
SMA	PSV(cm/s)	37.16 ± 10.64	42.72 ± 14.66**
	EDV(cm/s)	6.77 ± 2.38	8.74 ± 4.42***
	TAV(cm/s)	15.90 ± 5.02	17.90 ± 7.27
	RI	0.80 ± 0.05	0.79 ± 0.06
	PI	1.84 ± 0.45	1.89 ± 0.37
CA	PSV(cm/s)	51.38 ± 14.70	49.73 ± 13.53
	EDV(cm/s)	15.37 ± 6.77	13.89 ± 6.00
	TAV(cm/s)	28.22 ± 9.81	25 ± 8.07*
	RI	0.69 ± 0.09	0.72 ± 0.08*
	PI	1.32 ± 0.47	1.46 ± 0.40*

*p<0.05, **p<0.01, ***p<0.001
Data are the mean±s.d. unless otherwise indicated.
PSV: Peak systolic velocity; EDV: End-diastolic velocity; TAV: Time-averaged mean velocity; RI: Resistive index; PI: Pulsatile index; SMA: Superior mesenteric artery; CA: Celiac artery.

Table 3: Blood flow velocity variables in superior mesenteric artery (SMA) and celiac artery(CA) in 50 ELBW newborn.

SMA TAV also showed rising trend with advancing age although not statistically significant. On the contrary, CA BFV (PSV/EDV) showed negative trend, which was associated with high RI (P 0.025) and PI (P 0.027) with advancing age. CA TAV was significantly low at 48hr (P 0.023). The graphical representation of velocities in two major arteries is represented in figure 2.

13 preterm (table 1) were diagnosed with hemodynamically significant PDA. HsPDA was associated with high SMA PSV (44.40 ± 11.51 Vs. 35.11 ± 9.58, P 0.009) and low SMA EDV resulting high RI (0.86 ± 0.06 vs. 0.78 ± 0.04, P0.000) and high PI (2.19 ± 0.52 vs. 1.75 ± 0.38, P 0.004) compared to preterm without PDA. The adverse effect of HsPDA on mesenteric circulation persisted on day 2.11 infants were

diagnosed with significant PDA at 24hr of age and the number increased to 13 at 48hr of age (not shown in the table).

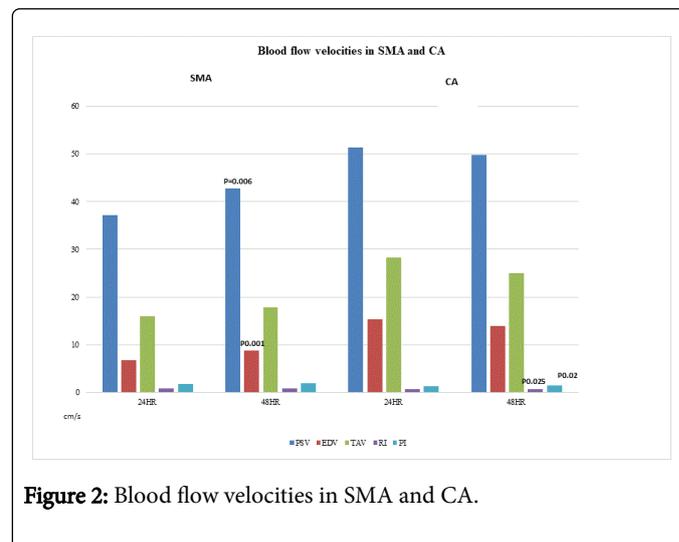


Figure 2: Blood flow velocities in SMA and CA.

Similar influence of HsPDA was observed on the CA BFV which was associated with high CA PSV (60.81 ± 13.64 Vs 48.71 ± 14.03) and low CAEDV resulting high RI (0.76 ± 0.10 vs. 0.67 ± 0.07, P 0.002) and high PI (1.66 ± 0.76 vs. 1.23 ± 0.30, P 0.007) on day1. This adverse effect of HsPDA on CA BFV was persisted on day 2 postnatal age.

Blood transfusion (n=8; table1) was associated with low SMA EDV (5.62 ± 2.97 vs. 6.98 ± 2.23), resulting high RI and PI in these babies. CA BFV influenced more adversely with BT compared to SMA resulting high PSV (66.18 ± 11.77 vs. 48.56 ± 13.56, P 0.001*) and high RI (0.77 ± 0.04 VS 0.71 ± 0.087, P 0.048*).

In SMA, Preterm with UAC (n=12; table 1) showed almost similar velocity pattern at 24hr (PSV: 35.83 ± 9.84 vs. 37.58 ± 10.98, EDV 6.75 ± 1.97 vs. 6.77 ± 2.53, TAV 15.12 ± 4.09 vs. 16.14 ± 5.30) and 48hr (PSV: 38.29 ± 9.18 vs. 44.11 ± 15.86, EDV 8.79 ± 3.55 vs. 8.72 ± 4.70, TAV 15.89 ± 5.69 vs. 18.53 ± 7.65) compared to preterm without UAC. CA BFV were also comparable in preterm with UAC and without UAC.

Anemia (n=6; table1) was associated with high SMA PSV (24hr: 43.41 ± 14.34 vs.36.30 ± 9.95, 48hr:44.50 ± 8.24 vs. 42.47 ± 15.38) and low EDV(24hr:6.41 ± 4.24 vs. 6.81 ± 2.09,48hr:8.66 ± 3.77 vs. 8.75 ± 4.54) on both the occasions, leading to high RI (0.83 ± 0.11 vs. 0.799± 0.05) and PI (1.82 ± 0.77 vs. 1.85 ± 0.40) compared to preterm with normal hemoglobin. This negative effect of anemia on SMA BFV was significant on day 2, resulting high PI (2.21 ± 0.26 vs. 1.84 ± 0.36*) and high RI (0.84 ± 0.02 vs. 0.78 ± 0.06).Similar influence of anemia was observed in CA, high PSV (24hr: 68.91 ± 9.89 vs. 48.98 ± 13.65 *) and low EDV.

Sepsis (n=4; table1) was associated with high CA BFV (PSV: 61.25 ± 12.33 vs. 50.52 ± 14.69, EDV: 22.82 ± 5.44 vs. 14.72 ± 6.53, P 0.02, TAV: 39.50 ± 11.79 vs. 27.23 ± 9.13, P 0.01) on day 1 and similar influence on mesenteric circulation was noted, which was not statistically significant.

Trophic feeding (n=7 at 24hr/21 at 48hr; table1) was associated with positive influence on SMA and CA velocities. SMA TAV (20.31 ± 9.16 Vs. 16.15 ± 4.99, P 0.044) was higher in trophic fed infants on day 2.

SGA preterm (n=20; table1) had low SMA velocities compared to AGA (n=30), whereas CA BFV were comparable in both the groups.

Discussion

Pulse wave Doppler has been used as a non-invasive parameter to assess the intestinal BFV in human newborns by measuring the blood flow in SMA and CA. Although there are some reports of physiological changes in intestinal blood-flow velocity after birth in healthy term infants [11,12] little is known about these changes in immature high risk preterm. To understand the maturation of intestinal circulation and pathophysiology of intestinal diseases in this population, we studied postnatal blood-flow velocity pattern in SMA, CA and factors influencing the blood flow by means of pulse Doppler ultrasound. Values at 24hr (20-30) were used as baseline reference values for the comparison.

Pappci et al. [1] and Coombs et al. [11], reported significant increase in SMA PSV and other velocities postnatally during the first month although velocities directly proportional to GA. Matsova et al. [3] and Kocvaroval et al. [13] showed significant increase in all SMA BFV resulting in low RI and PI in term and late preterm respectively. Agata et al. [12] and Martinussen [14] reported significant increase in SMA EDV compared to PSV in term infants during first 96hr of life, which predicts the improved intestinal perfusion compared to RI and other velocities. We also report that progressive increase in SMA BFV postnatally with significant increase in EDV and PSV-a finding in agreement with other investigators, which reflects improved intestinal perfusion. RI reflects vascular resistance, thus the index is inversely related to blood flow. A change in vascular resistance is presumed to influence diastolic BFV more than peak systolic BFV [14]. Under normovolemic conditions, the increase in PSV, EDV and TAV in the SMA are caused by a redistribution of abdominal systemic blood flow, because of the progressive opening of vascular beds due to a decrease in peripheral resistance under the influence of physiological factors like increasing blood pressure, increasing stroke volume and closure of the ductus arteriosus [2].

Pappci et al. [1] and Matsova et al. [3] in their studies showed positive trend in CA PSV, whereas CA EDV and TAV showed reducing trend resulting high RI and PI in preterm and term newborn. We reported negative trend in all CA velocities in first 48hr after birth resulting significantly high RI and PI – a finding in agreement with other reports possibly because of complex tributary system of celiac circulation [1].

Effect of significant PDA is not widely reported in CA, as it was studied in SMA. SMA EDV has been reported to decrease with symptomatic PDA [11,15,16]. Frank et al. [17] reported high SMA PSV and negative EDV with significant PDA with normalization to reference values after PDA closure. SMA diastolic BFV and TAV increases after closure of the ductus arteriosus with indomethacin was reported by Jakob et al. [18] and Shimada et al. [19]. El-Khuffash et al. [20] reported lower CA BFV in presence of PDA in his recent study. Consistent with these reports, our study also showed abnormal SMA (high PSV and low EDV) and abnormal CA BFV in presence of significant PDA.

Banerjee et al. [21] reported no significant change in SMA velocities after blood transfusion in ELBW preterm in agreement with other studies in term and old preterm infants. Pitzele et al. [22], demonstrated attenuated BFV response (low PSV) immediately post-transfusion in VLBW preterm. Nelle et al. [23] reported post-

transfusion decrease CA BFV in stable preterm. Our study showed compromised intestinal blood flow after transfusion in study population although effect was significant in CA (high PSV).

In the present study, the presence of UAC did not have any adverse effect on the SMA and CA BFV – a finding that is in agreement with other investigators [24,25]. Position of UAC was confirmed with a follow up x-ray done after the insertion (all the infants in the study population had high position UAC). We observed slightly low PSV in both major arteries with UAC in situ without compromising the perfusion. Roll et al. [24] and Shah et al. [25] demonstrated that there was no difference in blood-flow velocities in the SMA and celiac axis before and after removal of a UAC in the high position. On the contrary, Rand et al. [26] showed low PSV with the UAC in situ. Havranek et al. [27] concluded that Pre-prandial and postprandial SMA BFV responses to minimal enteral feedings were not affected by the presence of a UAC.

Delay in the introduction of enteral feed is major cause for postnatal growth restriction adding to the morbidity in preterm infants [28-30]. Enteral feeding is essential for the promotion of intestinal maturation and growth, as it increases the intestinal blood flow, stimulates intestinal motility and induces release of trophic factors. Leidig et al. [31] and Fang et al. [32] reported significant increase in PSV after feeding in preterm infants hence concluded positive correlation between increase SMA velocities and feed tolerance. Other investigators, Martinussen et al. [4] and Thompson et al. [33], reported increase pre-prandial SMA EDV and increase SMA PSV after trophic feed respectively. In agreement with these reports, our study showed higher velocities in both major arteries after trophic feeding indicating improved perfusion.

Animal models demonstrate that anemia can impair gut blood flow and increase oxygen extraction as a compensatory mechanism [34,35]. Dani et al. [36] and Grisen et al. [37] showed no change in SMA BFV in anemic preterm secondary to autoregulation, which was in agreement with two other studies, which showed that SMA BFV parameters were not altered by anaemia [2,38]. Effect of anemia on CA BFV not studied previously in preterm infants. Our study concluded that anemia is associated with compromised intestinal blood flow (more in SMA) in high risk preterm, which needs to be studied in larger trial.

Kempley et al. [39] reported a similar effect to adult systemic inflammatory response in preterm with sepsis in both SMA and CA, although significant effect in later vessel. In agreement with this report-our study reported increased velocities in culture positive septic preterm infants with significant hyperemia in celiac circulation, which may result in increased cardiovascular demands in sepsis. Consistent with previous report [40], our study demonstrated low SMA BFV in SGA preterm compared to AGA; whereas CA BFV in both the groups were comparable.

This is clinically relevant study, which gives us a basic idea of baseline blood velocity pattern in two major arteries in high risk preterm infants. This study contributes to understand the physiological changes at the major viscera during the postnatal period. This study not only identifies the various factors influencing the intestinal blood flow pattern, but also describes the rate at which blood flow is affected. The main strengths of this study were, it's prospective and adequately subjects size population. The other advantages were the strict inclusion and exclusion criteria. On the other hand, the study

had some limitations. Firstly, it was not a randomized trial and was conducted at single centre.

Conclusion

High risk preterm infants showed improved intestinal perfusion associated with increased SMA velocities after birth. CA BFV showed opposite trend in the same period. Preterm with significant PDA have attenuated blood velocities in both arteries.

Conflict of Interest

The authors declare no conflict of interest

References

1. Patrizia P, Carmen G, Francesco C, Caterina L, Carla MS, et al. (2009) Neonatal colour Doppler ultrasound study: normal values of abdominal blood flow velocities in the neonate during the first month of life. *Pediatr Radiol* 39:328-335.
2. Havranek T, Thompson Z, Carver JD (2006) Factors that influence mesenteric artery blood flow velocity in newborn preterm infants. *J Perinatol* 26:493-497.
3. Matasova K, Dokus K, Zubor P, Danko J, Zibolen M (2011) Physiological changes in blood flow velocities in the superior mesenteric and coeliac artery in healthy term fetuses and newborns during perinatal period. *J Matern Fetal Neonatal Med* 24:827-832.
4. Martinussen M, Brubakk AM, Linker DT, Vik T, Yao AC (1994) Mesenteric blood flow velocity and its relation to circulatory adaptation during the first week of life in healthy term infants. *Pediatric Res* 36: 334-339.
5. Ilves P, Lintrop M, Talvik I, Muug K, Asser K, Veinla M (2008) Developmental changes in cerebral and visceral blood flow velocity in healthy neonates and infants. *J Ultrasound Med* 27: 199-207.
6. Matheson PJ, Wilson MA, Garrison RN (2000) Regulation of intestinal blood flow. *J Surg Res* 93: 182-196.
7. Jacobson E (1991) The splanchnic circulation. *Gastrointestinal Physiology*, Mosby Year Book, St Louis, MO. Pp:142-161.
8. El-Khuffash AF, Slevin M, McNamara PJ, Molloy EJ (2011) Troponin T, N-terminal pro natriuretic peptide and a patent ductus arteriosus scoring system predict death before discharge or neurodevelopmental outcome at 2 years in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 96: 133-137.
9. Kluckow M, Jeffery M, Gill A, Evans N (2014) A randomized placebo-controlled trial of early treatment of the patent ductus arteriosus. *Arch Dis Child Fetal Neonatal Ed* 99: 99-104.
10. McNamara PJ, Sehgal A (2007) Towards rational management of the patent ductus arteriosus: the need for disease staging. *Arch Dis Child Fetal Neonatal Ed* 92: 424-427.
11. Coombs RC, Morgan ME, Durbin GM, Booth IW, McNeish AS (1992) Doppler assessment of human neonatal gut blood flow velocities: postnatal adaptation and response to feeds. *J Pediatr Gastroenterol Nutr* 15: 6-12.
12. Agata Y, Hiraishi S, Misawa H, Hirota H, Nowatari M (1994) Regional blood flow distribution and left ventricular output during early neonatal life: a quantitative ultrasonographic assessment. *Pediatr Res* 36: 811.
13. Kocvarova L, Mackovicova L, Matasova K, Jessica M (2011) Early postnatal changes in the superior mesenteric artery blood flow parameters in late preterm newborns. *J Matern Fetal Neonatal Med* 24: 827-832.
14. Martinussen M, Odden JP, Brubakk AM, Vik T, Bratlid D (1996) Validity of Doppler measurements of superior mesenteric artery blood flow velocity: comparison with blood flow measured by microsphere technique. *Eur J Ultrasound* 4: 55-62.
15. Van Bel F, Van Zwieren PH, Guit GL, Schipper J (1990) Superior mesenteric artery blood flow velocity and estimated volume flow duplex Doppler US study of preterm and term neonates. *Radiology* 174: 165-169.
16. Wong SN, Lo RN, Hui PW (1990) Abnormal renal and splanchnic arterial Doppler pattern in premature babies with symptomatic patent ductus arteriosus. *J Ultrasound Med* 9: 125-130.
17. Frank VB, Schipper J, Guit GL, Margotvan DB (1995) Blood velocity wave form characteristics of superior mesenteric artery and anterior cerebral artery before and after ductus arteriosus closure. *Eur J Ultrasound* 2: 183-189.
18. Jakob SM (2002) Clinical review: Splanchnic ischemia. *Crit Care* 6: 306-312.
19. Shimada S, Kasai T, Konishi M, Fujiwara T (1994) Effect of patent ductus arteriosus on left ventricular output and organ blood flows in preterm infants with respiratory distress syndrome treated with surfactant. *J Pediatr* 125: 270-277.
20. El-Khuffash A, Higgins M, Walsh K, Molloy EJ (2008) Quantitative Assessment of the Degree of Ductal Steal Using Celiac Artery Blood Flow to Left Ventricular Output Ratio in Preterm Infants. *Neonatology* 93: 206-212.
21. Banerjee J, Leung TS, Aladangady N (2016) Effect of blood transfusion on intestinal blood flow and oxygenation in extremely preterm infants during first Week of life. *Transfusion* 56: 808-815.
22. Pitzele A, Rahimi M, Armbrrecht E, Havranek T (2015) Packed red blood cell transfusion (PRBC) attenuates intestinal blood flow responses to feedings in pre-term neonates with normalization at 24 hours. *J Matern Fetal Neonatal Med* 28: 1770-1773.
23. Nelle M, Hocker C, Eugen PZ, Linderkamp O (1994) Effects of red cell transfusion on cardiac output and blood flow velocities in cerebral and gastrointestinal arteries in premature infants. *Arch Dis Child Fetal Neonatal Ed* 71: F45-F48.
24. Roll C, Hansler L (1998) Effect of umbilical arterial catheters on intestinal blood supply. *Acta Paediatr* 87: 955-959.
25. Shah JB, Bracero LA, Gewitz MH, Fish BG, Dweck HS (1998) Umbilical artery catheters and blood flow velocities in the superior mesenteric artery: effect of insertion, removal, aspiration, and bolus infusion. *J Clin Ultrasound* 26: 73-77.
26. Rand T, Weninger M, Kohlhauser C, Bischof S, Heinz-Peer G, et al. (1996) Effects of umbilical arterial catheterization on mesenteric hemodynamics. *Pediatr Radiol* 26: 435-438.
27. Havranek T, Johanboeke P, Madramootoo C, Carver JD (2007) Umbilical artery catheters do not affect intestinal blood flow responses to minimal enteral feedings. *J Perinatol* 27: 375-379.
28. Lemons JA, Bauer CR, Oh W, Korones SB, Papile L, et al. (2001) Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 through December 1996. *Pediatrics* 107: e1-e11.
29. Clark RH, Thomas P, Peabody J (2003) Extrauterine growth restriction remains a serious problem in prematurely born neonates. *Pediatrics* 111: 986-990.
30. Reber KM, Nankervis CA, Nowicki PT (2002) Newborn intestinal circulation Physiology and pathophysiology. *Clin Perinatol* 29: 23-39.
31. Leidig E (1989) Pulsed Doppler ultrasound blood flow measurements in the superior mesenteric artery of the newborn. *Pediatr Radiol* 19: 169-172.
32. Fang S, Kempley ST, Gamsu HR (2001) Prediction of early tolerance to enteral feeding in preterm infants by measurement of superior mesenteric artery blood flow velocity. *Arch Dis Child Fetal Neonatal Ed* 85: 42-45.
33. Thompson A, Cicero TS, Semih AG, Wang D, Ehrenkranz RA (2014) Intestinal Blood Flow by Doppler Ultrasound: The Impact of Gestational Age and Time from First Enteral Feeding in Preterm Neonates. *Amer J Perinatol* 31: 261-268.
34. Krimmel G, Baker R, Yanowitz T (2009) Blood transfusion alters the superior mesenteric artery blood flow velocity response to feeding in premature infants. *Am J Perinatol* 26: 99-105.

-
35. Szabo JS, Mayfield SR, Oh W, Stonestreet BS (1987) Postprandial gastrointestinal blood flow and oxygen consumption: effects of hypoxemia in neonatal piglets. *Pediatr Res* 21: 93-98.
 36. Dani C, Pratesi S, Fontanelli G, Barp J, Bertini G (2010) Blood transfusions increase cerebral, splanchnic, and renal oxygenation in anemic preterm infants. *Transfusion* 50: 1220-1226.
 37. Greisen G, Pryds O, Rosen I, Lou H (1988) Poor reversibility of EEG abnormality in hypotensive preterm neonates. *Acta Paediatr Scand* 77: 785-790.
 38. Abu-Amarah I, Ajikobi DO, Bachelard H, Cupples WA, Salevsky FC (1998) Responses of mesenteric and renal blood flow dynamics to acute denervation in anesthetized rats. *Am J Physiol* 275: 1543-1552.
 39. Kempley ST, Murdoch E (2000) Splanchnic hemodynamic disturbances in perinatal sepsis. *Arch Dis Child Fetal Neonatal Ed* 83: 139-142.
 40. Maruyama K, Koizumi T (2001) Superior mesenteric artery blood flow velocity in small for gestational age infants of very low birth weight during the early neonatal period. *J Perinat Med* 29: 64-70.