Published in final edited form as:

World J Pediatr Congenit Heart Surg. 2017 January ; 8(1): 62–68. doi:10.1177/2150135116668833.

Preoperative feeding and necrotizing enterocolitis: Is the fear justified?

Carly J Scahill, DO,

Department of Pediatrics, Division of Pediatric Cardiology, Medical University of South Carolina,
165 Ashley Ave MSC 915, Charleston, SC 29425

Eric M Graham, MD,

Department of Pediatrics, Division of Pediatric Cardiology, Medical University of South Carolina,
165 Ashley Ave MSC 915, Charleston, SC 29425

Andrew M Atz, MD,

Department of Pediatrics, Division of Pediatric Cardiology, Medical University of South Carolina,
165 Ashley Ave MSC 915, Charleston, SC 29425

Scott M Bradley, MD,

Department of Surgery, Division of Pediatric Cardiothoracic Surgery, Medical University of South Carolina, 96 Jonathan Lucas St, Charleston, SC 29425

Minoo N Kavarana, MD, and

Department of Surgery, Division of Pediatric Cardiothoracic Surgery, Medical University of South Carolina, 165 Ashley Ave, Charleston, SC 29425

Sinai C Zyblewski, MD

Department of Pediatrics, Division of Pediatric Cardiology, Medical University of South Carolina,
165 Ashley Ave MSC 915, Charleston, SC 29425

Abstract

Background—The potential for necrotizing enterocolitis (NEC) in neonates undergoing cardiac surgery has contributed largely to wide feeding practice variations and a hesitation to initiate enteral feeding during the preoperative period, specifically those patients with hypoplastic left heart syndrome.

Methods—A retrospective chart review of neonates undergoing cardiac surgery at a single institution between July 2011 and July 2013 was performed. The primary objective of this study was to determine if preoperative feeding was associated with necrotizing enterocolitis (NEC) in

Corresponding Author: Carly J. Scahill, DO, ¹Department of Pediatrics, Division of Pediatric Cardiology, Medical University of South Carolina, 165 Ashley Ave MSC 915, Charleston, SC 29425, Phone number: (843) 792-3300, Fax number: (843) 792-5878, scahill@musc.edu.

Meeting Presentations

1. Pediatric Cardiac Intensive Care Society's 10th International Conference, Miami, December 12, 2014
2. The 18th Annual Update on Pediatric and Congenital Cardiovascular Disease, Scottsdale, February 13, 2015

Conflict of Interest:

The authors declare that they have no conflict of interest

neonates requiring cardiac surgery. Univariable and multivariable analyses were performed to evaluate the relationship between preoperative feeding and NEC. Secondary outcomes including growth failure, total ventilator days and total length of stay were analyzed.

Results—One hundred thirty consecutive neonates who required cardiac surgery were included in the analysis. Preoperative feeding occurred in 61% (n=79). The overall prevalence of NEC was 9% (12/130), including 3 neonates with surgical NEC. There was no difference in the prevalence of NEC between the preoperative feeding and nil per os (NPO) groups. NPO preoperatively was associated with longer ventilator dependent days (p=0.01) but was not associated with worsened growth failure or longer length of stay.

Conclusion—In this study cohort, preoperative feeding was not associated with NEC. Larger prospective studies evaluating the safety and benefits of preoperative feeding in cardiac neonates are warranted.

Keywords

Congenital heart surgery; Congenital heart disease; Intensive care; Neonate; Nutrition; Preoperative care; Outcomes

Introduction

Congenital heart disease (CHD) is a well described risk factor for necrotizing enterocolitis (NEC). [1–7] The incidence of NEC in infants with CHD has been reported between 3.3 and 6.8%, which is 10- to 100-fold greater risk than that of the late pre-term and term newborn population. [3, 5] The potential for NEC in neonates undergoing cardiac surgery has contributed largely to wide feeding practice variations and a hesitation to initiate enteral feeding during the preoperative period, specifically those patients with hypoplastic left heart syndrome (HLHS).[8, 9]

The etiology of NEC in CHD infants is thought to be different from NEC in preterm infants. (3, 7, 10) Mesenteric hypoperfusion is believed to be a possible contributor to NEC in CHD infants.[3, 10–12] This is particularly true in patients with cardiac defects at risk for diastolic steal and flow reversal in the abdominal aorta. This diastolic steal phenomena has been described in patients with a large patent ductus arteriosus, ductal dependent lesions, shunted single ventricle physiology, truncus arteriosus and aortopulmonary window. [1, 2, 5, 6, 13] Additionally, low cardiac output states, possible intrinsic microvascular abnormalities, and compensatory mechanisms such as the “diving reflex” contribute to risks for mesenteric hypoperfusion. [11, 13]

Given wide inter-provider and institutional practice variation and the paucity of data regarding preoperative feeding in neonates with complex CHD, the objective of this study was to determine if preoperative enteral feeding was associated with NEC in neonates undergoing cardiac surgery.

Patients and Methods

The study design was a retrospective chart review of all neonates (≥ 31 days of age at admission) admitted to the pediatric cardiac intensive care unit who required neonatal cardiac surgery at the Medical University of South Carolina between July 2011 and July 2013. The Medical University of South Carolina's Institutional Review Board approved this study and a waiver of the need for parental consent. Exclusion criteria included infants who required extracorporeal membrane oxygenation support and those infants whose only surgery was either a patent ductus arteriosus ligation or pacemaker implantation. The primary risk factor was exposure to any amount of enteral feeds during the preoperative period. The primary outcome of interest was diagnosis of Modified Bell Stage IIa or higher NEC, either prior to or following cardiac surgery.[14] Furthermore, we investigated for an association between volume of feeds and NEC. Additional variables controlled for in multivariable analysis included single ventricle physiology, structural gastrointestinal abnormality, confirmed genetic abnormality, presence of umbilical artery catheter, need for inotropic support during the preoperative period, ductal dependence for systemic circulation and gestational age < 37 weeks. These variables were chosen because they have been previously described as potential risk factors for NEC in the literature. [1–3, 5, 6, 9, 10, 15, 16] Secondary outcomes included growth failure, measured by change in weight for age Z score (WAZ) from hospital admission to hospital discharge, total ventilator dependent days, total hospital length of stay and total intensive care unit length of stay.

Statistical methods

Means were compared on all normally distributed data using independent two-sample t-test. Mann-Whitney U test was used to compare medians on all nonparametric data. Cochran Mantel-Haenszel was used for univariable analysis. Multivariable analysis was preformed using a stepwise backward elimination logistic regression model with a removal probability of 0.3. Statistical analysis was completed with *IBM SPSS Statistics for Mac, Version 22.0* (SPSS, Inc. Chicago, IL). P values < 0.05 were considered statistically significant.

Results

There were 130 consecutive neonates who required cardiac surgery between July 2011 and July 2013 that met study inclusion/exclusion criteria. The cohort consisted of 24 subjects with hypoplastic left heart syndrome (19%) and 54 subjects with other single ventricle physiology (42%). Seventy-two subjects were ductal dependent for systemic circulation (55%). Eighty subjects had an umbilical artery catheter preoperatively (62%). Twenty-seven subjects were on inotropic support preoperatively (21%). Thirty-three subjects had a confirmed genetic abnormality (25%), 12 had a structural gastrointestinal abnormality (9%), and 19 were less than 37 weeks gestation (15%).

In this study cohort, 61% of neonates received enteral feeds ($n=79$) during the preoperative period. Amongst those who received enteral feeds during the preoperative period, 33 subjects received trophic feeds ($< 20\text{cc/kg/day}$), 32 subjects received greater than trophic feeds, and 14 subjects did not have specific volumes recorded in their medical records. Of

the patients with hypoplastic left heart syndrome, 54% were fed preoperatively with the majority (82%) fed only trophic volumes.

The prevalence of NEC in the entire cohort was 9% (12/130). There was no difference in the prevalence of NEC between the preoperatively fed and NPO groups ($p=0.43$). Of the patients receiving preoperative feeds 8% developed NEC (6/79). Of the patients who remained NPO preoperatively 12% developed NEC (6/51). Fig I. The prevalence of Modified Bell Stage IIIB NEC requiring surgical bowel resection was 2% ($n=3$). Of the 3 patients with surgical NEC, 1 subject was fed preoperatively. Among the 12 NEC affected subjects, 5 subjects had hypoplastic left heart syndrome, 3 had truncus arteriosus, 1 had a right ventricular dominant atrioventricular septal defect, 1 had interrupted aortic arch, ventricular septal defect and left ventricular outflow tract obstruction, 1 had d-transposition of the great arteries and 1 had a complex single ventricle (right ventricular dominant atrioventricular defect, double outlet right ventricle, transposition of the great arteries and pulmonary stenosis). All but one of the NEC affected subjects developed NEC postoperatively and all subjects with NEC survived to hospital discharge. No neonate admitted to the PCICU during the study period died as a result of NEC prior to undergoing cardiac surgery. There were no significant differences in patient demographics between the NEC group and the non NEC group. Table 1.

In univariable analysis, preoperative enteral feeding was not found to be associated with NEC (OR 0.62, CI 0.19–2.0, $p=0.43$). Additionally, higher volume feeds (> 20 cc/kg/day) was not associated with NEC (OR 4.04, CI 0.49 – 33.3, $p= 0.19$). In the multivariable analysis, preoperative enteral feeding was not associated with NEC ($p=0.38$). Table 2. Prematurity was the only variable associated with NEC ($p= 0.03$).

Secondary outcomes are reported in Table 3. Subjects who received enteral feeds in the preoperative period had less ventilator dependent days compared to subjects who remained NPO preoperatively, 5 days versus 7 days ($p =0.01$). However, there were no differences in hospital length of stay, intensive care unit length of stay or change in WAZ from hospital admission to hospital discharge.

Comment

In this study cohort of neonates undergoing cardiac surgery, enteral feeding during the preoperative period was not associated with development of NEC. These findings suggest that with appropriate risk stratification and monitoring, term gestation neonates with complex anatomy including ductal dependence for systemic circulation and single ventricle physiology can be safely fed during the preoperative period. Our study findings are relevant given the wide practice variation in perioperative feeding practices.[8, 9] Additionally, early postnatal nutrition and growth have been identified as key modifiable risk factors for long-term neurodevelopmental outcomes.[17,18]

While withholding enteral feeding preoperatively may seem like a protective strategy to decrease the risk of NEC, delayed enteral feeding may be incurring more harm than benefit. Neonates who undergo cardiac surgery have altered intestinal permeability extending into

post-operative day 14.[19] Drawing from the literature on preterm infants, delayed enteral feeding contributes to cellular atrophy in the gut, pathologically abnormal increases in gut permeability, delayed postnatal intestinal development and maturation, and motility problems.[20–22]. Early enteral feeding may be an important component of optimizing perioperative nutrition practices given its essential role in postnatal intestinal barrier maturation, cellular and mucosal development, and establishment of a healthy intestinal microbiome.[20–24]

There are limitations to this study. The retrospective study design only allows determination of associations and not causality. Additionally, retrospective studies are subject to information bias and lack of randomization. The decision to feed preoperatively was based on physician judgment, which may have led to selection bias. The single center nature of the study limits its external validity and the relatively small sample size increases the risk of a type II error. Original intention was to investigate if type and route of enteral feeds was associated with NEC, however due to missing data this could not be accomplished. Lastly, while transfusion associated necrotizing enterocolitis has been described in the literature it was not controlled for in multivariable analysis.[25] This was intentional given the majority of the cohort was exposed to blood products during cardiopulmonary bypass.

In conclusion, preoperative enteral feeding can be performed safely without increased risk of NEC. Future prospective studies in neonates undergoing cardiac surgery are warranted to further delineate the risks and benefits of preoperative feeding and to identify the best perioperative feeding practices.

Acknowledgments

This work was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) under Award Number T32 HL007710. The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

1. Becker KC, Hornik CP, Cotten CM, Clark RH, Hill KD, Smith PB, et al. Necrotizing Enterocolitis in Infants with Ductal-Dependent Congenital Heart Disease. *American journal of perinatology*. 2014
2. Carlo WF, Kimball TR, Michelfelder EC, Border WL. Persistent diastolic flow reversal in abdominal aortic Doppler-flow profiles is associated with an increased risk of necrotizing enterocolitis in term infants with congenital heart disease. *Pediatrics*. 2007; 119(2):330–5. [PubMed: 17272623]
3. Giannone PJ, Luce WA, Nankervis CA, Hoffman TM, Wold LE. Necrotizing enterocolitis in neonates with congenital heart disease. *Life sciences*. 2008; 82(7–8):341–7. [PubMed: 18187159]
4. Iannucci GJ, Oster ME, Mahle WT. Necrotising enterocolitis in infants with congenital heart disease: the role of enteral feeds. *Cardiology in the young*. 2013; 23(4):553–9. [PubMed: 23025968]
5. McElhinney DB, Hedrick HL, Bush DM, Pereira GR, Stafford PW, Gaynor JW, et al. Necrotizing enterocolitis in neonates with congenital heart disease: risk factors and outcomes. *Pediatrics*. 2000; 106(5):1080–7. [PubMed: 11061778]
6. Willis L, Thureen P, Kaufman J, Wymore E, Skillman H, da Cruz E. Enteral feeding in prostaglandin-dependent neonates: is it a safe practice? *The Journal of pediatrics*. 2008; 153(6): 867–9. [PubMed: 19014824]

7. Pickard SS, Feinstein JA, Popat RA, Huang L, Dutta S. Short- and long-term outcomes of necrotizing enterocolitis in infants with congenital heart disease. *Pediatrics*. 2009; 123(5):e901–6. [PubMed: 19403484]
8. Pasquali SK, Ohye RG, Lu M, Kaltman J, Caldarone CA, Pizarro C, et al. Variation in perioperative care across centers for infants undergoing the Norwood procedure. *The Journal of thoracic and cardiovascular surgery*. 2012; 144(4):915–21. [PubMed: 22698562]
9. Wernovsky G, Ghanayem N, Ohye RG, Bacha EA, Jacobs JP, Gaynor JW, et al. Hypoplastic left heart syndrome: consensus and controversies in 2007. *Cardiology in the young*. 2007; 17(Suppl 2): 75–86. [PubMed: 18039401]
10. Hebra A, Brown MF, Hirschl RB, McGeehin K, O'Neill JA Jr, Norwood WI, et al. Mesenteric ischemia in hypoplastic left heart syndrome. *Journal of pediatric surgery*. 1993; 28(4):606–11. [PubMed: 8483077]
11. Young CM, Kingma SD, Neu J. Ischemia-reperfusion and neonatal intestinal injury. *The Journal of pediatrics*. 2011; 158(2 Suppl):e25–8. [PubMed: 21238702]
12. Harrison AM, Davis S, Reid JR, Morrison SC, Arrigain S, Connor JT, et al. Neonates with hypoplastic left heart syndrome have ultrasound evidence of abnormal superior mesenteric artery perfusion before and after modified Norwood procedure. *Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*. 2005; 6(4):445–7.
13. Miller TA, Minich LL, Lambert LM, Joss-Moore L, Puchalski MD. Abnormal abdominal aorta hemodynamics are associated with necrotizing enterocolitis in infants with hypoplastic left heart syndrome. *Pediatric cardiology*. 2014; 35(4):616–21. [PubMed: 24154504]
14. Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Annals of surgery*. 1978; 187(1): 1–7. [PubMed: 413500]
15. Tabbutt S, Ghanayem N, Ravishankar C, Sleeper LA, Cooper DS, Frank DU, et al. Risk factors for hospital morbidity and mortality after the Norwood procedure: A report from the Pediatric Heart Network Single Ventricle Reconstruction trial. *The Journal of thoracic and cardiovascular surgery*. 2012; 144(4):882–95. [PubMed: 22704284]
16. Ravishankar C, Zak V, Williams IA, Bellinger DC, Gaynor JW, Ghanayem NS, et al. Association of impaired linear growth and worse neurodevelopmental outcome in infants with single ventricle physiology: a report from the pediatric heart network infant single ventricle trial. *The Journal of pediatrics*. 2013; 162(2):250–6. e2. [PubMed: 22939929]
17. Zyblewski SC, Nietert PJ, Graham EM, Taylor SN, Atz AM, Wagner CL. Randomized Clinical Trial of Preoperative Feeding to Evaluate Intestinal Barrier Function in Neonates Requiring Cardiac Surgery. *The Journal of pediatrics*. 2015; 167(1):47–51. e1. [PubMed: 25962930]
18. Berseth CL. Effect of early feeding on maturation of the preterm infant's small intestine. *The Journal of pediatrics*. 1992; 120(6):947–53. [PubMed: 1593357]
19. Mishra S, Agarwal R, Jeevasankar M, Deorari AK, Paul VK. Minimal enteral nutrition. *Indian journal of pediatrics*. 2008; 75(3):267–9. [PubMed: 18376096]
20. Neu J. Gastrointestinal development and meeting the nutritional needs of premature infants. *The American journal of clinical nutrition*. 2007; 85(2):629S–34S. [PubMed: 17284768]
21. Mallick IH, Yang W, Winslet MC, Seifalian AM. Ischemia-reperfusion injury of the intestine and protective strategies against injury. *Digestive diseases and sciences*. 2004; 49(9):1359–77. [PubMed: 15481305]
22. Maurer I, Latal B, Geissmann H, Knirsch W, Bauersfeld U, Balmer C. Prevalence and predictors of later feeding disorders in children who underwent neonatal cardiac surgery for congenital heart disease. *Cardiology in the young*. 2011; 21(3):303–9. [PubMed: 21272426]
23. Mohamed A, Shah PS. Transfusion associated necrotizing enterocolitis: a meta-analysis of observational data. *Pediatrics*. 2012; 129(3):529–40. [PubMed: 22351894]

Figure 1.

Table 1

Patient Demographics

Patient Characteristic	NEC (n=12)	No NEC (n=118)	P-value
Age at surgery, days (SD ^a)	8 (13)	10 (13)	0.22
Admission WAZ (SD)	-1.06 (0.8)	-1.0 (1.2)	0.54
Weight at surgery, kg (SD)	2.9 (0.4)	3.1 (0.6)	0.22
Gender n (%)			0.16
Male	10 (83%)	73 (62%)	
Race n (%)			0.58
Caucasian	5 (42%)	67 (57%)	
Black	6 (50%)	34 (29%)	
Hispanic	1 (8%)	13 (11%)	
Other	0 (0%)	4 (3%)	

^aSD = Standard Deviation

Table 2

Multivariable Logistic Regression Analysis: Patient variables associated with NEC

Patient variables ^a	Odds ratio	p-value
Preoperative feeds	1.8	0.38
Gestational age < 37 weeks	5.8	0.03
Structural gastrointestinal abnormality	4.5	0.08
Hypoplastic left heart syndrome	3.9	0.07
Genetic abnormality	2.2	0.29

^aStepwise backward elimination logistic regression using a removal probability of 0.3. Variables eliminated from model include: prostaglandins for systemic circulation, inotropic support, umbilical artery catheter and single ventricle physiology

Table 3

Secondary Outcomes in Preoperative Feed vs. No Preoperative Feed Groups

Patient Outcomes	Pre-op Feeds	No Pre-op Feeds	p-value
Duration of mechanical ventilation, days (SD ^a)	5 (14)	7 (17)	0.01
ICU ^b length of stay, days (SD)	16 (21)	15 (28)	0.61
Hospital length of stay, days (SD)	34 (41)	28 (46)	0.24
Change in WAZ (SD)	-0.72 (1.3)	-0.68 (2.3)	0.88

^aSD = Standard Deviation^bICU = Intensive Care Unit