TITLE: Enteral feeding practices in infants with congenital heart disease across European Pediatric Intensive Care Units: a European Society of Pediatric and Neonatal Intensive Care (ESPNIC) survey

CORRESPONDING AUTHOR: Lyvonne N Tume

Tume LN, Balmaks R, da Cruz EM, Latten L, Verbruggen S, Valla FV.

Lyvonne N Tume RN PhD
Associate Professor in Child Health
Faculty of Health and Applied Sciences
University of West of England, Bristol, UK
Glenside Campus
Blackberry Hill
Stapleton
Bristol
BS16 1DD
Lyvonne.Tume@UWE.ac.uk
+44 07710 412142

Reinis Balmaks MD, Dr. Med.
Assistant professor
Department of Clinical Skills and Medical Technologies
Riga Stradins University
16 Dzirciema
Riga, LV-1007
Latvia
reinis.balmaks@rsu.lv
+371-26535074

Eduardo da Cruz MD
Associate Medical Director, CHCO Heart Institute
Head, Pediatric Cardiac Critical Care Program & Inpatient Services
Director, Cardiac Intensive Care Unit
Children's Hospital Colorado
Tenured Professor of Pediatrics, Pediatric Cardiology and Intensive Care
University of Colorado Denver, School of Medicine
Eduardo.dacruz@childrenscolorado.org

Lynne Latten RD BSc (Hons)
Specialist Pediatric Dietician,
PICU, Alder Hey Children's NHS FT,
Eaton Rd, Liverpool L12 2AP

Lynne.Latten@alderhey.nhs.uk

Sascha Verbruggen MD, PhD
Consultant in Pediatric Intensive Care Medicine
Pediatric Intensive Care Unit
Erasmus MC - Sophia Children's Hospital
Wytemaweg 80, 3015 CN, Rotterdam,
The Netherlands
s.verbruggen@erasmusmc.nl

Frédéric V Valla MD, MSc
Consultant in Pediatric Intensive Care Medicine
Pediatric Intensive Care Unit
Hôpital Femme Mère Enfant, Hospices Civils de Lyon
59 bd Pinel, 69500 Lyon-Bron, France
Frederic.valla@chu-lyon.fr

On behalf of the members of the ESPNIC pediatric and congenital cardiac intensive care & mechanical circulatory support section, the metabolism-endocrinology-nutrition section, and the nurse science section.

No reprints will be ordered

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Enteral feeding practices in infants with congenital heart disease across European Pediatric Intensive Care Units: a European Society of Pediatric and Neonatal Intensive Care (ESPNIC) survey

Abstract

Objectives: To describe enteral feeding practices in pre and post-operative infants with congenital heart disease(CHD) in European Pediatric Intensive Care Units (PICU).

Design: Cross-sectional electronic survey

Setting: European pediatric intensive care units that admit infants with congenital heart disease pre and post-operatively.

Participants: One senior PICU physician or designated person per unit.

Interventions: None

Measurements and Main Results: Fifty nine PICUs from 18 European countries responded to the survey. PICU physicians were involved in the nutritional care of children with CHD in most (76%) PICUs, but less than 60% of units had a dedicated dietician. Infants with CHD were routinely fed pre-operatively in only 63% of the PICUs, due to ongoing concerns around prostaglandin (PGE1) infusion, the presence of umbilical venous and/or arterial catheters and the use of vasoactive drugs. In three quarters of the PICUs (76%) infants were routinely fed during the first 24 hours post-operatively. Units cited, the most common feeding method, both pre and post-operatively, was intermittent bolus feeds via the gastric route. Importantly, 69% of European PICUs still did not have written guidelines for feeding, but this varied for pre and post-operative patients.

Conclusions: Wide variations in practices exist in the nutritional care between European PICUs, which reflects the absence of local protocols and scientific society-endorsed

guidelines. This is likely to contribute to suboptimal energy delivery in this particularly vulnerable group.

INTRODUCTION

Ensuring adequate nutrition is vitally important for infants with congenital heart disease (CHD)(1,2). It is well known that these children, especially those with complex conditions such as single ventricle lesions, have a high incidence of growth delay and poor weight gain (1). Multiple factors including the presence of heart failure, stress of surgery, hepatomegaly, gastrointestinal dysfunction as well as reduced energy intake contribute to this nutritional deficiency (3,4). Furthermore, low weight at the time of surgical intervention is associated with increased mortality in infants with CHD and weight loss after congenital heart surgery predicts late death in these infants (5,6). Yet, commencing enteral feeding in infants with CHD remains inconsistent. Necrotizing Enterocolitis (NEC) is more common in neonates with CHD, especially those with single ventricle physiology (7,8,9). However, increasing evidence supports the safety of feeding these infants enterally both pre and post-operatively, even with single ventricle lesions (10,11,12). Literature remains scarce and most has described practices mainly in North America (13) or in critically ill children generally (14). Some studies have advocated for the use of consistent enteral feeding protocols that require minimal variability in practice (15). We theorized that in Europe, variability of practice with feeding in this fragile patient population is the norm and therefore, our aim in this study was to characterize the enteral feeding practices in pre and post-operative infants with CHD in European Pediatric Intensive care Units (PICUs) and to establish future research questions and priorities across Europe.

MATERIALS AND METHODS

We conducted a cross-sectional electronic survey (on Survey Monkey^{TM}) across European PICUs. A survey instrument developed in the US (13) was adapted by the authors to the European context and piloted on four PICU physicians for clarity and face validity

(Supplementary material). Changes were made after this probing phase, with some questions reworded and one question removed. As the previously published survey only asked about enteral feeding in ductal-dependent infants, we added a further section on post-operative CHD infants. The instrument was further refined within the study team and tested again on three different PICU physicians to improve face validity of the survey instrument. The final instrument was a 54-item closed and open-ended survey (in English). After European Society of Pediatric and Neonatal Critical Care (ESPNIC) approval, Institutional Board review (IRB) was gained in the Netherlands (MEC-2016-759) and the study was approved both by the United Kingdom (UK) Pediatric Intensive Care Society (PICS) Study group and as clinical audit within the UK and Ireland. A country lead addressed any IRB concerns in their country, and consent was implied by survey completion. This individual identified all PICUs that admit infants with CHD in their country. Subsequently, the ESPNIC PICU registry was used to identify and contact one attending physician for the selected PICUs to determine their interest to participate and the need for translation of the survey. Using this approach, we identified and contacted as many PICUs who admitted infants with CHD in Europe as possible. Previously no database of these PICUs existed across Europe. PICUs were only identifiable by country; no other unit-identifiable data was collected. If units agreed, then an email with a link to the e-survey was sent to one PICU Physician (to ensure one response per unit). The survey was undertaken between February and March 2017, with three reminders over a three-week period to maximize the survey response rate. Data was exported from Survey Monkey software Inc (San Mateo, USA) in a CSV file format into Microsoft Excel (Washington, USA) and directly into IBM SPSS v22 (IBM Corp, Armonk NY, USA) for analysis. Analysis was firstly descriptive and inferential analysis of categorical variables done to compare differences between size of unit, cardiac surgical volume, type of medical staffing and European region as defined in the ETHICUS study (16). Cardiac surgical volume was defined as per Hannan et al and Chang et al (17,18) with >170 cases per year defined as a high volume, 70 – 170 as medium volume, and <70 as a low volume centre. PICU physician involvement in care was converted to a binary variable (Yes/No) if a PICU physician was involved as part of the care team. Median and interquartile range (IQR) was used for most data, which was non-normally distributed, with means and standard deviation (SD) used in normally distributed. Chi Square tests were used to determine differences between categorical variables and we considered a p value of <0.05 to be significant; two tailed tests were used.

RESULTS

Fifty-nine PICUs from 18 European countries responded to the survey (Table 1). The mean PICU size was 13.1 beds (SD 5.8), with a mean cardiac surgical volume of 288 cases per year (SD 283). The total range of cases varied from 40 - 750 a year, with 73% units classed as high volume centers. In terms of demographics, around half (29/59; 49%) of the PICUs admitted both general and cardiac patients, whilst 24% (14/59) were specific cardiac PICUs. Ten percent of the units were cardiac only ICUs admitting both children and adults, while 7% were mixed PICU/Neonatal Intensive Care Units (NICUs). In terms of the clinical responsibility for the care of these children, in most (76% 45/59) units a pediatric intensivist was involved in the child's care. However, in 16% units, children were still managed by adult intensivists, cardiac surgeons and anesthesiologists. Respondents from only 38% (22/58) of the responding units stated they had any specialist dietetic input into the management of these children.

Pre-operative enteral feeding practices

Thirty-eight percent (22/59) of respondents stated that pre-operative infants were admitted to the NICU, so the PICU team had little involvement in their management pre-operatively. Children managed in a mixed general and cardiac PICU or a specialized cardiac PICU were significantly more likely to be fed, than if they were admitted to a NICU ($p < 0.001$).

In most units (35/51; 68%) infants had no formal nutritional assessment on admission, and in the 31% of the units where a nutritional assessment was performed, this ranged from a very comprehensive assessment involving anthropometry, biochemistry and history to just weight and length. Infants receiving prostaglandin (PGE1) infusion were routinely fed in only 63% (37/59) of the units. The mean PGE1 dose felt to be safe to feed on was 0.03 micrograms/kg/minute (SD 0.019), however, 28% of clinicians stated that the dose of PGE1 did not matter.

Those units who did not feed, cited the fear of necrotizing enterocolitis (NEC) and poor gut perfusion as the main reason. Only 31% units (17/54) had written guidelines for feeding these infants pre-operatively, but having a protocol was positively associated with enteral feeding ($p = 0.002$). In those units where patients were fed, this was primarily by intermittent bolus gastric feeds (68%) and 77% of the units stated the infants were fed with breast milk (if available) or with a standard 0.65-0.70kcal/ml infant formula. When assessing the factors that affected the clinician's decision to feed enterally, the survey documented that in only half (26/52; 50%) of the units were infants with an umbilical arterial catheter fed, whereas more (36/54; 67%) clinicians would feed if the infant had only an umbilical venous catheter. Just under half (25/54; 46%) of the respondents acknowledged that they would feed infants on vasoactive drugs, and 26% of these stated this was dose-dependent. Table 2 summarizes pre-operative feeding practices.

Parameters clinicians stated their units used to guide readiness to feed and assess feed tolerance pre-operatively for children receiving PGE1 infusion were: serum lactate level (67%); gastric residual volume (GRV) (63%); arterial blood gases (51%); diastolic blood pressure (DBP) (49%); the infants respiratory status (47%); echocardiographic data (45%); arterial oxygen saturation (Spo2) (31%); splanchnic near infra-red spectroscopy (sNIRS) (16%); cerebral near-infrared spectroscopy (cNIRS) (14%); abdominal radiographs (12%) and cerebral:somatic NIRS ratio (6%).

Post-operative enteral feeding practices

A third (30%) of the units stated that all infants would be routinely fed within 12-24 hours after surgery, however, in 54% of the units this practice was surgery or infant-specific. Fewer than half (39%) of the units had specific written guidelines for feeding post-operatively. Around half respondents (48%) cited specific surgical procedures after which their unit would withhold enteral feeding. Those procedures cited were as predominantly left sided obstructive lesions: coarctation of the aorta, aortic arch surgery and Norwood-Sano procedures. However, multiple other conditions or groups of children were cited, such as: Fontans with pleural effusions; infants with an open sternum, those infants on extracorporeal life support (ECLS), those who had received deep hypothermic circulatory arrest (DHCA) or 'unstable' patients. These data were not specific and not analyzed in depth for the purpose of this survey. In most units, (74%) infants with a peritoneal dialysis catheter in situ were fed, and in 64% of the units, infants on ECLS would also be fed. Over half of clinicians (61%) would feed infants receiving vasoactive drugs, but for 35% of them this was dose-dependent. In the nineteen individual responses around dose, 21% would support feeding any child on milrinone regardless of the dose, 21% cited an epinephrine dose of <0.1mcg/kg/minute and 10% a dopamine dose of <5mcg/kg/minute.

In those units where feeding would be started, in just under half (44%) the aim was to achieve specific energy targets post-operatively, but half of the responses related that fluid restriction was the driving factor that determined amount of feeding possible. There were large variations in the energy targets cited by clinicians. Clinicians from twenty-two units responded about their specific energy targets, but this varied hugely, ranging from 30 kcal/kg to 120kcal/kg. Most units (74%) used hypocaloric, trophic enteral feeding with 63% stating the infants would be fed by intermittent bolus via the gastric route. A smaller proportion of units (20%) used continuous feeding via the gastric route and even fewer units (10%) used post-pyloric feeding.

If an infant could not be fed enterally, in 72% of the units they would start parenteral nutrition (PN). However, the timing of commencing PN was variable. Forty-eight units responded to this question, and in 42% (20/48) of them PN would be started within the first 24 hours, in 14% within 48h, and in 12% within the first 48-72 hours. Overall, 69% would initiate PN within the first 3 days after surgery. Table 3 summarizes the feeding practices post-operatively. Parameters used to assess readiness to feed post-operatively were similar to the parameters used pre-operatively (Table 4).

Indications cited by clinicians as concerning to withhold feeds post-operatively were broadly abdominal signs/symptoms (27%) and high gastric residual volumes (27%). Other identified factors were: cardiovascular instability (16%), followed by vomiting (11%), signs of

NEC (7%), bloody stools (6%), high serum lactates (3%), for procedures (3%) and for declining NIRS values (1%).

There was no relationship between unit surgical volume (p=0.123), pediatric intensivist involvement in care (p=0.154), dedicated dietician hours (p=0.948), type of PICU (p=0.717) European region (p=0.665) or the presence of written protocols for feeding (p=0.105) on whether children were routinely fed within the first 24 hours post-operatively. However, larger volume surgical centers appeared to feed children more often, but this was not statistically significant. There was no relationship between involvement of a pediatric intensivist and whether they used trophic feeding (p=0.210), had defined energy targets (p=0.462), whether they fed on vasoactive medications (p=0.378) or whether they fed on ECLS (p=0.187).

DISCUSSION

Although other studies have examined practices around feeding of cardiac infants, this is the first and largest study to specifically examine the pre- and post-operative feeding practices specifically across Europe. Most clinicians representing the analyzed units did not undertake comprehensive nutritional assessments in these children, a recommendation in the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines (19,20). Recommendations for this baseline assessment include the use of anthropometry (21), yet this was rarely done. In this group of children with CHD (unlike many other critically ill children), there is an opportunity to improve pre-operative nutritional assessment.

The likelihood of enteral feeding pre-operatively was significantly impacted by the fact that most units did not have guidelines for feeding pre-operatively, and the fact that many patients were admitted to neonatal units where preoperative feeding was not common practice. There is increasing evidence of the positive impact of multidisciplinary feeding protocols on energy delivery in these infants (11,12). Given the relative simplicity of producing guidelines, this would seem an easy first step in improving enteral nutrition (EN). More units had guidelines for post-operative feeding, which may reflect that post-operatively these infants were more often managed in a PICU rather than NICU but also shows the lack of continuity within a hospital regarding nutrition policies.

In a third of units, infants on PGE1 infusions were still not routinely fed pre-operatively. There are no randomized studies demonstrating the safety of feeding on PGE1. However, more than half of teams do feed these children enterally, and numerous cohort studies suggest that this is safe, if adequately monitored, even in the most severe single ventricle lesions (10,11,22,23). Moreover, achieving adequate nutrition pre-operatively in infants with CHD impacts patient outcomes (5,6,24,25) Interestingly, despite of the fact that in a third of units these infants are not fed, most (82%) clinicians responded that they did not perceive a higher incidence of NEC in the infants that were enterally fed. This suggests a historical fear of adverse outcomes (predominantly NEC) rather than practice based on evidence. We also identified a fear of feeding these infants with umbilical catheters (UAC) in situ. One trial (26) and a prospective observational study (27) in preterm neonates found that having a UAC in situ did not affect mesenteric blood flow or lead to a greater risk of feed intolerance or NEC. Indeed, often the placement of these lines, as opposed to other vascular access, is organizational practice, and does not always correlate to disease severity. We postulate that the fear of these devices may arise from clinicians' experience in pre-term infants. However, a USA survey of neonatal nutrition practices in 2009 (28), reported that 75% of clinicians did feed infants with UACs and 93% with umbilical venous catheters (UVCs), significantly higher than what we found.

Fewer studies have examined practices around enteral feeding post-operatively, except in specific conditions such as single ventricle lesions and Hypoplastic Left Heart Syndrome (HLHS) (10,12-15). Clinicians predominantly cited left sided obstructive lesions, as surgical procedures in which they would delay feeding. However, many responses were heterogeneous, and appeared to relate to local organization-specific practices, with little evidence to support them.

Energy targets post-operatively varied markedly with no uniform practice, which almost certainly relates to lack of guidance for the optimal targets in these infants. One study (29) measured energy expenditure on post-operative patients and suggested a figure of 59kcal/kg/d for non-bypass patients, rising to 74kcal/kg/d for those after cardiopulmonary bypass. Energy expenditure was higher in those who were malnourished pre-operatively. Actual requirements to achieve growth in these infants are poorly defined and predictive equations poorly correlate with actual energy expenditure (29,30). Indirect calorimetry (IC) although recommended, it is only available in a minority (14%) of PICUs internationally (14) and is rarely possible to use in the acute postoperative phase due to the presence of high fraction of inspired oxygen (FiO2) , endotracheal tube leaks, pleural air leaks or intra-cardiac shunting.

European clinicians remain concerned about enteral feeding on vasoactive drugs, but post-operatively, concerns appeared to be dose-dependent. Little evidence exists to support the safety of feeding on vasoactive medicines in critically ill children or neonates. One prospective study (31) has investigated the safety of post-pyloric feeding in critically ill children in shock and found this safe, although with higher gastrointestinal complications than in children without shock. A further retrospective study found enteral feeding in critically ill children receiving vasoactive drugs posed no greater gastrointestinal complications than not feeding, and showed a trend to lower mortality (32).

There are few studies to determine the best parameters to monitor feed tolerance or predict risks either pre or post-operatively in infants with CHD. A prospective pilot study found low mesenteric NIRS at admission (33) was associated with gastrointestinal complications and feeding tolerance in children after heart surgery. However, the value of the most commonly cited parameters such as gastric residual volume (GRV) and serum lactate levels remain unknown. The use of GRV in particular is being increasingly challenged in critically ill patients as a poorly valid marker of feeding tolerance (34). Raised serum lactate levels after pediatric heart surgery are correlated with poor outcomes (35), thus might be justifiable as a marker of increased enteral feeding risk, however, the threshold risk level is unknown.

There is little evidence to support the optimal method of enteral feeding in infants with CHD. A small, randomized trial in critically ill children, compared gastric EN using bolus versus continuous instillation and demonstrated no difference in gastrointestinal complications (36). However, a randomized trial of post-pyloric (small bowel) versus gastric feeding in critically ill children showed better achievement of energy targets in the small bowel fed group, with no difference in complications (37).

We found that when the decision not to enterally feed was made, most respondents stated their unit would initiate parenteral nutrition (PN) within 3 days of admission. Although, a randomized trial in 1440 critically ill children (39% of whom were cardiac surgical) suggests that delaying PN for up to a week was superior to early PN (38), the optimal timing of PN initiation is still debated.

European Pediatric intensivists, appear to exercise some caution in enteral feeding of these infants, in relation to the perceived risk of NEC. NEC is clearly a condition that can be catastrophic, but that remains multifactorial and has not been shown to be affected by enteral feeding in large cohort studies (7, 8, 39, 40). The incidence of NEC in CHD infants, is relatively low 0.3% – 3.3% (7,8,9) (and severe forms of NEC are even rarer) although in single ventricle lesions it is higher. However, 57% of the CHD infants who developed NEC in the aforementioned studies were <37 weeks gestation, prematurity being a risk factor for NEC in this setting. Indeed, preterm neonates are a different population per se, with a higher risk of NEC (regardless the presence of CHD) of around 5-12% (39, 40) (an incidence that varies dependent on the definition). We speculate that European pediatric intensivists may be influenced regarding their perception of risk of NEC and feeding by their experience and former training in neonatology. Recent neonatal studies however support that delaying starting EN does not reduce the incidence of NEC and feeding with maternal milk reduces the incidence of NEC (39, 40). However, the pathophysiology of NEC in terms infants with CHD may be different, affected by inadequate gut perfusion or hemodynamic compromise rather than by immaturity.

This study has a number of limitations that we acknowledge. As with any survey there is the bias of self-reporting, which provides no validation of the accuracy of the data provided, and we asked only one clinician to respond per unit, which was intentional to reduce conflicting data but may influence its own bias. Additionally, based on previous point-prevalence surveys (14) reported practices may reflect a more positive situation than what actually occurs. Despite our best efforts, we could not identify contacts in all European countries, although responses from 59 PICUs in 18 European countries make this the largest survey of feeding in infants with CHD within Europe, other surveys have mainly represented a North American perspective. Furthermore, using a survey design, did not allow us to determine the identification of any association between feeding practices and mortality, morbidity or any other to postoperative outcomes.

Importantly this study has allowed us to identify eight priorities for research in children with CHD, in no particular priority order these are: identifying the barriers to and improving the implementation of nutritional guidelines; to identify the energy expenditure and optimal energy requirements in three states: 1) extubated, 2) intubated and 3) intubated and heavily sedated and muscle relaxed infants; to determine prospectively the impact of enteral feeding on the incidence of NEC on PGE1 infusion; to prospectively study the impact of different EN feeding methods (intermittent versus continuous feeding) in infants both on vasoactive support and without; to determine the utility, value and impact on outcomes of routinely measuring GRV pre and post-operatively; to develop and validate a nutritional screening tool and a 'readiness to feed' risk score in CHD infants; to determine how best to optimize nutritional delivery to meet energy goals and to investigate the impact of an intervention to liberalize non-IV fluid restrictions (with enteral feed) on clinical outcomes post-operatively.

CONCLUSIONS

Little evidence exists to direct best practice in enteral feeding on infants with CHD. This survey has showed considerable variation and little consistency in nutritional practices across European PICUs, with many practices often based on suggestive fears extrapolated from other subgroups of patients (mainly preterm infants). Although in most European countries a pediatric intensivist was involved in the care of these infants, few had dedicated input from dieticians, and given that ensuring optimal nutrition is vital in these children this is concerning. The presence of feeding protocols significantly impacted on the likelihood of feeding pre-operatively yet few units had one. Wide variations in energy targets cited post-operatively reflect the lack of guidance around this area. Clinicians remain heavily driven by fluid restriction, and serum lactate level and gastric residual volume are the two most common parameters used to assess readiness to feed and feed tolerance. The latter of which is being increasingly questioned as a valid or useful marker to guide feeding. This study has identified eight priorities for future research and raises a number of opportunities to implement consistent guidelines for enteral feeding practice in this patient population.

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TABLE 1 Responding units per European country

Country	European region	No. responding units	Percentage of respondents
Belgium	Central	2	3.4%
Croatia	Central	2	3.4%
Estonia	Northern	1	1.7%
Finland	Northern	1	1.7%
France	Central	8	13.6%
Germany	Central	9	15.3%
Italy	Southern	4	6.8%
Latvia	Northern	1	1.7%
Lithuania	Northern	1	1.7%
Norway	Northern	1	1.7%
Poland	Central	3	5.1%
Portugal	Southern	2	3.4%
The Netherlands	Northern	4	6.8%
Slovenia	Central	1	1.7%
Spain	Southern	8	13.6%
Switzerland	Central	1	1.7%
Sweden	Northern	2	3.4%
UK	Northern	7	11.9%

TABLE 2 Summary of pre-operative enteral feeding practices

Nutritional variable	Percent of total PICUs (n=59)	Details
Conduct a nutritional assessment on admission	31% units	Assessment varied from height/weight to comprehensive assessment
Presence of written feeding guidelines	31% units	
Feeding method used	68% intermittent gastric feeds	
Feed formula used	77% Breast milk or standard 0.7kcal/ml infant feed	
Top 3 parameters used to assess feed readiness or tolerance	Serum lactate 69% Gastric residual volume 62% Arterial blood gas 55%	
Routinely feed on PGE1 infusion	63% units	42% stated dose-dependent with mean dose would feed on 30nng/kg/min
Routinely feed infants with an umbilical artery catheter	50% units	
Routinely feed infants with an umbilical venous catheter	67% units	
Routinely feed on vasoactive drugs	46% units	Stated dose-dependent, but variable drugs and doses

Abbreviations: PGE1 Prostaglandin Infusion

TABLE 3 Summary of post-operative feeding practices

Nutritional variable	Percent of total PICUs (n=59)	Details
Presence of written feeding guidelines	39% units	
Routinely feed all infants within 12-24 hours post-op	30% units	54% stated lesion-specific, with left sided obstructive lesions the main conditions to delay EN
Targeted energy post-operatively	Variable range 30kcal/kg – 120kcal/kg	50% stated mainly driven by fluid restrictions
Routinely feed using trophic (sub caloric feeds)	74% units	
Feeding method used	63% Intermittent gastric feeds	
Top 3 parameters used to assess feed readiness or tolerance	Stable hemodynamics 87% Gastric residual volume 67% Serum lactate 62%	
If EN contraindicated timing of PN	69% would start within the first 3 days	
Routinely feed infants with a peritoneal dialysis catheter	74% units	
Routinely feed on ECLS	64% units	
Routinely feed on vasoactive drugs	61% units	Dependent on drugs and doses

Abbreviations: EN Enteral Nutrition; PN: Parenteral Nutrition ; ECLS : Extracorporel Life Support

TABLE 4 Comparison of parameters used to assess readiness for and tolerance to enteral feeding in infants with congenital heart disease pre and post operatively

Pre-operative parameters		Post-operative parameters	
Serum lactate	**67.3%**	'Stable' hemodynamics	87.5%
Gastric residual volume	**63.3%**	Gastric residual volume	66.7%
Blood gas	**51%**	Serum lactate	62.5%
Diastolic blood pressure	**49%**	Systemic blood pressure	58.3%
Respiratory status	**46.9%**	Fluid allowance to feed	50%
Echocardiogram	**44.9%**	Blood gas	45.8%
Arterial oxygen saturation	**30.6%**	Echocardiogram	37.5%
Splanchnic NIRS	**16.3%**	Abdominal X-rays	27.1%
Cerebral NIRS	**14.3%**	Splanchnic NIRS	12.5%
Abdominal X-rays	**12.2%**	Cerebral NIRS	10.4%
Cerebral:somatic NIRS ratio	**6.1%**	Cerebral:somatic NIRS ratio	6.3%

Abbreviations: NIRS: Near Infrared Spectroscopy