Does time to theater matter in simple gastroschisis?

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ABSTRACT

Objective A recent publication has suggested that expedited time to theater in gastroschisis results in higher rates of primary closure and decreases the length of stay (LOS). This study primarily aims to assess the impact of time to first management of neonates with gastroschisis on the LOS.

Methods Neonates admitted between August 2013 and August 2020 with gastroschisis were included. Data were collected retrospectively, and neonates with complex gastroschisis were excluded. Variables including gestation, birth weight, time of first management, primary/delayed closure and use of patch were evaluated as possible confounding variables. The outcome measures were time to full feeds, time on parenteral nutrition (PN) and LOS. Univariate and multivariate linear regression analyses were performed. P<0.05 was regarded as significant.

Results Eighty-six neonates were identified, and 16 were then excluded (eight patients with complex gastroschisis, eight patients with time to first management not documented). The median LOS for those who underwent primary closure was 21 days (interquartile range (IQR) =16–29) and for those who underwent silo placement and delayed closure was 59 days (IQR=44–130). The mean time to first management was 473 min (standard deviation (SD) =146 min), with only 20% of these infants being operated on at less than 6 hours of age. Univariate and multivariate analyses demonstrated no relationship between time to first management and LOS (r²=0.00, p=0.82) but did demonstrate a consistent positive association between time to first feed and LOS and delayed closure, resulting in a longer time to full feeds and a longer time on PN.

Conclusions The time to first management was not associated with a change in LOS in these data. Further prospective evaluation of the impact of reducing the time to first feed on the LOS is recommended.

Level of evidence IV.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Achieving primary closure is the strongest determinant of reducing the length of stay (LOS) of infants with simple gastroschisis. Reducing the time to first management after birth may increase the rate of primary closure and further reduce the LOS.

WHAT THIS STUDY ADDS

⇒ The time between birth and primary closure did not have a significant impact on the LOS in this study. Reducing the time to theater did not achieve a higher rate of primary closure in this series. An association between time to first feed and LOS is consistently demonstrated.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Investigation of whether prospectively instigating early feeding in infants with gastroschisis can result in a reduced LOS requires prospective evaluation.

INTRODUCTION

Gastroschisis is the most common congenital abdominal wall defect, estimated to affect between 3.6 and 4.4 per 10 000 live births in the UK.[1] It is increasing in prevalence and has been identified by the chief medical officer of the UK as a research priority.[2 3] The majority of gastroschisis is simple (85%), with excellent survival exceeding 90% in high-income countries.[1 4 5] Complex gastroschisis, defined as gastroschisis with intestinal atresia, perforation or stenosis, represents a much higher risk cohort with complex clinical courses and a worse prognosis.[6] Neonates with simple gastroschisis have an average length of stay (LOS) of around 1 month.[7] This represents a significant cost for healthcare providers and is associated with family disruption and stress. While best care is always a clinician's focus, with the National Health Service reporting £13.4 billion of outstanding debt at the end of the 2019/2020 tax year, service planning to facilitate high-quality delivery of care, which results in reduced LOS and thus reduces costs, is an important consideration.[8]

Strategies regarding the initial management and timing of intervention in simple gastroschisis are controversial. Current trends within the UK demonstrate that approximately 58% are managed by primary closure and 40% by silo.[1] The silo group is inherently more heterogeneous. Some will have a preformed silo placed in a non-theater setting, some of whom would have been suitable for primary closure. Some will have a silo placed in theater when primary reduction is not possible. Multicenter UK data demonstrate that babies

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managed by primary closure have a shorter LOS than those managed by initial preformed silo (median 34 vs 38 days).[1 9] More recent evidence suggests that expedited time to theater improves the primary closure rate to 77% with shorter time to full feeds (TFF) and shorter LOS (median 19 and 22.5 days, respectively).[10]

The aim of this study was to determine the relationship between time to first management (TFM) and LOS in simple gastroschisis. Although TFM was the focus of our study, other variables, including gestation, birth weight (BW), time of procedure (day 08:00–19:59 or night 20:00–07:59), primary/delayed closure and use of patch, were evaluated as possible confounding variables. The primary outcome measures were TFF, time on parenteral nutrition (TPN) and LOS.

METHODS

This study was undertaken in a UK pediatric surgical tertiary center as a service evaluation of the care of children with gastroschisis and was registered with the institution. Neonates with antenatally diagnosed gastroschisis were delivered in a level III maternity and neonatal hospital and stabilized prior to transfer to the pediatric surgical center for definitive management. Preformed silo placement was performed in the maternity hospital if the neonate was unfit for transfer or if a prolonged delay to theater was expected; in this instance, the silo would be placed by a member of the pediatric surgical team, and this would be considered a delayed repair. TFM was defined as the time from delivery to the time of first management of gastroschisis, which could be time to the theater, time of bedside reduction or time of placement of bedside silo.

Inclusion criteria:
► Infants with gastroschisis admitted to the pediatric surgical center between August 2013 and August 2020, identified using the BadgerNet database and searching for 'gastroschisis'.
► Simple gastroschisis.
► Time from birth to first management could be extracted from the notes.

Exclusion criteria:
► Complex gastroschisis. This was determined using the criteria described by Molik *et al* and included babies with atresia, congenital necrosis, perforation, or volvulus.[6]
► No documentation of the time of first management.

Data were collected retrospectively from case notes, including gestation, BW, sex, time of birth, time to first set of observations in theater, surgical procedures, vascular access and time to first feed. Outcome variables including TFF, duration of parenteral nutrition (PN) and LOS (time from birth to time of discharge, inclusive of those undergoing primary or staged/delayed closure) were recorded. When babies underwent gastroschisis management in a non-theater setting, the time of the procedure as recorded in the notes was used. Time

of birth and time of procedure were coded as 0 if they occurred during 'day-time hours' between 08:00 and 19:59 and 1 if they occurred 'out of hours' between 20:00 and 07:59. In our institution, there is no standardized approach to the initiation of feeding regarding timing, volume, or rate of advancement, which is at the discretion of the clinician. Where feasible, breast feeding or expressed breast milk provision is our preference, but the family's wishes are always respected and combination feeding is often used when available breast milk supplies do not meet the requirements of the infant.

Statistical analysis
Data are described using percentages, were tested for normality and are presented as the mean and standard deviation(SD) or median and interquartile range (IQR) as appropriate. Parametric data were compared using an unpaired Student's t-test, and non-parametric data were compared using an unpaired Mann-Whitney U test. Categorical data were compared using Fisher's exact test and are described using odds ratios (ORs) and 95% confidence intervals (CIs). When data points were missing, the baby was excluded from the analysis. Univariate linear regression analysis was performed for the outcome measures of LOS, duration of PN and TFF. The variables gestation, mode of delivery (vaginal or cesarean section), BW, time from birth to procedure, type of line (tunneled central line or peripherally inserted central catheter (PICC)), primary or delayed closure and use of abdominal patch were initially analyzed. These variables were then included in multivariate analysis to determine if any association persisted.

Subanalysis of the association between TFM and the use of primary closure compared with the placement of a silo was undertaken using univariate logistic regression. The TFM and the outcomes of TFF, duration of PN and LOS were compared in the subgroup of infants who underwent primary closure using univariate linear regression analysis. Statistical significance was determined using $p < 0.05$.

RESULTS
Demographics
Eighty-six neonates were identified, 16 were excluded (eight with complex gastroschisis (there was one mortality in this group) and eight who did not have a record of time to the first management). Thus, 70 babies met the inclusion criteria, 41 male and 29 female. The median gestation at birth was 36+4/40 weeks (IQR=35+2 weeks to 37+4 weeks), and the mean BW was 2.47±0.55 kg. A total of 42/70 (60%) babies were delivered vaginally. The mean time from birth to first management was 473±146 min, with 14/70 (20%) babies undergoing primary closure or silo placement within 6 hours of birth. Infants born during daytime hours had the same delay to theater as those born overnight (479 min vs 466 min,

p=0.72). There was no mortality in this group of babies with simple gastroschisis.

Primary closure was achieved in 41/70 babies (59%), one of which was performed in the intensive care unit. Twenty-nine (41%) underwent primary silo placement, with 4/29 (14%) silos placed in a non-theater setting. Fisher's exact test comparing time to theater within 6 hours and the type of first management (primary closure vs silo placement) did not demonstrate a significant difference in the rate of primary closure in those managed within 6 hours (42.8%) and those managed at 6 hours or beyond (62.5%), p=0.23. This was also demonstrated in logistic regression, where no significant association was demonstrated between TFM and primary versus silo placement (OR=1.00, 95% CI 0.997 to 1.004, p=0.66).

The first feed was given at a median of 9.5 days (IQR=6–20 days) of age. A total of 3/41 (7%) of those undergoing primary closure and 9/29 (31%) undergoing delayed closure required further laparotomy following abdominal closure (3 necrotizing enterocolitis, 6 adhesional obstruction, 1 fundoplication, 1 compartment syndrome, 1 segmental volvulus). The odds of undergoing further laparotomy were higher after delayed closure than after primary closure (OR=5.70, 95% CI 1.51–20.75, p=0.021).

A total of 47/70 (67%) babies had a tunneled central line as their first form of centrally positioned intravenous access, 21/70 (30%) had a PICC, and 1/70 (1%) had a non-tunneled central line. The median TFF was 23 days (IQR=15–42 days), the median duration of PN was 25 days (IQR=15–44 days) and the median LOS was 30 days (IQR=19–54 days). Infants undergoing primary closure of gastroschisis had a significantly shorter LOS than those undergoing delayed closure (21 days (IQR=16–29 days) vs 59 days (IQR=44–130 days), p<0.0001).

Univariate analysis of factors that may influence the duration of PN, TFF and LOS

Univariate analysis of the variables that may influence the duration of PN, TFF and LOS is displayed in table 1. A significant negative correlation was demonstrated between gestation and BW with LOS but not with the TFF or the duration of PN. There is a significant correlation between increased TFF, duration of PN and LOS when the procedure is performed 'out-of-hours' and when a delayed closure is undertaken (ie, a silo is placed in the first procedure).

Multivariate analysis of factors that may influence the duration of PN, TFF and LOS

Multivariate linear regression analysis (table 2) demonstrates a persistent significant association between achieving primary closure and a reduced TFF and a reduced duration of PN compared with those undergoing delayed closure when the model is adjusted for all other variables. However, an association with LOS was not demonstrated in this analysis. The TFM of an infant with

Table 1 Univariate association between variables and the outcomes of time to full feeds, duration of parenteral nutrition and length of stay

Variables	Time to full feeds (days)		Duration of PN (days)		Length of stay (days)	
	r^2	P value	r^2	P value	r^2	P value
Gestation (weeks) 36+4 (35+3 to 37+4)	−0.06	0.06	−0.06	0.05	**−0.07**	**0.04**
Birth weight (kg) 2.52 (2.09–2.81)	−0.05	0.08	−0.05	0.08	**−0.08**	**0.02**
Mode of delivery 0: 43 (61%); 1: 27 (39%)	0.002	0.75	0.002	0.73	0.004	0.61
Time of birth 0: 39 (56%); 1: 31 (44%)	0.05	0.08	0.06	0.08	0.00	0.45
Time from birth to procedure (mins) 463 (370–547)	0.03	0.16	0.03	0.15	0.00	0.82
Time of procedure 0: 30 (43%); 1: 40 (57%)	**0.09**	**0.02**	**0.08**	**0.02**	**0.10**	**0.01**
Primary versus delayed closure 0: 41 (59%); 1: 29 (41%)	**0.28**	**<0.0001**	**0.28**	**<0.0001**	**0.31**	**<0.0001**
No patch versus patch closure 0: 54 (77%); 1: 16 (23%)	**0.12**	**0.005**	**0.12**	**0.004**	**0.18**	**0.0005**
Days to first feed 9.5 (6.0–19.8)	**0.21**	**0.0001**	**0.21**	**0.0001**	**0.36**	**<0.0001**

Mode of delivery (0—vaginal, 1—cesarean section), time of birth (0—08:00 to 19:59, 1—20:00 to 07:59), time of procedure (0—08:00 to 19:59, 1—20:00 to 07:59), primary (0) versus delayed (1) closure, no patch (0) versus patch (1).
Data were presented as median (IQR) or number (percentage).
IQR, interquartile range; PN, parenteral nutrition.

Table 2 Multivariate linear regression analysis of variables found to be associated with the outcomes of time to full feeds, duration of parenteral nutrition and length of stay in univariate regression analysis

Variables	Time to full feeds (days) Est (95% CI)	P value	Duration of PN (days) Est (95% CI)	P value	Length of stay (days) Est (95% CI)	P value
Gestation (weeks)	−4.1 (−11.0 to 2.8)	0.23	−4.2 (−11.0 to 2.6)	0.22	−5.9 (−13.9 to 2.1)	0.15
Birth weight (kg)	0.00 (−0.02 to 0.03)	0.62	0.00 (−0.01 to 0.03)	0.61	0.00 (−0.02 to 0.03)	0.86
Mode of delivery	−6.1 (−27.6 to 15.3)	0.57	−6.3 (−27.6 to 15.0)	0.56	−0.83 (−26.7 to 25.0)	0.95
Time of birth	−19.8 (−41.4 to 1.9)	0.07	−20.0 (−41.5 to 1.5)	0.07	−9.02 (−35.0 to 17.0)	0.49
Time of procedure	18.6 (−3.3 to 40.5)	0.09	18.3 (−3.5 to 40.0)	0.10	20.5 (−5.9 to 46.9)	0.13
Time from birth to first management (mins)	0.04 (−0.04 to 0.11)	0.31	0.04 (−0.0 to 0.1)	0.30	−0.01 (−0.09 to 0.07)	0.82
Primary versus delayed closure	**16.5 (9.8 to 76.0)**	**0.01**	**43.0 (10.1 to 75.9)**	**0.01**	32.4 (−6.7 to 71.5)	0.10
No patch versus patch closure	−11.2 (−44.0 to 21.6)	0.50	−11.0 (−43.6 to 21.6)	0.50	−0.1 (−39.5 to 39.2)	>0.99
Days to first feed	0.98 (−0.7 to 2.6)	0.23	0.97 (−0.6 to 2.6)	0.23	**2.34 (0.5 to 4.2)**	**0.01**

Time of procedure (0—08:00 to 19:59, 1—20:00 to 07:59), primary (0) versus delayed (1) closure, no patch (0) versus patch (1). The results shown are the estimated relationship between the variable and outcome (r^2) and the 95% CI.
CI, confidential interval; PN, parenteral nutrition.

gastroschisis is not associated with a significant reduction in the TFF, duration of PN or LOS.

Earlier administration of the first feed is associated with a reduced LOS but is not associated with a reduced time to achieving full feeds or a reduced duration of PN. Figure 1 demonstrates a significant correlation between the days to first feed and the LOS in infants undergoing primary closure but not for infants undergoing delayed closure.
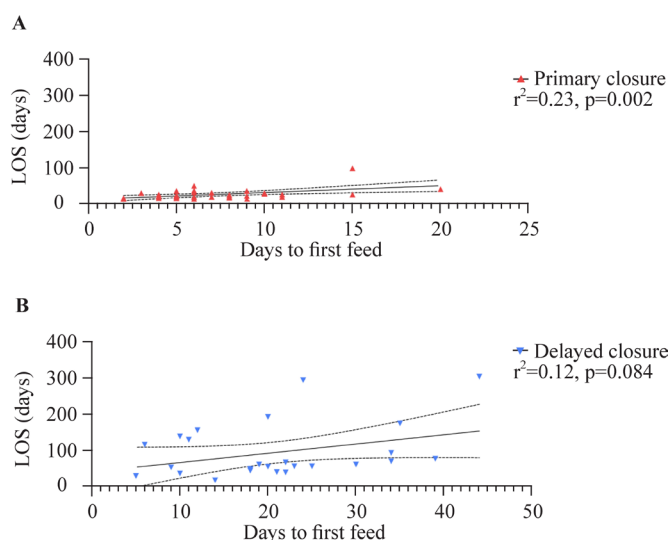
For infants undergoing primary closure, the median TFF was 17 days (IQR=13–22 days), the duration of PN was 16 days (IQR=13–22 days) and the LOS was 21 days (IQR=16–29 days). No significant association was demonstrated between TFM and TFF and LOS (figure 2A,B).

DISCUSSION

The incidence of gastroschisis has increased threefold over the last decade, with the estimated cost of gastroschisis care rising from 3.6 million in 1996 to 15 million by 2005.[11] In addition to the economic impact, parents of infants who require long stays in neonatal intensive care units experience negative psychological effects, including issues pertaining to attachment and the development of their parenting role.[12] For these reasons, it is vital as clinicians that we consider how we can safely limit the time neonates spend in the hospital.

It is demonstrated that younger gestation and lower BW infants have a longer LOS, but this does not significantly impact their TPN or their TFF. Standardized care and enhanced recovery protocols have been shown to improve outcomes across a wide range of pediatric surgical conditions.[13 14] Several studies have highlighted that protocolized care in institutional 'care bundles' may positively impact mechanical ventilation and rates of primary closure.[15–17] While Joharifard's group did not

Figure 1 Association between the days to first feed and length of stay (LOS) for infants undergoing primary closure (A) and delayed closure (B). A line of best fit and 95% CIs are shown. CI, confidential interval.
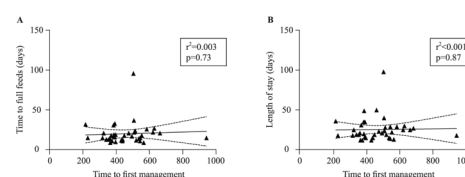
Figure 2 Association between the time to first management and the outcomes of time to full feeds (A), and length of stay (LOS) (B). A line of best fit and 95% CIs are shown. No significant association is demonstrated. CI, confidential interval.

demonstrate a reduction in the duration of TPN or LOS, they did achieve a 95% rate of TFM <6 hours after delivery with a median duration of TPN of 20 days (vs 25 in our cohort). This again supports the potential impact of time to first intervention. Early first feed has been previously suggested to improve outcomes from gastroschisis,[18 19] and the results shown here suggest that early feeds may be associated with a reduction in LOS, particularly in infants undergoing primary closure. However, early feeding has not been shown to have a significant association with a reduction in TPN or the TFF, in keeping with previous research.[18]

It is accepted that primary closure is associated with reduced LOS in infants with gastroschisis, a finding strongly supported by the data within this study.[20 21] Infants undergoing primary closure had a significantly lower rate of further laparotomies than infants undergoing delayed closure. Aprahamian's group was the first to consider the impact of expedited theater to improve rates of primary closure. They described combining immediate attempted reduction and primary closure along with mucolytic bowel irrigation, resulting in rates of primary closure of 77%.[10] This is substantially higher than the 59% receiving primary closure in this group. The findings of our study do not demonstrate that earlier intervention results in a higher likelihood of achieving primary closure. However, in Aprahamian's group, the median time to theater was 1.8 hours compared with a median time to theater of 7.9 hours in this study. To achieve this fourfold reduction in time to theater, there must be colocated maternity services and a dedicated pediatric theater.

Aprahamian proposes that for every 1-hour delay in time to theater, there is a 5.5% increase in LOS for those undergoing primary closure. Within this study, no correlation was demonstrated between TFM and TFF, duration on PN or LOS in the group as a whole or in the group achieving primary closure. Furthermore, the TFF and LOS are comparable in those undergoing primary closure in Aprahamian's group (19 and 22.5 days) and within this series (17 and 21 days).

Strengths and limitations
This study demonstrates the current reality of care of infants with gastroschisis in a center where maternity services are not colocated. There are several limitations to the study, particularly the exclusion of eight infants who did not have documentation of TFM, the lack of a standardized feeding pathway, which may have resulted in variability around the approach to postoperative feeding, and the retrospective nature of the data collection. As a rare condition for a single center to research, findings are limited by the relatively small sample size for performing multivariate statistics. Furthermore, alternative approaches to gastroschisis, particularly including the use of preformed silos in the majority of infants with gastroschisis, have not been examined in this cohort.

Conclusion
Time to first procedure has not been demonstrated to be associated with an improvement of any of the three outcome measures, and while the TFM in this cohort is longer than is reported in centers where maternity and pediatric surgical services are colocated, the TFF and LOS are comparable to other studies in infants undergoing primary closure. The implementation of standardized care bundles, particularly focusing on time to first feed, as well as the investigation of whether reducing the TFM to below 6 hours can result in a higher rate of primary closure requires prospective evaluation.

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REFERENCES
1 Owen A, Marven S, Johnson P, *et al*. Gastroschisis: a national cohort study to describe contemporary surgical strategies and outcomes. *J Pediatr Surg* 2010;45:1808–16.
2 Donaldson LJ. *On the state of the public health: annual report of the Chief Medical Officer 2004*. London: Health Do, 2005.
3 Kilby MD. The incidence of gastroschisis. *BMJ* 2006;332:250–1.
4 Tauriainen A, Sankilampi U, Raitio A, *et al*. The Association of perinatal and clinical factors with outcomes in infants with gastroschisis-a retrospective multicenter study in Finland. *Eur J Pediatr* 2021;180:1875–83.
5 Brebner A, Czuzoj-Shulman N, Abenhaim HA. Prevalence and predictors of mortality in gastroschisis: a population-based study of 4803 cases in the USA. *J Matern Fetal Neonatal Med* 2020;33:1725–31.
6 Molik KA, Gingalewski CA, West KW, *et al*. Gastroschisis: a plea for risk Categorization. *J Pediatr Surg* 2001;36:51–5.
7 Pédiatrique TCPSNLRCdC. *CAPSNet 2015 annual report*. 2016.
8 Anandaciva S. *Financial debts and loans in the NHS*. Fund TK, 2020.
9 Bradnock TJ, Marven S, Owen A, *et al*. Gastroschisis: one year outcomes from national cohort study. *BMJ* 2011;343:d6749.

10   Pearl RH, Esparaz JR, Nierstedt RT, *et al*. Single center protocol driven care in 150 patients with gastroschisis 1998-2017: collaboration improves results. *Pediatr Surg Int* 2018;34:1171–6.

11   Keys C, Drewett M, Burge DM. Gastroschisis: the cost of an epidemic. *J Pediatr Surg* 2008;43:654–7.

12   Al Maghaireh DF, Abdullah KL, Chan CM, *et al*. Systematic review of qualitative studies exploring parental experiences in the neonatal intensive care unit. *J Clin Nurs* 2016;25:2745–56.

13   Arena S, Di Fabrizio D, Impellizzeri P, *et al*. Enhanced recovery after gastrointestinal surgery (ERAS) in pediatric patients: a systematic review and meta-analysis. *J Gastrointest Surg* 2021;25:2976–88.

14   Brindle ME, McDiarmid C, Short K, *et al*. Consensus Guidelines for Perioperative Care in Neonatal Intestinal Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations. *World J Surg* 2020;44:2482–92.

15   Joharifard S, Trudeau MO, Miyata S, *et al*. Implementing a standardized gastroschisis protocol significantly increases the rate of primary sutureless closure without compromising closure success or early clinical outcomes. *J Pediatr Surg* 2022;57:12–7.

16   Haddock C, Al Maawali AG, Ting J, *et al*. Impact of multidisciplinary standardization of care for gastroschisis: treatment, outcomes, and cost. *J Pediatr Surg* 2018;53:892–7.

17   DeUgarte DA, Calkins KL, Guner Y, *et al*. Adherence to and outcomes of a university-consortium gastroschisis pathway. *J Pediatr Surg* 2020;55:45–8.

18   Raduma OS, Jehangir S, Karpelowsky J. The effect of standardized feeding protocol on early outcome following gastroschisis repair: a systematic review and meta-analysis. *J Pediatr Surg* 2021;56:1776–84.

19   Hobson D, Spence K, Trivedi A, *et al*. Differences in attitudes to feeding post repair of gastroschisis and development of a standardized feeding protocol. *BMC Pediatr* 2019;19:475.

20   Gurien LA, Dassinger MS, Burford JM, *et al*. Does timing of gastroschisis repair matter? A comparison using the ACS NSQIP pediatric database. *J Pediatr Surg* 2017;52:1751–4.

21   Banyard D, Ramones T, Phillips SE, *et al*. Method to our madness: an 18-year retrospective analysis on gastroschisis closure. *J Pediatr Surg* 2010;45:579–84.

Table 1. Univariate association between variables and the outcomes of time to full feeds, duration of parenteral nutrition and length of stay

Variables	Time to full feeds (days)		Duration of PN (days)		Length of stay (days)	
	r^2	p	r^2	p	r^2	p
Gestation	-0.06	0.06	-0.06	0.05	**-0.07**	**0.04**
Birth Weight	-0.05	0.08	-0.05	0.08	**-0.08**	**0.02**
Mode of delivery	0.002	0.75	0.002	0.73	0.004	0.61
Time of birth	0.05	0.08	0.06	0.08	0.00	0.45
Time from birth to procedure (min)	0.03	0.16	0.03	0.15	0.00	0.82
Time of procedure	**0.09**	**0.02**	**0.08**	**0.02**	**0.10**	**0.01**
Primary vs delayed closure	**0.28**	**<0.0001**	**0.28**	**<0.0001**	**0.31**	**<0.0001**
No patch vs patch closure	**0.12**	**0.005**	**0.12**	**0.004**	**0.18**	**0.0005**
Time of first feed	**0.21**	**0.0001**	**0.21**	**0.0001**	**0.36**	**<0.0001**

Mode of delivery (0 - vaginal, 1 - caesarean section), Time of Birth (0 - 8am - 7:59pm, 1 - 8pm - 7:59am), Simple (0) vs complex (1), Time of Procedure (0 - 8am - 7:59pm, 1 - 8pm - 7:59am), Primary (0) vs delayed (1) closure, No patch (0) vs patch (1), Type of line (0 - tunnelled central line, 1 - PICC).

Table 2. Multivariate linear regression analysis of variables found to be associated with the outcomes of time to full feeds, duration of PN and length of stay in univariate regression analysis

Variables	Time to full feeds (days)		Duration of PN (days)		Length of stay (days)	
	Est (95% CI)	p	Est (95% CI)	p	Est (95% CI)	p
Gestation	-4.1 (-11.0 - 2.8)	0.23	-4.2 (-11.0-2.6)	0.22	-5.9 (-13.9 - 2.1)	0.15
Birth Weight	0.00 (-0.02 - 0.03)	0.62	0.00 (-0.01 - 0.03)	0.61	0.00 (-0.02 - 0.03)	0.86
Mode of delivery	-6.1 (-27.6-15.3)	0.57	-6.3 (-27.6 - 15.0)	0.56	-0.83 (-26.7 - 25.0)	0.95
Time of birth	-19.8 (-41.4-1.9)	0.07	-20.0 (-41.5 - 1.5)	0.07	-9.02 (-35.0 - 17.0)	0.49
Time of procedure	18.6 (-3.3 - 40.5)	0.09	18.3 (-3.5 - 40.0)	0.10	20.5 (-5.9 - 46.9)	0.13
Time from birth to first management	0.04 (-0.04 - 0.11)	0.31	0.04 (-0.0-0.1)	0.30	-0.01 (-0.09 - 0.07)	0.82
Primary vs delayed closure	**16.5 (9.8 - 76.0)**	**0.01**	**43.0 (10.1-75.9)**	**0.01**	32.4 (-6.7 - 71.5)	0.10
No patch vs patch closure	-11.2 (-44.0 - 21.6)	0.50	-11.0 (-43.6 - 21.6)	0.50	-0.1 (-39.5 - 39.2)	>0.99
Days to first feed	0.98 (-0.7-2.6)	0.23	0.97 (-0.6-2.6)	0.23	**2.34 (0.5 - 4.2)**	**0.01**

Time of Procedure (0 - 8am - 7:59pm, 1 - 8pm - 7:59am), Primary (0) vs delayed (1) closure, No patch (0) vs patch (1). Results shown are the estimated relationship between the variable and outcome (r^2) and the 95% confidence interval of this.