**Title: Improving growth of infants with congenital heart disease using a consensus-based nutritional pathway**

**Authors:**

Luise V Marino1,3,4, Mark J Johnson2,4, Natalie J Davies1, Catherine S Kidd1, Julie Fienberg1, Trevor Richens4, Tara Bharucha4, R Mark Beattie4,5, Anne-Sophie E Darlington6

**Affiliations:** University Hospital Southampton NHS Foundation Trust; Department of Dietetics/ SLT 1, Department of Neonatal Medicine2, Department of Paediatric Cardiology 3, Department of Gastroenterology4, NIHR Biomedical Research Centre Southampton5, University Hospital Southampton NHS Foundation Trust and University of Southampton; School of Health Sciences 6

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**Corresponding author:** Luise Marino, University Hospital Southampton NHS Foundation Trust, Southampton, UK S016 6YD Tel: + 44 (0) 23 8079 6000 Email: Luise.marino@uhs.nhs.uk

**Objective:** Infants with congenital heart disease (CHD) often experience growth failure prior to surgery, which is associated with increased length of paediatric-intensive-care unit of stay (PICU-LOS) and post-operative complications. This study assessed the impact of a pre-operative, consensus-based nutritional pathway (including support from a multi-disciplinary team) on growth and clinical outcome.

**Design:** Single-centre prospective pilot study

**Setting:** Tertiary paediatric cardiology surgical centre

**Patients:** Infants with CHD

**Intervention:** Infants with CHD were followed for up to 4-months-of-age before cardiac surgery and then to 12-months-of-age following the implementation of the consensus-based nutritional-pathway (Intervention group: November 2017-August 2018), with outcomes compared to a historic control group. The nutrition pathway involved a dietitian contacting parents of infants with the highest risk of growth failure weekly; reviewing weight gain and providing feeding support.

**Main outcome measure:** Growth (weight-for-age, WAZ, and height-for-age-z-score, HAZ) at 4 and 12 months-of-age

**Results:** 44 infants in the intervention group were compared to 38 in the control group. Median (inter quartile range) change in WAZ from birth to 4 months-of-age (-0.9 (-1.5, 0.7)) and from birth to 12 months-of-age (-0.09 (-1.3, 1.1)) in the intervention group compared to the control group (-1.5 (-2.0, -0.4) (p=0.04) at 4 months-of age and at 12 months-of-age (-0.4 (1.9, 0.2) (p=0.03)). HAZ at 4 months-of-age was -0.7 (-1.4, -0.1) vs. -1.0 (-1.9, -0.3) (p=0.6) in the intervention and control groups respectively, and at 12 months-of-age HAZ was -0.7 (-1.9, -0.07)in the intervention group vs.-1.6 (-2.6, -0.4) in the control group (p=0.04). Duration of PICU-LOS was 8.2±11.6 days intervention vs. 18.3±24.0 days control (p=0.006).

**Conclusion:** Overall weight was well maintained and growth improved in infants who followed the pre-operative nutritional-pathway. The duration of PICU-LOS was significantly lower in the intervention group, which may be due to improved nutritional status, although this requires further investigation.

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| **What we know:*** Infants with congenital heart disease (CHD) often experience growth failure
* Poor growth in infants is associated with increased risk of post-operative complications and paediatric intensive care unit length of stay (PICU-LOS)
* Ensuring optimal growth before surgery has been identified as an important factor to improve short and longer term outcomes
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| **What this study adds:*** Using a consensus-based nutritional pathway in daily clinical practice is possible for health care professionals and parents to use
* The use of a consensus-based nutritional pathway, including nutrient energy dense feed and regular monitoring by a dietitian, is associated with improved growth and shorter intensive care stay
* Further work is required to test the use of a consensus based nutritional pathway in a large multicentre study
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**Introduction**

Congenital heart disease (CHD) is the most common congenital anomaly, occurring in around 1% of live births worldwide ([1-3](#_ENREF_1)), with a reported UK prevalence of univentricular physiology of 0.16 per 1,000 live births ([4](#_ENREF_4)) and ventricular septal defects (VSD) of 3.5 infants per 1,000 births ([5](#_ENREF_5)). Advances in medical and surgical management have resulted in improved clinical outcomes ([1](#_ENREF_1), [6](#_ENREF_6)). However, nutritional impairment and poor growth amongst infants with CHD is common ([7-9](#_ENREF_7)), and can have an adverse impact on clinical outcomes ([10](#_ENREF_10)).

The majority of infants with CHD have a normal weight at birth ([11](#_ENREF_11)). However, during the first few months of life many experience growth failure, with a decline in weight-for-age z scores (WAZ) and height-for-age z scores (HAZ) of -0.8 and -0.5 respectively ([8](#_ENREF_8), [9](#_ENREF_9), [12](#_ENREF_12), [13](#_ENREF_13)). The prevalence of moderate malnutrition (defined as a WAZ of <-2) in infants with CHD is between 21-29% ([7-9](#_ENREF_7)), and poor perioperative growth is associated with an increased risk of morbidity and mortality ([10](#_ENREF_10), [14](#_ENREF_14)).

Children with CHD with persistent malnutrition have reduced post-operative resilience and longer length of paediatric intensive care unit length of stay (PICU-LOS)([15](#_ENREF_15)), which is likely to be due to diminished immune response and functional reserve, leading to impaired metabolic control ([16](#_ENREF_16), [17](#_ENREF_17)). As such, intervening early in life with the use of nutrient-energy dense infant feeds in addition to an infant’s usual milk may reduce growth impairment, thereby improving growth and clinical outcomes. This concept has been demonstrated in other chronic diseases such as cystic fibrosis ([18](#_ENREF_18)).

The most severe forms of CHD, e.g. hypoplastic left heart syndrome, are not surgically repairable, and patients are often offered staged surgical palliation creating a univentricular circulation, and many of these infants are now included in home monitoring programs seeking to improve growth and reduce mortality between stages of surgical repair ([19](#_ENREF_19), [20](#_ENREF_20)). Conversely, those with VSDs and at risk of congestive heart failure are usually not included, despite growth being at significant risk ([21](#_ENREF_21), [22](#_ENREF_22)). In order to improve nutritional outcomes amongst infants with CHD before surgery, a consensus based pre-operative nutrition pathway has been developed ([23](#_ENREF_23)), with the aim of i) reducing variation in nutrition management of infants with CHD, ii) promoting early use of energy-nutrient dense infant feeds (e.g. 100kcal and 2.6g protein per 100ml) to reduce the risk of faltering growth and iii) reducing the prevalence of persistent malnutrition prior to surgery. The purpose of this study was to test the use and impact of the consensus based pre-operative nutrition pathway ([23](#_ENREF_23)) within a tertiary paediatric cardiology service.

**Methods**

**Development of the pre-operative nutritional pathway**

The details of the development of the consensus-based pre-operative nutrition care pathway are published elsewhere ([24](#_ENREF_24)), but briefly the following process was used: 1) initial development of pathway using available evidence, 2) initial stakeholder meeting to finalise draft guidelines and develop questions 3) a modified Delphi process based on 2 rounds of anonymous online survey, 4) regional cardiac conference and pathway revision, 5) final expert meeting and pathway finalization ([24](#_ENREF_24)). The pathway contains five sections: i) assess nutrition risk, ii) classify growth, iii) consider how and iv) what an infant is drinking and eating, iv) determine nutrition risk and appropriate care plan (A, B or C, see Figure 1).

**Participant study enrolment**

Infants (≤12 months) with CHD awaiting surgery were prospectively enrolled (November 2017 – August 2018) at a single tertiary centre (University Hospital Southampton NHS Foundation Trust). Parents of eligible infants with CHD were approached during the first month of life by the study team. Parents who provided informed consent were regularly contacted by a dietitian from the Paediatric Cardiology Nutrition Multi-disciplinary team (PCNMDT). At each contact parents provided information on growth and nutritional intake. At enrolment, infants were assigned a nutrition care plan according to predefined nutritional risk factors, and followed-up until the time of surgery or 4 months-of-age. Following surgery, infants continued to receive nutrition support as part of standard nutrition practice from a paediatric dietitian until 12 months of age. Exclusion criteria included infants with other diseases which may impact on feeding e.g. neurological-disorders, oncological diagnoses, respiratory disease, primary gut disorders and renal disease.

*A priori* we included children with known growth perturbations such as trisomy 21 or Di-George syndrome (22q.11 micro-deletion), as we were interested in providing nutrition support to all infants considered to have increased nutrition risk. However, there are limitations to this approach as growth in infants with CHD and genetic conditions may have different predicted growth trajectories and so where available, syndrome-appropriate growth charts were used.

**Paediatric Cardiology Nutritional multi-disciplinary team**

As part of this study, a PCNMDT was formed, which included Paediatric Congenital Cardiac Nurses, Speech and Language Therapists and specialist paediatric dietitians. The team held weekly meeting to discuss patients. Standardised electronic patient record templates for Nutrition Care Plans A, B and C were created, which were given to parents and other health care professionals (HCPs) involved in the care of these infants, including their General Practitioners (Figure 1). Dietitians involved in the study also visited nine district general hospitals within the Wessex Region to introduce the consensus-based pre-operative nutrition pathway, explain the pathway referral criteria, and answer queries.

As part of the PCNMDT, information was recorded relating to the infants: diagnosis, feed type, most recent weight, weight gain. Infants’ progress was discussed in terms of growth, actual versus recommended intake, method of feeding (i.e. oral, nasogastric or jejunal feeding tube and percutaneous endoscopic gastrostomy) and parental reported symptoms such as reflux or vomiting. A revised nutrition care plan was formulated together with individual patient goals, which was then communicated to parents/carers and associated HCPs.

**Historic control and clinical outcomes**

Clinical outcomes including growth, duration of mechanical ventilation and PICU-LOS during the first year of life of the study group were compared to a historic control group from the same organisation. This was infants with CHD requiring surgery, cared for by the same regional cardiology service during 2012 – 2013, representing a time before structured routine nutrition input and follow up of infants was implemented. There are 11 Surgical Cardiac Centres in the United Kingdom. The Southampton-Oxford Network receives referrals from 23 district general hospitals as far north as Northamptonshire and as far south as Cornwall and the Channel Islands. As such infants with CHD awaiting surgery are widely dispersed throughout a large regional Paediatric-Cardiac-Networks provision of nutrition support from a paediatric-dietitian varies considerably. Surgical strategy had not changed significantly during these two time periods.

**Outcomes**

Clinical outcomes were; 1) growth; WAZ and HAZ at 4 months-of-age and 12 months-of-age, 2) duration of mechanical ventilation (MV) on PICU and 3) PICU-LOS.

**Definitions of moderate malnutrition**

Z-scores were calculated using WHO Anthro software version 3.3.3 2011 ([25](#_ENREF_25)). Moderate malnutrition was defined as a WAZ ≤-2 ([26](#_ENREF_26)). For ex-preterm infants weight z-scores were corrected using the Fenton growth charts for preterm infants ([27](#_ENREF_27)) and for infants with Trisomy 21 ([28](#_ENREF_28)).

**Statistical analysis**

SPSS version 21 (Chicago, IL) was used for statistical analysis. Median and interquartile range (IQR) was used to summarise data where given that the sample size was small and therefore unable to be assessed formally for normality in a robust manner. Categorical variables are expressed as frequencies and percentages. Non-parametric tests (Mann Whitney) were used to examine differences between outcome variables; HAZ, WAZ, MV and PICU-LOS. A *p* value of <0.05 was considered statistically significant.

This study was approved by a NHS research ethics committee (West of Scotland Research Ethics Service, reference 17/WS/0084).

**Results**

Fifty-four patients parents were approached to participate in the study; of which 44 completed the study (hereafter termed the intervention group, Figure 2). These were compared to a historical cohort of 38 infants (hereafter termed the control group). Patient characteristics of both the control and intervention groups are shown in Table 1.

**Nutrition care plans in the intervention group**

 During the intervention period the majority of infants were on Nutrition Care plan C (64%) with the remainder on Nutrition Care Plan B. The majority (54.6%) of infants were managed using nutrient-energy dense feed (including extensively hydrolysed) alone, with the remainder given a combination of nutrient energy dense feed and breastmilk (27%), or standard infant formula (15.6%). A minority (1.8%) of infants during the intervention period received an amino acid infant formula. 39.2% of infants in the intervention period were reported to have symptoms of reflux and 30% required a enteral feeding tube.

**Growth during the first year of life**

Growth outcomes are summarised in Table 2 and figure 3. There was a significant reduction in the median (IQR) change in WAZ from birth to 4 months-of-age (-0.9 (-1.5, 0.7)) and from birth to 12 months-of-age (-0.09 (-1.3, 1.1)) in the intervention group compared to the control group (-1.5 (-2.0, -0.4) (p=0.04) at 4 months-of age and at 12 months-of-age (-0.4 (1.9, 0.2) (p=0.03)), see figure 3a). There were no significant differences between the intervention and control groups for WAZ at baseline, 4 months and 12 months (figure 3b), nor were there for weight for length z scores at 4 months and 12 months (figure 3c). Median (IQR) HAZ at 4 months in the intervention was similar at -0.7 (-1.4, -0.1) compared to the control groups -1.0 (-1.9, -0.3) (p=0.06) respectively. However, at 12months median (IQR) HAZ was significantly greater in the intervention group at -0.7 (-1.9, -0.07) - compared to -1.6 (-2.6, -0.4) in the control group (p=0.04), figure 3d).

The prevalence of moderate malnutrition (WAZ <-2) at 4 months-of-age was 20% in the intervention group and 28% in the control group (p=0.7). At 12 months-of-age, the prevalence of moderate malnutrition was 14% in the intervention group and 28% in the control group (p=0.1).

**Duration of mechanical ventilation and PICU-LOS**

Cumulative duration of mechanical ventilation during the first year of life was significantly shorter in the intervention group compared to the control group (5.1±8.2 vs 11.7±15.8 days, p=0.009). PICU-LOS in the intervention group was significantly shorter compared to the control group (8.2±11.6 days vs 18.3±24.0 days, p=0.006) (Figure 4). Age of palliative/corrective surgery was 7.3±4.9 months in the intervention and 4.0±3.2 in the control (p=0.001).

**Discussion**

This single centre prospective cohort study has shown the use of consensus based standardized pre-operative nutrition pathway has the potential to improve both growth and important clinical outcomes in infants with CHD, and may warrant testing in a larger cohort of infants in a multicentre study. With a median (IQR) change in WAZ from birth to 12 months of nearly zero, the use of the pathway enabled these infants to achieve growth along birth centile lines, avoiding the faltering growth often seen.

Based on recommendations from Golden *et al.* ([16](#_ENREF_16)), our pathway aimed to prevent the early growth faltering commonly seen in infants with CHD by increasing both the quality and quantity of dietary nutrients prior to surgery by a focus on the use of a nutrient-energy dense feed in addition to, or alongside, an infant’s usual milk. Short term use of nutrient-energy dense infant feeds amongst these infants is associated with improved weight gain and achievement of nutritional targets ([29](#_ENREF_29), [30](#_ENREF_30)). Overall, the use of nutrient dense infant formula was well tolerated, although 30% of the cohort did have symptoms of reflux or required an enteral feeding tube. The following strategies are employed to improve tolerance feed tolerance 1) inserting a naso-gastric feeding tube to provide bolus or continuous feeds via an enteral feeding pump 2) changing to an extensively hydrolysed version of the nutrient energy dense feed and 3) if those strategies did not provide symptom resolution the enteral feeding tube was advanced to a naso-jejunal tube.

 Although, the fall in WAZ between birth and both 4 and 12 months-of-age were significantly reduced in the intervention group compared to the control group, it is important to note that weight gain alone or improved weight for height does not indicate nutritional rehabilitation in the presence of stunting or low height for age, as it suggests there is insufficient nutrients to support linear growth, resulting in overweight stunted children([31](#_ENREF_31)), which is increasingly reported in older children with CHD ([32](#_ENREF_32)). As such improving linear growth during the first year of life is a priority and may reduce cardiovascular risk in later life ([33](#_ENREF_33)). In this study linear growth at 12 months-of-age was significantly improved in infants with CHD who followed the pre-operative nutrition pathway, when compared to a historic control.

A proportion of the cohort continued to have moderate malnutrition, with a low WAZ at 4 months-of-age (20%) despite seemingly adequate amounts of nutrition and dietetic support, which is similar to those described by other groups ([34-36](#_ENREF_34)). El-Koofy *et al*. ([37](#_ENREF_37)) describes the use of Nutrition Care plans based on a traffic light system as part of a programme of nutritional rehabilitation in 50 infants with left to right cardiac shunts. Plans were graded from green, through amber to red, where the red plan represented more aggressive nutritional management for the highest risk infants or those with the poorest growth This resulted in a significant improvement in the prevalence of moderate malnutrition from 28% prior to implementation, to 23% afterwards, representing similar figures to those described in the present study. Gongwer *et al.* ([34](#_ENREF_34)) reported significant improvements in changes to WAZ from baseline to 6 months following the implementation of a structured approach to the nutritional care of inpatient infants with CHD, which included daily nutrition review and a weekly nutrition team assessment. However, at exit from the programme the median WAZ was still low at -3.5, suggesting that although there was improved weight gain, overall the cohort was significantly malnourished.

 Many factors affect growth in infants with CHD ([38-40](#_ENREF_38)). Heart failure is common, which increases metabolic demands, and may result in acute and chronic mesenteric hypoperfusion ([41](#_ENREF_41)), compromising intestinal absorption of nutrients ([42](#_ENREF_42), [43](#_ENREF_43)), and subsequently limiting growth. Gastroesophageal reflux disease (GORD) ([44](#_ENREF_44), [45](#_ENREF_45)) may also contribute towards poor intake and subsequent poor growth ([46](#_ENREF_46)). In the present study cohort almost 40% of infants were reported to have GORD, which may have contributed towards reduced oral intake.

Clinical outcomes were improved in infants who followed the pre-operative nutritional pathway, with significant reductions in the duration of MV and PICU-LOS compared to a historic control. We have previously described poorer post-operative resilience amongst children with CHD who had persistent malnutrition (e.g. stunting with a HAZ of <-2) at the time of surgery, which was associated with a significantly increased risk of PICU-LOS ([15](#_ENREF_15)) . Others have described a relationship between persistent malnutrition and poorer clinical outcomes ([47](#_ENREF_47), [48](#_ENREF_48)). While the reduced duration of MV and PICU-LOS in this cohort may be as a result of improved nutritional status, this may be also be as a result of other factors such as changes in surgical or post-operative medical management. However, the mean age for palliative/corrective surgical procedures in the intervention group was later, and one explanation for this may be that continued good growth meant that the need for imminent surgical intervention was not as pressing, and so surgery could be deferred as medical management appeared adequate. This requires further investigation amongst a larger cohort of infants within a prospective randomised national study that is sufficiently powered to confidently detect differences in clinical outcomes.

There are a number of limitations to this study, which include the use of historic control group rather than a prospectively enrolled cohort. We were also not able to accurately determine daily intake of infant milk and the exact proportion of nutrient-energy dense feeds when mixed with breastmilk or standard infant formula. The sample size of both cohorts was also small, which although allowed us to draw some conclusions about efficacy, is not sufficiently powered to be assured the effects seen are reproducible, particularly with respect to the duration of MV and PICU-LOS.

**Conclusions:**

This single centre study has shown that the use of consensus based standardized nutritional pathway in in infants with CHD before surgery is feasible, and has the potential to improve growth and clinical outcomes.

Overall growth significantly improved in infants who followed the pre-operative nutritional-pathway, with a reduced fall in WAZ from birth and better linear growth at 12 months-of-age, which may be as a result of the early use of nutrient-energy dense infant formula to prevent growth faltering. The duration of MV and PICU-LOS was significantly lower in the intervention group, but other factors associated with medical/ surgical management may have contributed to these improvements, which warrant further investigation in a larger cohort of infants in a national, multi-centre study.

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**CONTRIBUTORS STATEMENT:**

Authors made the following contribution to the manuscript: (1) Luise Marino formulated the original idea and wrote the initial nutritional pathway, collated the parent information, completed statistical analysis and drafted the manuscript. (2) Luise Marino, Natalie Davies, Catherine Kidd, Julie Fienberg were involved in consenting parents to participate in the study. (3) Ann-Sophie Darlington, Mark Beattie, Mark Johnson, Trevor Richens and Tara Bharucha, contributed to revising the manuscript for important intellectual content, (4) and all authors provided final approval of the version to be submitted.

**References**

1. van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. Journal of the American College of Cardiology. 2011;58(21):2241-7.

2. Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Seminars in thoracic and cardiovascular surgery Pediatric cardiac surgery annual. 2010;13(1):26-34.

3. Hoffman JI, Kaplan S. The incidence of congenital heart disease. Journal of the American College of Cardiology. 2002;39(12):1890-900.

4. Coats L, O'Connor S, Wren C, O'Sullivan J. The single-ventricle patient population: a current and future concern a population-based study in the North of England. Heart. 2014;100(17):1348-53.

5. Sands AJ, Casey FA, Craig BG, Dornan JC, Rogers J, Mulholland HC. Incidence and risk factors for ventricular septal defect in "low risk" neonates. Archives of disease in childhood Fetal and neonatal edition. 1999;81(1):F61-3.

6. Petersen S PV, Rayner M. Congenital Heart Disease Statistics. British Heart Foundation Health Promotion Research Group

 [Internet]. 2003.

7. Marino LV, Magee A. A cross-sectional audit of the prevalence of stunting in children attending a regional paediatric cardiology service. Cardiology in the young. 2016;26(4):787-9.

8. Toole BJ, Toole LE, Kyle UG, Cabrera AG, Orellana RA, Coss-Bu JA. Perioperative nutritional support and malnutrition in infants and children with congenital heart disease. Congenital heart disease. 2014;9(1):15-25.

9. Vaidyanathan B, Nair SB, Sundaram KR, Babu UK, Shivaprakasha K, Rao SG, et al. Malnutrition in children with congenital heart disease (CHD) determinants and short term impact of corrective intervention. Indian pediatrics. 2008;45(7):541-6.

10. Eskedal LT, Hagemo PS, Seem E, Eskild A, Cvancarova M, Seiler S, et al. Impaired weight gain predicts risk of late death after surgery for congenital heart defects. Archives of disease in childhood. 2008;93(6):495-501.

11. Hehir DA, Rudd N, Slicker J, Mussatto KA, Simpson P, Li SH, et al. Normal interstage growth after the norwood operation associated with interstage home monitoring. Pediatric cardiology. 2012;33(8):1315-22.

12. Marino LV, Magee A. A cross-sectional audit of the prevalence of stunting in children attending a regional paediatric cardiology service. Cardiology in the young. 2015:1-3.

13. Cheung MM, Davis AM, Wilkinson JL, Weintraub RG. Long term somatic growth after repair of tetralogy of Fallot: evidence for restoration of genetic growth potential. Heart. 2003;89(11):1340-3.

14. Mitting R, Marino L, Macrae D, Shastri N, Meyer R, Pathan N. Nutritional status and clinical outcome in postterm neonates undergoing surgery for congenital heart disease. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2015;16(5):448-52.

15. Marino LV, Meyer R, Johnson M, Newell C, Johnstone C, Magee A, et al. Bioimpedance spectroscopy measurements of phase angle and height for age are predictive of outcome in children following surgery for congenital heart disease. Clinical nutrition (Edinburgh, Scotland). 2017.

16. Golden MH. Proposed recommended nutrient densities for moderately malnourished children. Food and nutrition bulletin. 2009;30(3 Suppl):S267-342.

17. Mehta NM, Duggan CP. Nutritional deficiencies during critical illness. Pediatric clinics of North America. 2009;56(5):1143-60.

18. Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al. ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis. Clinical nutrition (Edinburgh, Scotland). 2016;35(3):557-77.

19. Oster ME, Ehrlich A, King E, Petit CJ, Clabby M, Smith S, et al. Association of Interstage Home Monitoring With Mortality, Readmissions, and Weight Gain: A Multicenter Study from the National Pediatric Cardiology Quality Improvement Collaborative. Circulation. 2015;132(6):502-8.

20. Miller-Tate H, Stewart J, Allen R, Husain N, Rosen K, Cheatham JP, et al. Interstage weight gain for patients with hypoplastic left heart syndrome undergoing the hybrid procedure. Congenital heart disease. 2013;8(3):228-33.

21. Weintraub RG, Menahem S. Early surgical closure of a large ventricular septal defect: influence on long-term growth. Journal of the American College of Cardiology. 1991;18(2):552-8.

22. Correia Martins L, Lourenco R, Cordeiro S, Carvalho N, Mendes I, Loureiro M, et al. Catch-up growth in term and preterm infants after surgical closure of ventricular septal defect in the first year of life. European journal of pediatrics. 2016;175(4):573-9.

23. Marino LV, Johnson MJ, Hall NJ, Davies NJ, Kidd CS, Daniels ML, et al. The development of a consensus-based nutritional pathway for infants with CHD before surgery using a modified Delphi process. Cardiology in the young. 2018;28(7):938-48.

24. Keller HH, McCullough J, Davidson B, Vesnaver E, Laporte M, Gramlich L, et al. The Integrated Nutrition Pathway for Acute Care (INPAC): Building consensus with a modified Delphi. Nutrition journal. 2015;14:63.

25. WHO WHO. WHO Anthro (version 3.2.2, January 2011). 2015.

26. WHO WHO. Growth reference 5-19 years: BMI-for-age (5-19years) 2015. Available from: <http://www.who.int/growthref/who2007_bmi_for_age/en/>.

27. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC pediatrics. 2013;13:59.

28. Zemel BS, Pipan M, Stallings VA, Hall W, Schadt K, Freedman DS, et al. Growth Charts for Children With Down Syndrome in the United States. Pediatrics. 2015;136(5):e1204-11.

29. Marino LV ER, Morton K, Verbruggen SCAT, Joosten KFM. Peptide nutrient-energy dense enteral feeding in critically ill infants to reach nutritional targets – a comparison study. Journal of Human Nutrition and Dietetics. 2019.

30. Zhang H, Gu Y, Mi Y, Jin Y, Fu W, Latour JM. High-energy nutrition in paediatric cardiac critical care patients: a randomized controlled trial. 2018.

31. Popkin BM, Richards MK, Montiero CA. Stunting is associated with overweight in children of four nations that are undergoing the nutrition transition. J Nutr. 1996;126(12):3009-16.

32. Steele JM, Preminger TJ, Erenberg FG, Wang L, Dell K, Alsaied T, et al. Obesity trends in children, adolescents, and young adults with congenital heart disease. Congenital heart disease. 2019.

33. Fedchenko M, Mandalenakis Z, Dellborg H, Hultsberg-Olsson G, Bjork A, Eriksson P, et al. Cardiovascular risk factors in adults with coarctation of the aorta. Congenital heart disease. 2019.

34. Gongwer RC, Gauvreau K, Huh SY, Sztam KA, Jenkins KJ. Impact of a Standardized Clinical Assessment and Management Plan (SCAMP(R)) on growth in infants with CHD. Cardiology in the young. 2018;28(10):1093-8.

35. Fitria L, Caesa P, Joe J, Marwali EM. Did Malnutrition Affect Post-Operative Somatic Growth in Pediatric Patients Undergoing Surgical Procedures for Congenital Heart Disease? Pediatric cardiology. 2019;40(2):431-6.

36. Vaidyanathan B, Radhakrishnan R Fau - Sarala DA, Sarala Da Fau - Sundaram KR, Sundaram Kr Fau - Kumar RK, Kumar RK. What determines nutritional recovery in malnourished children after correction of congenital heart defects? (1098-4275 (Electronic)).

37. El-Koofy N, Mahmoud AM, Fattouh AM. Nutritional rehabilitation for children with congenital heart disease with left to right shunt. The Turkish journal of pediatrics. 2017;59(4):442-51.

38. Forchielli ML, McColl R, Walker WA, Lo C. Children with congenital heart disease: a nutrition challenge. Nutrition reviews. 1994;52(10):348-53.

39. Surmeli-Onay O, Cindik N Fau - Kinik ST, Kinik St Fau - Ozkan S, Ozkan S Fau - Bayraktar N, Bayraktar N Fau - Tokel K, Tokel K. The effect of corrective surgery on serum IGF-1, IGFBP-3 levels and growth in children with congenital heart disease. (0334-018X (Print)).

40. Dinleyici EC, Kilic Z Fau - Buyukkaragoz B, Buyukkaragoz B Fau - Ucar B, Ucar B Fau - Alatas O, Alatas O Fau - Aydogdu SD, Aydogdu Sd Fau - Dogruel N, et al. Serum IGF-1, IGFBP-3 and growth hormone levels in children with congenital heart disease: relationship with nutritional status, cyanosis and left ventricular functions. (0172-780X (Print)).

41. Ellis CL, Rutledge JC, Underwood MA. Intestinal microbiota and blue baby syndrome: probiotic therapy for term neonates with cyanotic congenital heart disease. Gut microbes. 2010;1(6):359-66.

42. Davis D, Davis S, Cotman K, Worley S, Londrico D, Kenny D, et al. Feeding difficulties and growth delay in children with hypoplastic left heart syndrome versus d-transposition of the great arteries. Pediatric cardiology. 2008;29(2):328-33.

43. Cavell B. Gastric emptying in infants with congenital heart disease. Acta paediatrica Scandinavica. 1981;70(4):517-20.

44. Cavell B. Effect of feeding an infant formula with high energy density on gastric emptying in infants with congenital heart disease. Acta paediatrica Scandinavica. 1981;70(4):513-6.

45. St Pierre A, Khattra P, Johnson M, Cender L, Manzano S, Holsti L. Content validation of the infant malnutrition and feeding checklist for congenital heart disease: a tool to identify risk of malnutrition and feeding difficulties in infants with congenital heart disease. Journal of pediatric nursing. 2010;25(5):367-74.

46. Blasquez A, Clouzeau H, Fayon M, Mouton JB, Thambo JB, Enaud R, et al. Evaluation of nutritional status and support in children with congenital heart disease. European journal of clinical nutrition. 2016;70(4):528-31.

47. Bechard LJ, Duggan C, Touger-Decker R, Parrott JS, Rothpletz-Puglia P, Byham-Gray L, et al. Nutritional Status Based on Body Mass Index Is Associated With Morbidity and Mortality in Mechanically Ventilated Critically Ill Children in the PICU. Critical care medicine. 2016;44(8):1530-7.

48. Grippa RB, Silva PS, Barbosa E, Bresolin NL, Mehta NM, Moreno YM. Nutritional status as a predictor of duration of mechanical ventilation in critically ill children. Nutrition (Burbank, Los Angeles County, Calif). 2016.