Journal of Pediatric Surgery 56 (2021) 1564–1569

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg.org

Head circumference in infants undergoing Foker process for long-gap esophageal atresia repair: Call for attention

Dusica Bajic[a,b,*], Samuel S. Rudisill[a,c], Russell W. Jennings[b,d]

[a] Department of Anesthesiology, Critical Care, and Pain Medicine, Boston Children's Hospital, 300 Longwood Avenue, Bader 3, Boston, MA 02115, USA
[b] Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA
[c] Rush Medical College at Rush University, 600 S. Paulina Street, Chicago, IL 60612, USA
[d] Department of Surgery, Esophageal and Airway Treatment Center, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA, 02115, USA

ARTICLE INFO

Article history:
Received 5 May 2020
Revised 14 January 2021
Accepted 18 January 2021

Keywords:
Brain
Development
Infancy
LGEA
MRI
Pediatric

ABSTRACT

Introduction: We extended our pilot study in infants following long-gap esophageal atresia (LGEA) repair to report head circumference, an easily obtainable indirect measure of brain size. Data are presented in the context of previously reported body weight and T2-weighted MRI measures of intracranial and brain volumes.

Methods: Clinical information and head circumference were obtained for term-born ($n = 13$) and premature ($n = 13$) infants following LGEA repair with Foker process, as well as healthy term-born controls ($n = 20$) <1-year corrected age who underwent non-sedated research MRI. General Linear Model univariate analysis with corrected age at scan as a covariate and Bonferroni adjusted p values assessed group differences.

Results: We report no difference in head circumference between the three groups. Such findings paralleled trends in body weight and total intracranial volume but not in brain volume as previously reported for the same pilot cohort.

Discussion: Results suggest uncompromised somatic and head growth after repair of LGEA. In contrast, a novel finding of discrepancy between head circumference (novel data) and brain size (previously published data) in the same cohort suggests that head circumference might not be the best indirect measure of brain size in selected group of patients.

Level of Evidence

Prognostic Study - Level I: High-quality prospective cohort study with > 80% follow-up, and all patients enrolled at same time point in disease

Study of Diagnostic Test – Level I: Testing previously developed diagnostic criteria in a consecutive series of patients and a universally applied "gold" standard

1. Introduction

In humans, the period between the third trimester of pregnancy and the second year of life represents a critical phase of neurodevelopment characterized by dramatic brain growth [1,2]. Suboptimal brain growth during this window is known to have long-term implications in cognitive and behavioral function [3–6], thus monitoring of brain volume and growth trajectory is an important component of infant care. For decades, routine clinical practice has relied on head circumference as a safe, quick, inexpensive, and reproducible tool for estimating intracranial volume [7] and brain size [8] in otherwise healthy infants and toddlers, as well as developmentally normal premature infants weighing more than 1000 g at birth [9]. Specifically, head circumference has been shown to strongly correlate with brain size in several (1) postmortem cases (in small-for-gestational-age infants) [10,11], as well as (2) CT-based [12], and (3) MR-based studies [13,14] of premature infants at term-equivalent age. Thus, measured as the distance around the cranium overlying the greatest supraorbital and occipital protuberances, it is an effective proxy of brain size in neonates and infants [15]. Current American Academy of Pediatrics *Bright Futures* guidelines recommend head circumference to be measured at each physical examination from birth to 24 months of age, with serial measurements plotted on composite graphs to illustrate growth trajectory [16,17]. In doing so, any abnormality in growth patterns indicating pathology (e.g. hydrocephalus, subdural

Abbreviations: ANOVA, Analysis of variance; CA, Corrected age; ECMO, Extracorporeal membrane oxygenation; ICV, Intracranial volume; GA, Gestational age; HSD, Honestly significant difference; LGEA, Long-gap esophageal atresia; MRI, Magnetic resonance imaging; TEF, Tracheo-esophageal fistula.

* Corresponding author at: Boston Children's Hospital, Department of Anesthesiology, Critical Care and Pain Medicine, 300 Longwood Avenue, Bader 3, Boston, MA 02115-5737, United States.
E-mail address: dusica.bajic@childrens.harvard.edu (D. Bajic).

https://doi.org/10.1016/j.jpedsurg.2021.01.030
0022-3468/

hematoma, effusion) or altered neurodevelopment becomes readily apparent [18,19].

Recent literature suggests that critical illness (e.g. chronic lung disease, patent ductus arteriosus, postnatal infection, or need for mechanical ventilation) is an important risk factor for altered brain development [20,21]. The impact of prolonged and repeated anesthetic exposure on brain development is unclear and remains a controversial topic (see Reviews [22,23]). In addition to altered feeding [24,25], infections affecting infants while in the neonatal intensive care unit have been linked to a range of abnormalities in brain development and increased risk of neurological sequelae [26]. Moreover, there is growing evidence in the literature to support the notion that infants with congenital gastrointestinal anomalies who experience multiple stressors while hospitalized early in life [24,27] are at increased risk for brain injury [28–30] and poor long-term neurodevelopmental outcomes [31–35]. Indeed, we recently reported brain findings [36–38] and globally reduced brain volumes [36,38,39] in a pilot cohort of infants following *long-gap* esophageal atresia (LGEA) repair with Foker process [37,40]. While previously validated in healthy infants, it is not clear if measures of head circumference provide reliable assessments of brain size in the context of critical illness and perioperative care. Therefore, the goal of current study is to evaluate head circumference in our unique pilot cohort of infants following LGEA repair, who also underwent research brain MRI allowing for intracranial and brain volumes quantification [36,39,41].

Esophageal atresia, although a rare congenital anomaly with a stable prevalence around the world [42], represents one of the most common gastrointestinal birth defects, with reported incidence ranging from 1 in 2500 to 1 in 4500 live births [43,44]. Unlike *short-gap* esophageal defects that can be repaired by direct anastomosis (requiring one major surgery and pain treatment within 5 days) [45], longer disconnect (> 3 cm) as seen in LGEA requires more complex treatment. One treatment option for LGEA at our institution is the Foker process [46–48], which facilitates tension-induced growth of esophageal ends prior to final anastomosis. The unique aspect of such treatment is that infants with LGEA undergo repeated thoracotomy requiring prolonged sedation associated with physical dependence to the drugs of sedation [37,40]. Indeed, our recent retrospective report showed that opioids and benzodiazepines, which are administered in tandem for sedation lead to physical dependence after just 5 days of treatment [40]. Representative treatment duration as part of the Foker process course in infants undergoing repair for LGEA was previously illustrated (*Fig. 1* in [36] and *Fig. 1* in [37]) spanning a period of week(s). Such complex perioperative critical care in early life, [20,21] may predispose infants born with LGEA to (mal)adaptations in brain development [37,38]. In this report, we present novel findings of head circumference in selected pilot cohort of term-born and premature infants following LGEA repair with Foker process in comparison to normative control group. To assess validity of head circumference as an indirect measure of brain size, we present head circumference (*novel data*) together with brain size measures (*with permission to reprint* [36,39,41]) of the same cohort.

2. Methods

2.1. Study design and participants

Our current report of head circumference is an extension of previous studies [36,39,41] that were approved by the Boston Children's Hospital Institutional Review Board as a 'no more than minimal risk' study (IRB- P000007855). Informed written parental consent was obtained prior to subject participation (June 2015-March 2019), in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Considering that data presented is from the same infant study subjects, the previously described methodological approaches for (1) recruitment criteria and (2) MRI scanning process apply here [36,39]. We analyzed 3 groups: (i) term-born patients, (ii) preterm patients, and (iii) term-born healthy controls. Patients' eligibility criteria included term-born (37 to 42 weeks GA at birth) and moderate-to-late preterm (28 to 36 weeks GA at birth) patients <1 year gestation-corrected age who underwent surgery for Foker process for LGEA repair [46-48] and developed sedative dependency. A representative timeline illustrating the sequence of perioperative critical care was presented previously [36,37]. Exclusion criteria included (1) extreme prematurity (<28 weeks GA); (2) extra-corporeal membrane oxygenation exposure; (3) cranial ultrasound findings (e.g. ventricular enlargement with or without gray matter and/or ventricular hemorrhage); (4) neurological disease (e.g. seizures); (5) chromosomal abnormalities (e.g. Down syndrome); (6) prenatal drug exposure; and/or (7) MRI incompatible implants. Normative control infants <1 year old with no prior exposure to surgery, anesthesia, or sedation served as a reference baseline, and were not age or gender matched. Table 1 summarizes demographic and clinical characteristics at the time of the MRI scan (reprinted with permission [41]). The number of patient subjects was consistent throughout (n = 13/group),

Table 1
Study Cohort Demographic Characteristics.

	Term-born Patients with LGEA	Premature Patients with LGEA	Controls
Number Analyzed	13	13	20
Sex (male), n (%)	7 (54%)	8 (62%)	17 (85%)
Average GA at birth (weeks) ± SD	38.5 ± 1.1	32.2 ± 2.9	39.3 ± 1.15
Median CA at scan [range] (months)	5.4 [0.7–13.0]	3.8 [1.4–7.5]	4.5 [0.5–12.3]
Multiple births, n (%)	1 (8%)	2 (15%)	1 (5%)
Primary diagnoses			
Isolated LGEA, n (%)	3 (23%)	3 (23%)	0
LGEA with TEF, n (%)	5 (38%)	9 (69%)	0
Other, n (%)	5 (38%)	1 (8%)	0

Table 1. Summarizes demographic and clinical characteristics of all subjects included in the analysis from the 3 groups (term-born and premature patients, and controls). Table information is reprinted with permission [41]. Number of patient subjects was consistent throughout while the number of controls was different for each analysis: body weight (n = 20; Fig. 1A), head circumference (n = 10; Fig. 1B – novel data), and T2-weighted quantification of intracranial and total brain volumes (n = 17; Fig. 1C-E). Primary diagnoses are shown stratified based on noncardiac congenital anomaly diagnoses: (1) isolated LGEA, (2) LGEA with TEF, and (3) Other - that included LGEA as part of VACTERL association (without cardiac involvement). Typically, infants diagnosed with VACTERL exhibit ≥3 of the characteristic features (viz. Vertebral defects; Anal atresia; Cardiac defects; Tracheo-Esophageal fistula; Renal anomalies; Limb abnormalities). None of the enrolled patients had exposure to extracorporeal membrane oxygenation. For other exclusion criteria, see Methods section. Abbreviations: GA, gestational age; CA, corrected age; LGEA, long-gap esophageal atresia; SD, standard deviation; TEF, tracheo-esophageal fistula.

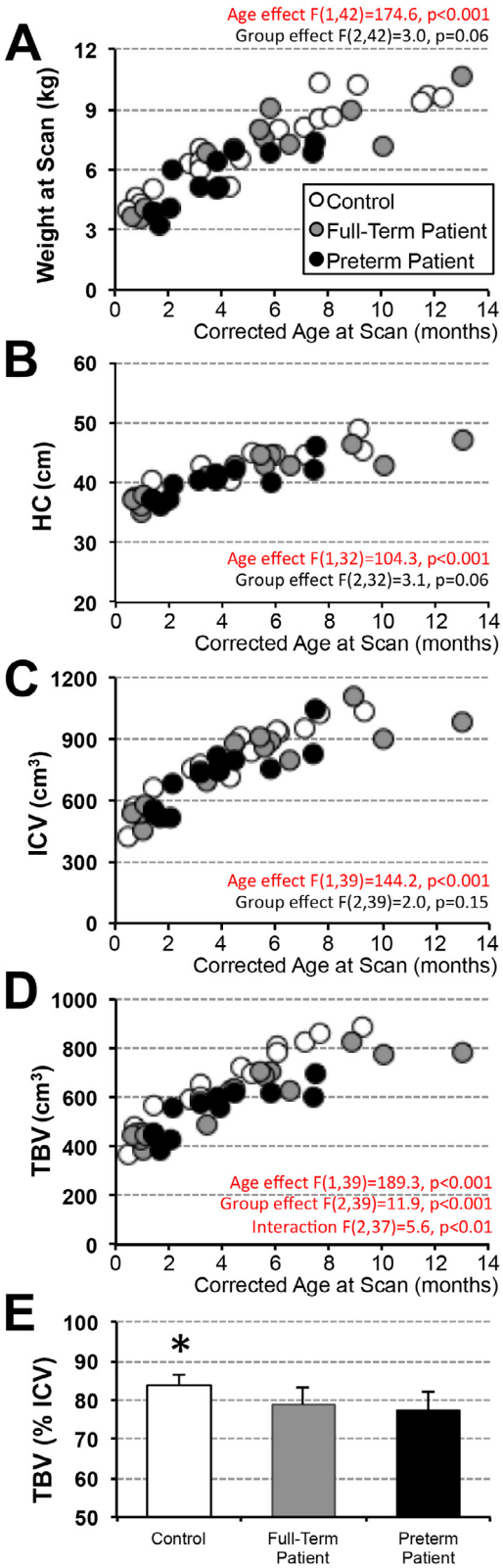

Fig. 1. Metrics of body weight (A), head (B and C), and brain size (D and E) following Foker process for long-gap esophageal atresia repair. Our pilot study [36,39,41] analyzed 3 groups: (1) term-born controls (open circles; n = 20 (A), n = 10 (B); n = 17 (C-E)), (2) term-born patients (gray circles; n = 13), and (3) premature patients (black circles; n = 13). Novel data with respect to head circumference (cm) are presented in Panel B while the remaining panels were *reprinted with permission* [36,39,41]. Data was collected following completion of perioperative critical care with Foker process; at the time of MRI scan. All measures significantly increased with advancing age irrespective of group status (A-D). Despite trend for group differences, we report no significant differences in body weight at MRI scan between the groups ($F(2,42)$ = 3.01, p = 0.06; Panel A; *with permission from* [41]). Head size measures are shown as head circumference (cm; Panel B – novel data) and intracranial volumes (ICV; cm^3; Panel C; *with permission from* [39]), and also show no group differences. In contrast, brain size shown as total brain volume (TBV; cm^3; Panel D; *with permission from* [39]) and normalized brain volume (% ICV; Panel E; *data updated from* [36]) demonstrates significantly smaller size for both term-born and premature patients in comparison to controls ($p<0.001$ in Panel D as demonstrated by General Linear Model univariate analysis; $p<0.01$ in Panel E as per one-way ANOVA), without differences between term-born and premature patients. Data in Panels C-E are updated with addition of 2 control subjects (n = 17) when compared to our previous T2-weighted analysis reports (n 13 in [36] and n = 15 in [39]; *reproduced with permission*). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

while the number of controls was different depending on the analysis: body weight (n = 20; Fig. 1A), head circumference (n = 10; Fig. 1B), and T2-weighted quantification of intracranial and total brain volumes (n = 17; Fig. 1C-E).

2.2. Clinical measures

Clinically relevant information was obtained by the research team at the time of MRI scan (controls and patients), or was collected from pre-existing data measures from electronic medical records (PowerchartR, Cerner, London, UK) for patients. This included birth details, diagnoses, surgical events, sedation treatment, measures of body weight (kg; Fig. 1A – reprinted with permission [41]), and head circumference (cm; Fig. 1B – novel data). When head circumference was measured, non-reusable paper tape measure that could not be stretched was applied snugly around the widest possible head circumference – from the most prominent part of the forehead (often 1–2 fingers above the eyebrow) around to the widest part of the back of the head. Preliminary data of associations between head/brain measures and various clinical exposure metrics were presented in part as an abstract, [49] and will be published elsewhere.

2.3. MRI acquisition, pre-processing, and segmentation

As outlined in the Introduction, we present head circumference (*novel data*) together with brain size measures (*with permission to reprint* [36,39,41]) of the same cohort. This will allow for evaluating validity of head circumference as an indirect measure of brain size in selected cohort of infants after LGEA repair. All infants underwent a non-sedated research scan after completion of all perioperative treatment for Foker process using a 'feed and wrap' approach [50–53]. For more details on handling infants in the scanner, refer to our previous reports [36,39]. Infants were scanned in late evenings or at night using a 3T Trio-Tim MRI system equipped with 32-channel receive-only head coil and body-transmission (Siemens Healthcare Inc., USA). As previously described [36,38,39], structural T2-weighted images were acquired using a fast spin echo sequence [TR/TE=12,624/110 ms; FA=120°; FOV = 180 × 180 mm^2; 63 slices, 2 mm thickness; voxels=0.35 × 0.35 mm^2]. T2 images were collected for all scanned term-born and premature patients (n = 13/group), and data was updated with additional 2 control subjects (n = 17/20) in comparison to the cohort presented in our previous report [39]. Please refer to our previously published comprehensive description [36] of T2-weighted preprocessing and tissue-types segmentation methodology for intracranial (Fig. 1C – reprinted with permission [36,39]) and brain volume quantifications (cm^3; Fig. 1D and E – reprinted with permission [36,39]).

2.4. Statistical analyses

As this was a pilot study and no prior information was available regarding brain volumes in the selected cohort of infants with LGEA, a convenience sample size of 13 patients/group was chosen based on the anticipated number of eligible infants at our institution and an estimated 50% enrollment rate. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, v.23.0; IBM Corporation, Armonk, NY). Normal distribution of all continuous variables was confirmed using the Shapiro-Wilk test. Comparison of end-point measures [weight (kg), head circumference (cm), absolute intracranial and brain volumes (cm^3)] between the three groups was assessed using a General Linear Model univariate analysis with corrected age at scan as a covariate and Bonferroni adjusted p values. The interaction (viz. test of parallelism) was reported when significant. Mean normalized brain measures (% intracranial volume) were compared between groups using a one-way analysis of variance (ANOVA) with Tukey's HSD (honestly significant difference) test. Statistical significance was assessed at the $\alpha < 0.05$.

3. Results

The current study of head circumference (Fig. 1B) is presented in the context of previously reported results on total body weight (Fig. 1A) [41], intracranial (Fig. 1C), and total brain volume (Fig. 1D and E) [36,39,41] of the pilot cohort: term-born and premature infant patients born with LGEA without concomitant cardiac abnormalities ($n = 13$/group) after treatment with Foker process in comparison to otherwise healthy controls ($n = 20$). Recruited patients had no previously known brain findings (e.g., presence of cranial ultrasound findings), symptoms that would implicate neurological disease (e.g., stroke, seizures), or head growth impairment.

3.1. Somatic and head size

Despite a trend of smaller total body weight in premature patients, we did not find any significant differences in body weight (kg) among groups [41] (Fig. 1A; reprint with permission from *Fig. 1* [54]). In parallel to the body weight patterns, our results in the same pilot cohort showed no differences in measures of head size between groups - in terms of head circumference (cm; novel data) or intracranial volume (cm^3; previously published *[39]*). Specifically, as graphically represented in Fig. 1A-C, all measures significantly increased with advancing age during the first year of life, irrespective of the group status: body weight ($F(1,42) = 174.6$, $p < 0.001$; Fig. 1A [54]), head circumference ($F(1,32) = 104.3$, $p < 0.001$; novel data - Fig. 1B), and intracranial volume ($F(1,39) = 144.2$, $p < 0.001$; Fig. 1C; reprint with permission from *Fig. 2A [39]*). However, there were no differences among the 3 groups for any of the listed measures at the time of scan: weight ($p = 0.06$), head circumference ($p = 0.06$ – novel data) or intracranial volume ($p = 0.15$).

3.2. Brain size

Surprisingly, in contrast to somatic body and head measures, previously published data of both absolute (Fig. 1D; reprint with permission from *Fig. 2B* in [39]) and normalized total brain volume (as % intracranial volume; Fig. 1E; data updated from *Fig. 8A*' [36]) was significantly smaller in both term-born and premature patients following Foker process in comparison to controls.

4. Discussion

The current report in a pilot cohort of term-born and premature infants following Foker repair for LGEA, in comparison to infant controls, implicates discrepancy between indirect (viz. head circumference) and direct measures of brain size (viz. 3D volume by MRI) as demonstrated by our novel and previously published data [36,39,41], respectively.

4.1. Somatic and head size following long-gap esophageal atresia repair

Similarly to body weight [41], our novel data do not show any group differences related to head circumference (Fig. 1B). This novel finding is further supported by 3D quantification of intracranial space volume of the same pilot cohort (Fig. 1C; reprinted with permission). Together, such results implicate adequate body and head size/growth in the setting of complex perioperative critical care of LGEA repair with Foker process. Our novel findings of lack of group differences in head circumference are in contrast to a previously reported study by Gischler et al. [55] of 16 infants with *short*-gap esophageal atresia without sedative dependency, which exhibited smaller weight and height in comparison to the norm, as well as slightly smaller head circumference that was within 0.5 standard deviation of the norm. Although short-gap esophageal atresia is repaired quickly, infants are often nutritionally restricted in the postoperative period, possibly due to metabolic demands of the surgery, new onset of gastro-intestinal reflux, and/or poor oral food intake [56,57]. It is also possible that perioperative critical care practices have significantly improved over the past decade to improve somatic growth – especially in infants with LGEA where the importance is placed on (i) pre-operative nutrition by enteral feeds via gastrostomy tube, (ii) administration of total parenteral nutrition during the Foker process, and (iii) gastrostomy-jejunostomy tube feeds post-operatively until the oral food intake is satisfactory.

4.2. Head and brain size discrepancy following long-gap esophageal atresia repair

Our novel results showing a *lack of differences* in head circumference in selected cohort of infant patients following Foker process for LGEA repair in comparison to normative control group–are especially important in the context of previously reported decreased brain size in the same cohort [36,38,39]. This striking finding of discrepancy between head size (as presented in this report) and smaller brain volumes in our pilot cohort [36,38,39] raises concerns for (1) validity of head circumference as an indirect measure of brain size in selected group of infants following LGEA repair with Foker process, and (2) their future proper neurological follow up. It was described recently that infants undergoing neonatal surgery for noncardiac congenital anomalies (including those with esophageal atresia) are at risk of brain injury [28]. Although we shared the list of identified qualitative radiological findings (ranging from delayed myelination to more serious findings of subdural hematomas and strokes; *Fig. 5* in [36]; *Fig. 2* in [37]; *Table 3* in [38]), the etiology underlying decreased brain size following Foker process in infants with LGEA is unknown. Our recent small series case report, albeit including sicker infants, implicates a possible '*dual-hit*' etiology: pre-existing, previously unrecognized findings that worsen over the course of perioperative critical care [38]. Further research is warranted into potential mechanisms of (mal)adaptations in brain size and its discordance with head size.

4.3. Neurobehavioral sequelae following Foker process for LGEA repair

While several studies have investigated the long-term effects of major surgery, anesthesia exposure, and prolonged sedation on the developing brain [31,58–61], the cumulative impact of complex and lengthy perioperative critical care as part of Foker process

in infants born with LGEA is unknown. Until such studies illuminate possible long-term neurobehavioral sequelae of pre/perinatal and pre-/post-Foker stressors on brain development in infants born with LGEA, commonly applied metrics of (1) head circumference should probably not be used as a sole, indirect measure of brain size in selected group of critically ill infants. Similarly, despite easy accessibility of (2) serial head ultrasound approaches [62], midsagittal visualization of anterior-posterior length of corpus callosum as an indirect measure of brain size might not be a sensitive enough measure either (see *Fig. 2* in [54]). Instead, the increased risk for possible impaired brain growth and associated neurodevelopmental sequelae warrants a dedicated interdisciplinary team tuning up all aspects of care, including: (i) advancement in surgical technique (to minimize administration of repeated anesthesia and prolonged sedation), (ii) scrupulous monitoring of infants' risk factors (viz. comorbidities and surgical complications), (iii), serial neurological exams, (iv) structured early intervention programs, (v) further improvement in nutrition, (vi) implementation of a constructive playful enriching environment, and (vii) adequate early education of parents on what to expect during critical years of development.

4.4. Study limitations

Our pilot study results should not be generalized until future studies that possibly include other referral centers, address several of the study limitations previously discussed [36,39,41] regarding the (1) *Study Groups*: we lack a true control group since there is no alternate treatment for LGEA that does not involve surgery, and there is a limited number of infants with prolonged sedation (without surgery) [40] or otherwise healthy preterm infants that did not require medical care; (2) *Study Size*: we had a limited number of subjects scanned at older time points (>8 months of age), particularly in that of the preterm patient group. Age-related changes in end-point measures were accounted for during statistical analysis by using a GLM with gestation-corrected age at scan as a covariate; (3) *Sex Differences*: unlike the balanced sex distributions in patient groups, the control group consisted of mostly males (Table 1); (4) *Timing of the Brain MRI*: subjects in our one-time cross-sectional study were scanned at a wide range of corrected ages, introducing a potential bias. Future analyses should include uniform age range distribution and additional time points for head and brain measures (e.g. pre- and post-Foker treatment).

5. Conclusion

Although future studies with larger cohorts should evaluate growth of the calvarium and brain of infants born with LGEA [38], our pilot study's take home message questions whether head circumference represents an appropriate tool to indirectly assess brain size in infants undergoing Foker process for LGEA repair. Discussed head/brain size discrepancy in the selected group of infants with LGEA should also call for long-term neurological follow up.

Author contributions

Authorship credit was based on substantial contributions to (1) the conception and manuscript design (all authors); (2) data summary (DB and SSR) and interpretation of data (all authors); (3) drafting the article (all authors) or critical revision for important intellectual content (all authors); (4) final approval of the version to be published (all authors).

Funding

The NIDA K08 DA035972–01 and Boston Children's Hospital 2019 OFD/BTREC/CTREC Faculty Career Development Fellowship supported this work (DB).

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgments

The authors express tremendous gratitude to infants and their parents who participated in this study. Authors would also like to thank Chandler R.L. Mongerson, MSci for technical help with formating Fig. 1. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

[1] Penzes P, Cahill ME, Jones KA, VanLeeuwen JE, Woolfrey KM. Dendritic spine pathology in neuropsychiatric disorders. Nat Neurosci 2011;14(3):285–93.
[2] Cockerill J, Uthaya S, Dore CJ, Modi N. Accelerated postnatal head growth follows preterm birth. Arch Dis Child Fetal Neonatal Ed 2006;91(3):F184–7.
[3] Vohr B. Long-term outcomes of moderately preterm, late preterm, and early term infants. Clin Perinatol 2013;40(4):739–51.
[4] Kuban KC, Allred EN, O'Shea TM, Paneth N, Westra S, Miller C, et al. Developmental correlates of head circumference at birth and two years in a cohort of extremely low gestational age newborns. J Pediatr 2009;155(3):344–9 e1-3.
[5] Kidokoro H, Anderson PJ, Doyle LW, Woodward LJ, Neil JJ, Inder TE. Brain injury and altered brain growth in preterm infants: predictors and prognosis. Pediatrics 2014;134(2):e444–53.
[6] Babson SG, Henderson NB. Fetal undergrowth: relation of head growth to later intellectual performance. Pediatrics 1974;53(6):890–4.
[7] Bray PF, Shields WD, Wolcott GJ, Madsen JA. Occipitofrontal head circumference–an accurate measure of intracranial volume. J Pediatr 1969;75(2):303–5.
[8] Bartholomeusz HH, Courchesne E, Karns CM. Relationship between head circumference and brain volume in healthy normal toddlers, children, and adults. Neuropediatrics 2002;33(5):239–41.
[9] Sheth RD, Mullett MD, Bodensteiner JB, Hobbs GR. Longitudinal head growth in developmentally normal preterm infants. Arch Pediatr Adolesc Med 1995;149(12):1358–61.
[10] Cooke RW, Lucas A, Yudkin PL, Pryse-Davies J. Head circumference as an index of brain weight in the fetus and newborn. Early Hum Dev 1977;1(2):145–9.
[11] Lemons JA, Schreiner RL, Gresham EL. Relationship of brain weight to head circumference in early infancy. Hum Biol 1981;53(3):351–4.
[12] Lindley AA, Benson JE, Grimes C, Cole TM 3rd, Herman AA. The relationship in neonates between clinically measured head circumference and brain volume estimated from head CT-scans. Early Hum Dev 1999;56(1):17–29.
[13] Cheong JL, Hunt RW, Anderson PJ, Howard K, Thompson DK, Wang HX, et al. Head growth in preterm infants: correlation with magnetic resonance imaging and neurodevelopmental outcome. Pediatrics 2008;121(6):e1534–40.
[14] Maunu J, Parkkola R, Rikalainen H, Lehtonen L, Haataja L, Lapinleimu H, et al. Brain and ventricles in very low birth weight infants at term: a comparison among head circumference, ultrasound, and magnetic resonance imaging. Pediatrics 2009;123(2):617–26.
[15] Harris SR. Measuring head circumference: update on infant microcephaly. Can Fam Phys 2015;61(8):680–4.
[16] Use of World Health Organization and CDC Growth Charts for Children Aged 0–59 Months in the United States. Accessed March 2020 at: http://www.cdc.gov/growthcharts/.
[17] Grummer-Strawn LM, Reinold C, Krebs NF. Centers for disease C, prevention. Use of World Health Organization and CDC growth charts for children aged 0-59 months in the United States. MMWR Recomm Rep 2010;59(RR–9):1–15.
[18] Nellhaus G. Head circumference from birth to eighteen years. practical composite international and interracial graphs. Pediatrics 1968;41(1):106–14.
[19] Sniderman A. Abnormal head growth. Pediatr Rev 2010;31(9):382–4.
[20] Grunau RE, Whitfield MF, Petrie-Thomas J, Synnes AR, Cepeda IL, Keidar A, et al. Neonatal pain, parenting stress and interaction, in relation to cognitive and motor development at 8 and 18 months in preterm infants. Pain 2009;143(1–2):138–46.
[21] Rice D, Barone S Jr. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environ Health Perspect 2000;108(Suppl 3):511–33.
[22] Loepke AW, Soriano SG. An assessment of the effects of general anesthetics on developing brain structure and neurocognitive function. Anesth Analg 2008;106(6):1681–707.
[23] McCann ME, Soriano SG. Does general anesthesia affect neurodevelopment in infants and children? BMJ 2019;367:l6459.

[24] Pierro A, Eaton S. Metabolism and nutrition in the surgical neonate. Semin Pediatr Surg 2008;17(4):276–84.
[25] Scheurer JM, Zhang L, Plummer EA, Hultgren SA, Demerath EW, Ramel SE. Body composition changes from infancy to 4 years and associations with early childhood cognition in preterm and full-term children. Neonatology 2018;114(2):169–76.
[26] Chau V, Brant R, Poskitt KJ, Tam EW, Synnes A, Miller SP. Postnatal infection is associated with widespread abnormalities of brain development in premature newborns. Pediatr Res 2012;71(3):274–9.
[27] Ramel SE, Brown LD, Georgieff MK. The impact of neonatal illness on nutritional requirements-one size does not fit all. Curr Pediatr Rep 2014;2(4):248–54.
[28] Stolwijk LJ, Keunen K, de Vries LS, Groenendaal F, van der Zee DC, van Herwaarden MYA, et al. Neonatal Surgery for noncardiac congenital anomalies: neonates at risk of brain injury. J Pediatr 2017;182:335–41 e1.
[29] De Cunto A, Paviotti G, Travan L, Bua J, Cont G, Demarini S. Impact of surgery for neonatal gastrointestinal diseases on weight and fat mass. J Pediatr 2015;167(3):568–71.
[30] Schwarzenberg SJ, Georgieff MK. Committee on N. advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. Pediatrics 2018;141(2).
[31] Laing S, Walker K, Ungerer J, Badawi N, Spence K. Early development of children with major birth defects requiring newborn surgery. J Paediatr Child Health 2011;47(3):140–7.
[32] Stolwijk LJ, Lemmers PM, Harmsen M, Groenendaal F, de Vries LS, van der Zee DC, et al. Neurodevelopmental outcomes after neonatal surgery for major noncardiac anomalies. Pediatrics 2016;137(2):e20151728.
[33] Prado EL, Dewey KG. Nutrition and brain development in early life. Nutr Rev 2014;72(4):267–84.
[34] Ramel SE, Gray HL, Christiansen E, Boys C, Georgieff MK, Demerath EW. Greater early gains in fat-free mass, but not fat mass, are associated with improved neurodevelopment at 1 year corrected age for prematurity in very low birth weight preterm infants. J Pediatr 2016;173:108–15.
[35] Pfister KM, Zhang L, Miller NC, Ingolfsland EC, Demerath EW, Ramel SE. Early body composition changes are associated with neurodevelopmental and metabolic outcomes at 4 years of age in very preterm infants. Pediatr Res 2018;84(5):713–18.
[36] Mongerson CRL, Wilcox SL, Goins SM, Pier DB, Zurakowski D, Jennings RW, et al. Infant brain structural MRI analysis in the context of thoracic noncardiac surgery and critical care. Front Pediatr 2019;7:315.
[37] Hodkinson DJ, Mongerson CRL, Jennings RW, Bajic D. Neonatal functional brain maturation in the context of perioperative critical care and pain management: a case report. Heliyon 2019;5(8):e02350.
[38] Rudisill SS, Wang JE, Jaimes C, Mongerson CRL, Hansen AR, Jennings RW, et al. Neurologic injury and brain growth in the setting of long-gap esophageal atresia perioperative critical care: a pilot study. Brain Sci 2019(9).
[39] Mongerson CRL, Jennings RW, Zurakowski D, Bajic D. Quantitative MRI study of infant regional brain size following surgery for long-gap esophageal atresia requiring prolonged critical care. Int J Dev Neurosci 2019;79:11–20.
[40] Solodiuk JC, Jennings RW, Bajic D. Evaluation of Postnatal Sedation in Full-Term Infants. Brain Sci 2019;9(5).
[41] Mongerson CRL, Jaimes C, Zurakowski D, Jennings RW, Bajic D. Infant corpus callosum size after surgery and critical care for long-gap esophageal atresia: qualitative and quantitative MRI. Sci Rep 2020;10(1):6408.
[42] Sfeir R, Michaud L, Salleron J, Gottrand F. Epidemiology of esophageal atresia. Dis Esophagus 2013;26(4):354–5.
[43] Moore KL, Persaud TVN, Torchia MG. The developing human, clinically oriented embryology. 10th ed. Philadelphia, PA: Elsevier; 2015.
[44] van der Zee DC, van Herwaarden MY, Tytgat SH, Maffi M, Lima M. Esophageal Atresia and Tracheoesophageal Fistula. Neonatal surgery. Lima M, R O, editors. Cham: Springer; 2019.
[45] Hunt RW, Perkins EJ, King S. Peri-operative management of neonates with oesophageal atresia and tracheo-oesophageal fistula. Paediatr Respir Rev 2016;19:3–9.
[46] Foker JE, Kendall Krosch TC, Catton K, Munro F, Khan KM. Long-gap esophageal atresia treated by growth induction: the biological potential and early follow-up results. Semin Pediatr Surg 2009;18(1):23–9.
[47] Kunisaki SM, Foker JE. Surgical advances in the fetus and neonate: esophageal atresia. Clin Perinatol 2012;39(2):349–61.
[48] Bairdain S, Hamilton TE, Smithers CJ, Manfredi M, Ngo P, Gallagher D, et al. Foker process for the correction of long gap esophageal atresia: primary treatment versus secondary treatment after prior esophageal surgery. J Pediatr Surg 2015;50(6):933–7.
[49] Shen J, Rudisill SS, Wang JT, Jennings RW, Zurakowski D, Bajic D. Association of anesthesia and sedation exposure with brain MRI in critically ill infants. Society for Pediatric Pain Medicine (SPPM) Abstract Nassau, Bahamas; 2020.
[50] Almli CR, Rivkin MJ, McKinstry RC. Brain Development Cooperative G. The NIH MRI study of normal brain development (Objective-2): newborns, infants, toddlers, and preschoolers. Neuroimage 2007;35(1):308–25.
[51] Raschle N, Zuk J, Ortiz-Mantilla S, Sliva DD, Franceschi A, Grant PE, et al. Pediatric neuroimaging in early childhood and infancy: challenges and practical guidelines. Ann N Y Acad Sci 2012;1252:43–50.
[52] Tocchio S, Kline-Fath B, Kanal E, Schmithorst VJ, Panigrahy A. MRI evaluation and safety in the developing brain. Semin Perinatol 2015;39(2):73–104.
[53] Paterson SJ, Badridze N, Flax JF, Liu WC, Benasich AA. A method for structural mri scanning of non-sedated infants. Chicago: Rutgers University; 2004.
[54] Mongerson CRL, Jennings RW, Main SA, Jois MS, Zurakowski D, Bajic D. Infant corpus callosum volumes following thoracic noncardiac surgery for long-gap esophageal atresia. 2019 American Society of Anesthesiology Annual Meeting Orlando, FL; 2019. Oct 19-23, 2019.
[55] Gischler SJ, Mazer P, Duivenvoorden HJ, van Dijk M, Bax NM, Hazebroek FW, et al. Interdisciplinary structural follow-up of surgical newborns: a prospective evaluation. J Pediatr Surg 2009;44(7):1382–9.
[56] Stadil T, Koivusalo A, Svensson JF, Jonsson L, Lilja HE, Thorup JM, et al. Surgical treatment and major complications within the first year of life in newborns with long-gap esophageal atresia gross type A and B - a systematic review. J Pediatr Surg 2019;54(11):2242–9.
[57] Koivusalo AI, Sistonen SJ, Lindahl HG, Rintala RJ, Pakarinen MP. Long-term outcomes of oesophageal atresia without or with proximal tracheooesophageal fistula - Gross types A and B. J Pediatr Surg 2017;52(10):1571–5.
[58] Walker K, Badawi N, Holland AJ, Halliday R. Developmental outcomes following major surgery: what does the literature say? J Paediatr Child Health 2011;47(11):766–70.
[59] Walker K, Holland AJ, Winlaw D, Sherwood M, Badawi N. Neurodevelopmental outcomes and surgery in neonates. J Paediatr Child Health 2006;42(12):749–51.
[60] Wilder RT, Flick RP, Sprung J, Katusic SK, Barbaresi WJ, Mickelson C, et al. Early exposure to anesthesia and learning disabilities in a population-based birth cohort. Anesthesiology 2009;110(4):796–804.
[61] Andropoulos DB. Effect of Anesthesia on the developing brain: infant and fetus. Fetal Diagn Ther 2018;43(1):1–11.
[62] Meijler G, Steggerda S. Neonatal cranial ultrasonography. 3 ed. Springer International Publishing; 2019.