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Early cerebral and intestinal oxygenation in the risk assessment of necrotizing enterocolitis in preterm infants

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ABSTRACT

Background and aim: Predicting necrotizing enterocolitis (NEC) might help in preventing its devastating consequences. We aimed to investigate whether early cerebral and intestinal tissue oxygen saturation (rSO_2) and fractional tissue oxygen extraction (FTOE) predict the onset of NEC.
Study design: Prospective observational case-control study.
Subjects: Infants with gestational age (GA) < 32 weeks were included. For every NEC case we matched two controls based on GA, birth weight (BW), and a patent ductus arteriosus.
Outcome measures: Cerebral oxygenation and intestinal oxygenation were prospectively monitored two-hours daily during the first five days after birth and once a week thereafter until five weeks after birth or until NEC developed. We used Kaplan-Meier analyses to determine the ability of near-infrared spectroscopy (NIRS) measurements, including their variability, to predict the development of NEC.
Results: We included ten infants (median (range) GA 27.1 (24.6–29.4) weeks, BW 903 (560–1630) grams) who developed NEC at median postnatal day 13 (range: 4–43 days), and 20 matched controls. Infants with cerebral rSO_2 < 70% within the first 48 h after birth developed NEC significantly more often than infants with cerebral rSO_2 ≥70% (odds ratio 9.00 (95% CI 1.33–61.14). Intestinal FTOE was higher in infants who developed NEC compared to controls during the last NIRS measurement at median 2 days (range: 1–7) before NEC onset (median 0.65 vs. 0.44).
Conclusions: Cerebral oxygenation monitoring early after birth might be valuable in the risk assessment of NEC development. Additionally, our results suggest that intestinal oxygenation is impaired before the onset of clinical NEC.

1. Introduction

Necrotizing enterocolitis (NEC) is a severe gastrointestinal disease in preterm infants, with mortality rates up to 40% [1]. Short-term and long-term disabilities occur frequently [2–5]. Preventing development of NEC is currently considered the best strategy to minimize these devastating consequences [6]. Besides a preterm intestinal epithelium predisposed to an exaggerated inflammatory response to the present microbiome, impaired mesenteric perfusion inducing bowel hypoxia and ischemia is suggested to be one of the factors playing a role in the development of NEC [7].

Immature intestinal perfusion in newborn animals has been demonstrated, with less vasodilatory response to systemic hypoxemia, compared to older animals [8]. Local autoregulatory control of intestinal blood flow during low perfusion is only detectable weeks after term birth, making the intestines vulnerable to states of low perfusion

Abbreviations: cFTOE, cerebral fractional tissue oxygen extraction; CoVar, coefficient of variation; intFTOE, intestinal fractional tissue oxygen extraction; NEC, necrotizing enterocolitis; NIRS, near-infrared spectroscopy; PDA, patent ductus arteriosus; r_cSO_2, regional cerebral tissue oxygen saturation; $r_{int}SO_2$, regional intestinal tissue oxygen saturation; SGA, small for gestational age; SpO_2, arterial oxygen saturation

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pressure during the perinatal period [9]. Furthermore, in preterm infants it is supposed that a dysregulation between locally produced vasodilatory and vasoconstrictive compounds may result in ischemic intestine and contribute to the development of necrotizing enterocolitis [10,11].

Near-infrared spectroscopy (NIRS) measures regional tissue oxygen saturation (rSO_2) non-invasively. When peripheral arterial oxygen saturation (SpO_2) is obtained simultaneously, fractional tissue oxygen extraction (FTOE) can be calculated [12]. FTOE is thought to reflect the balance between oxygen delivery and consumption, and might therefore be used as an early indicator of inadequate tissue perfusion [12]. Using NIRS in a piglet model, it was reported that lower abdominal oxygen saturations and higher abdominal oxygen variation occurred before NEC develops [13,14]. This hypothesis is further supported by the finding that after NEC onset, there is a relation between both cerebral and intestinal ischemia (assessed using NIRS) and plasma levels of intestinal fatty acid- binding protein (marker for intestinal damage) [15].

Measuring tissue oxygenation could also be helpful for predicting the onset of NEC in preterm infants [16,17]. Patel et al. found lower mean intestinal rSO_2 ($r_{int}SO_2$) values in the first week after birth in preterm infants who later on developed NEC than in controls, although the controls were born after longer gestation and with higher birth weights [18]. Additionally, there is conflicting literature with regard to variability of abdominal oxygen levels and its association with NEC [13,19]. We previously found lower cerebral rSO_2 (r_cSO_2) after NEC onset in infants who subsequently developed complicated NEC, compared to infants with uncomplicated NEC [20]. Measurements of r_cSO_2 might provide additional information concerning the overall hemodynamic condition before NEC development.

We therefore investigated the possibility to use cerebral and intestinal tissue oxygen saturation values measured by NIRS in the first days after birth up to NEC development, to predict which high-risk infants went on to develop NEC.

2. Study design

2.1. Patient population

We performed an observational case-control study. Patients and controls were derived from a cohort prospectively collected at the neonatal intensive care unit (NICU) of University Medical Center Groningen between October 2012 and February 2014. The purpose of this exploratory study was to find early non-invasive markers that might help in the risk assessment of NEC development, in order to be able to define a very high risk group early after birth. NEC incidence in all preterm infants admitted to our NICU was 7% during the previous 3 years.

The study was registered in the Dutch Trial Registry under number NTR4153. We intended to include 100 consecutive preterm infants at high risk for developing NEC. High risk was defined as being born at a gestational age (GA) of < 30 weeks or a birth weight (BW) below 1000 g, or at a GA of < 32 weeks with a BW below 1200 g. For this study, focusing on cerebral and abdominal oxygenation in relation to NEC development, we only included infants of whom we managed to obtain NIRS values within 48 h after birth. Exclusion criteria were: abdominal wall defects, major congenital deformations, and confirmed NEC diagnosis prior to inclusion. We obtained written informed parental consent in all cases within 72 h after birth. The study was approved by the institutional ethics review board of University Medical Center Groningen.

From this cohort, we selected all NEC cases and matched two controls to each infant who developed NEC, using the following criteria, in descending order of importance: GA (max deviation 1 week), BW (closest to index, no maximum deviation), and the presence of a hemodynamically significant patent ductus arteriosus (PDA).

2.2. NEC diagnosis

NEC diagnosis was confirmed when pneumatosis intestinalis, portal venous gas, or both were present on abdominal radiographic examination, and three authors (AB, EK, JH) classified the infants according to Bell's stages [21] afterward.

2.3. Near-infrared spectroscopy

We used the INVOS 5100C monitor (INVOS™ 5100C (Medtronic, Dublin, Ireland)) with neonatal INVOS™ somatic oximeters to measure r_cSO_2 and $r_{int}SO_2$. For r_cSO_2 we randomly placed the sensor on the left or right frontoparietal side of the head and for $r_{int}SO_2$ centrally just below the umbilicus. Sensors were kept in place using Mepitel® (Mölnlycke, Sweden) with or without an elastic bandage. The measurement was supervised by one of the researchers to ensure proper sensor placement. We performed NIRS measurements 2 h per day, starting within 48 h after birth, next every day until day 5 after birth, and weekly thereafter until the fifth week (day 36 after birth), until the infant was discharged from the NICU, or until NEC developed, whichever came first. During correct sensor placement, we chose not to exclude values of 15% or 95% from the analyses, the lowest and highest values possible for INVOS.

2.4. Clinical variables

We collected clinical data from patient reports: type of feeding, the administration of antenatal steroids, multiple gestations, cause of prematurity, GA, BW, gender, Apgar scores, treatment with antibiotics after birth, first hemoglobin and hematocrit levels within 48 h after birth, presence and grade of intra-ventricular hemorrhage, postnatal age at time of NEC onset, mortality, and length of NICU stay. Furthermore, we documented ventilator use, presence of a hemodynamically significant PDA, and use of medication (inotropes, red blood cell transfusions, volume expansion, ibuprofen). During the study period in infants receiving respiratory support with supplementary oxygen, the clinical SpO_2 target range was set between 85% and 93% (with alarm limits of 80% to 93%).

2.5. Data analysis and statistical analysis

We collected cerebral and intestinal rSO_2 values once every 6 s and SpO_2 once every 5 s. SpO_2 values were collected continuously using Nellcor® (Medtronic, Dublin, Ireland) software. Next, FTOE values were calculated $((SpO_2 - rSO_2) / SpO_2)$ for the cerebral and intestinal region separately, using synchronized rSO_2 and SpO_2 values, which led to two paired data per minute. We allowed the first 10 min of each NIRS measurement for stabilization. As a result, 110 min of available data could be used to calculate the daily mean values of r_cSO_2, $r_{int}SO_2$, cFTOE, and intFTOE. Unless a documented malplacement of the sensor occurred, all these clinical NIRS data were included in the analysis. We did not take into account the timing of feeding in relation to the timing of the NIRS measurements. Since 27 out of 30 infants received bolus feeds every 2 h, the two-hour NIRS measurements will have included both pre- and postprandial values in these infants. Three infants were over 1250 g and were therefore fed every 3 h, one index baby and it's two controls.

To determine whether r_cSO_2, $r_{int}SO_2$, cFTOE and/or intFTOE values predicted the onset of NEC, we used mean values from the first two-hour measurement after birth, which were obtained within 48 h after birth. Since it was previously found that low rSO_2 values corresponded to the onset of NEC [13,15,18], we chose to use the 25th percentile for r_cSO_2 and $r_{int}SO_2$ values and the 75th percentile for cFTOE and intFTOE values of all infants in this study as a cut-off. The use of the 25th percentile was supported by receiver operating characteristic curve analysis. Next, we compared infants below the 25th percentile with infants above the 25th percentile regarding rSO_2, and similarly below and above the 75th percentile

regarding FTOE. We performed Kaplan-Meier plots and used the log-rank test to determine if occurrence of NEC was significantly different in the Kaplan-Meier plots for the different groups: low versus high rSO_2 and FTOE values. Then, we performed logistic regression analyses and calculated odds ratios for those variables that had significantly different Kaplan-Meier curves. To adjust for possible confounders, we entered GA, BW, and small for gestational age (SGA) in the model.

We also determined the course of cerebral and intestinal rSO_2 and FTOE in individual infants. We used the Mann-Whitney test to test differences in median values of the last mean cerebral and intestinal rSO_2 and FTOE values before NEC development between the cases and values of the same day of life in the controls.

Finally, we determined the variability of cerebral and intestinal rSO_2 measurements of the first NIRS measurement after birth and of the last NIRS measurement prior to NEC development. For this purpose, we calculated the coefficient of variation of the 2 h measurements (CoVar, SD/mean). We used the Mann-Whitney test to determine whether the two groups differed regarding CoVar.

We used SPSS 22.0 software for Windows (IBM SPSS Statistics 22, IBM Corp., Armonk, New York, USA) for statistical analyses. We considered $P < .05$ to be statistically significant.

3. Results

Of the 99 infants that were finally included in the study, 11 infants, all preterm, developed NEC. Ten of these 11 infants had available NIRS measurements (Fig. 1). In one infant who developed NEC during the study, parents refused any further NIRS measurements. All three independent raters agreed 100% on the NEC diagnosis (≥Bell 2). Out of the remaining 88 infants, we matched twenty as controls. Of the ten infants with NEC, two infants were eventually classified as Bell's stage 2 and eight infants as Bell's stage 3 of whom six infants developed a bowel perforation.

Median postnatal age at time of NEC onset was 13 (range: 4–43) days. This led to a potential 64 measurements in the NEC group, and 128 in the control group. In the NEC infants we were able to calculate mean r_cSO_2 values for 62/64 (97%) 2-hour periods and mean $r_{int}SO_2$ values for 20/64 (31%) 2-hour periods. In the controls we were able to calculate mean r_cSO_2 values for 122/128 (95%) 2-hour periods and mean $r_{int}SO_2$ values for 41/128 (32%) 2-hour periods. Placing the infraumbilical sensor was often not possible due to the presence of an umbilical venous catheter taped to the infraumbilical skin and/or due to lack of space in very low birth weight infants.

We present clinical characteristics of the study population in Table 1. Apart from higher mortality rates in cases than in controls, no differences were observed.

3.1. Cerebral and intestinal rSO_2 and FTOE values in the first days after birth and the development of NEC

The 25th percentiles of r_cSO_2 and $r_{int}SO_2$ were 70% and 30%, respectively. The 75th percentiles of cFTOE and intFTOE were 0.23 and 0.65, respectively. From the Kaplan-Meier analyses, we saw that infants with r_cSO_2 values < 70%, i.e. the 25th percentile (n = 7), developed NEC significantly more often (n = 5) in the first 43 days after birth than infants with r_cSO_2 values > 70% (n = 23, NEC in n = 5), $P = .005$ (Fig. 2). Using r_cSO_2 values < 70%, sensitivity was 50% (95% CI 20–80%) and specificity was 90% (95% CI 67–98%) for predicting NEC. Using logistic regression analysis, we found that the risk of NEC increased with odds ratio 9.00 (95% CI 1.33–61.14, $P = .03$) if infants had r_cSO_2 values < 70% on their first measurement on day 1 or 2. Adjusting for GA, BW, and SGA did not result in a relevant change in the OR for low r_cSO_2 (Table 2).

We did not find an association between intestinal oxygenation values after birth and NEC development.

Mean SpO_2 values during the two-hour measurement were not significantly different between cases and controls (median: 91% (range: 48–99%) versus 90% (range: 84–97%), $P = .69$). The one infant with a mean SpO_2 of 48% had a severe RDS during the first day after birth, resulting in prolonged episodes of extreme hypoxia. This infant, born after 25 weeks of GA, 810 g, developed NEC 15 days after birth.

3.2. Cerebral and intestinal rSO_2 and FTOE values the week prior to NEC onset

The course of cerebral and intestinal rSO_2 and FTOE in individual infants who developed NEC did not reveal any specific patterns (data not shown).

The last NIRS measurement before NEC development was obtained at a median of two days (range: 1–7) prior to NEC development; median

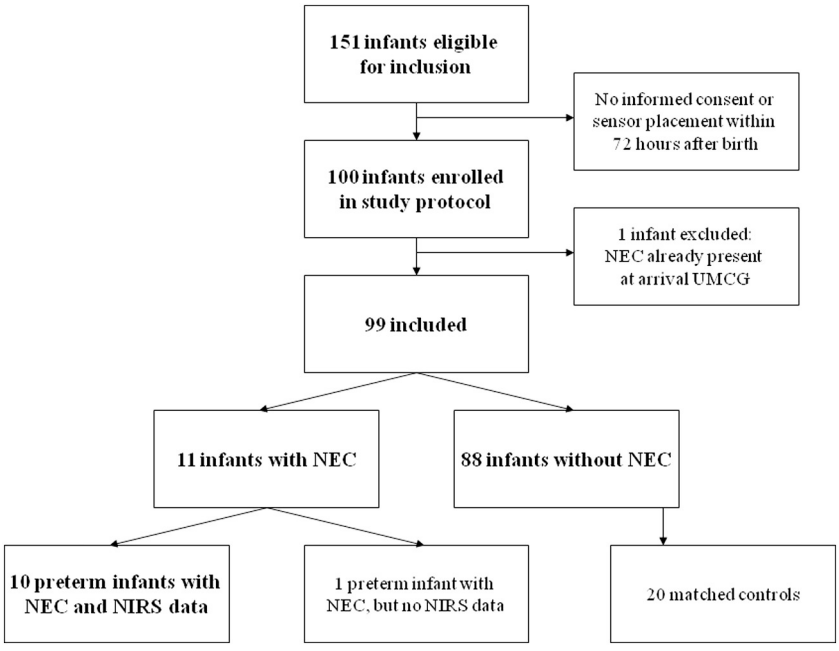

Fig. 1. Flow diagram of the study.

Table 1
Patient characteristics of preterm infants with NEC and their matched controls.

	NEC cases (n = 10)	Controls (n = 20)
Gestational age (weeks)[a]	27.1 (24.6–29.4)	27.6 (25.0–29.7)
Birth weight (grams)[a]	903 (560–1630)	960 (615–1330)
Small for gestational age	2 (20%)	3 (15%)
PDA treated with Ibuprofen[a]	5 (50)	8 (40)
Male	6 (60)	10 (50)
Multiple gestations	3 (30)	4 (20)
Antenatal steroids	9 (90)	18 (90)
PPROM (> 24 h)	3 (30)	3 (15)
Spontaneous premature birth	3 (30)	10 (50)
Induction of birth		
	2 (20)	2 (10)
- Maternal reason	2 (20)	4 (20)
- Fetal reason	0 (0)	1 (5)
- Combination of both		
Apgar score 1 min	4 (1–7)	5 (2 – 10)
Apgar score 5 min	7 (1–9)	7 (3 – 10)
Type of feeding 48 h after birth		
	1 (10)	10 (50)
- Unknown	4 (40)	0 (0)
- Formula	2 (20)	1 (5)
- Mother's milk	3 (30)	9 (45)
- Combination		
Type of feeding day before NEC onset		
	2 (20)	
- Unknown	1 (10)	
- Formula	4 (40)	
- Mother's milk	3 (30)	
- Combination		
Antibiotics for < 48 h	8 (80)	17 (85)
Antibiotics for > 48 h	7 (70)	13 (65)
Mechanical ventilation		
	0 (0)	4 (20)
- ≤ 48 h after birth	8 (80)	12 (60)
- > 48 h after birth		
Intraventricular hemorrhage		
	7 (70)	17 (85)
- None	2 (20)	1 (5)
- Grade I	1 (10)	2 (10)
- Grade II	0 (0)	0 (0)
- Grade III/IV		
Hemoglobin within 48 h after birth	9.3 (6.5–10.5)	9.2 (6.8–12.5)
Hematocrit within 48 h after birth	0.42 (0.31–0.50)	0.42 (0.31–0.59)
RBC transfusion	8 (80)	13 (65)
RBC transfusion within 48 h before NEC onset	3 (38)	
Fluid resuscitation	6 (60)	8 (40)
Inotropes	4 (40)	3 (15)
	0	2
- Within 48 h after birth	4	0
- During NEC		
Length NICU stay (days)	46 (6–89)	39 (9–103)
Mortality	4 (40)	1 (5)

Data are expressed as median (range) or as number (percentage). NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; PDA, patent ductus arteriosus; PPROM, preterm premature rupture of membranes; RBC, red blood cell.

[a] Criteria for selection of control group.

postnatal day was eight (3–36) days (Fig. 3). We found significantly higher intFTOE values in the NEC infants than in controls on the same day after birth, median 0.65 (0.49–0.84) versus 0.44 (0.17–0.70), 95% CI of difference −0.4–0.0, $P = .04$ (Fig. 3). $R_{int}SO_2$ tended to be lower and cFTOE values higher in cases than in controls ($r_{int}SO_2$, median 33% versus 48%, $P = .09$; cFTOE, median 0.36 versus 0.24, $P = .08$, Fig. 3).

SpO_2 values were not significantly different between cases and controls, with median 92% (86–100%) versus 90% (84–99%), $P = .16$.

3.3. Variability

Both within 48 h after birth and before NEC onset, variability of

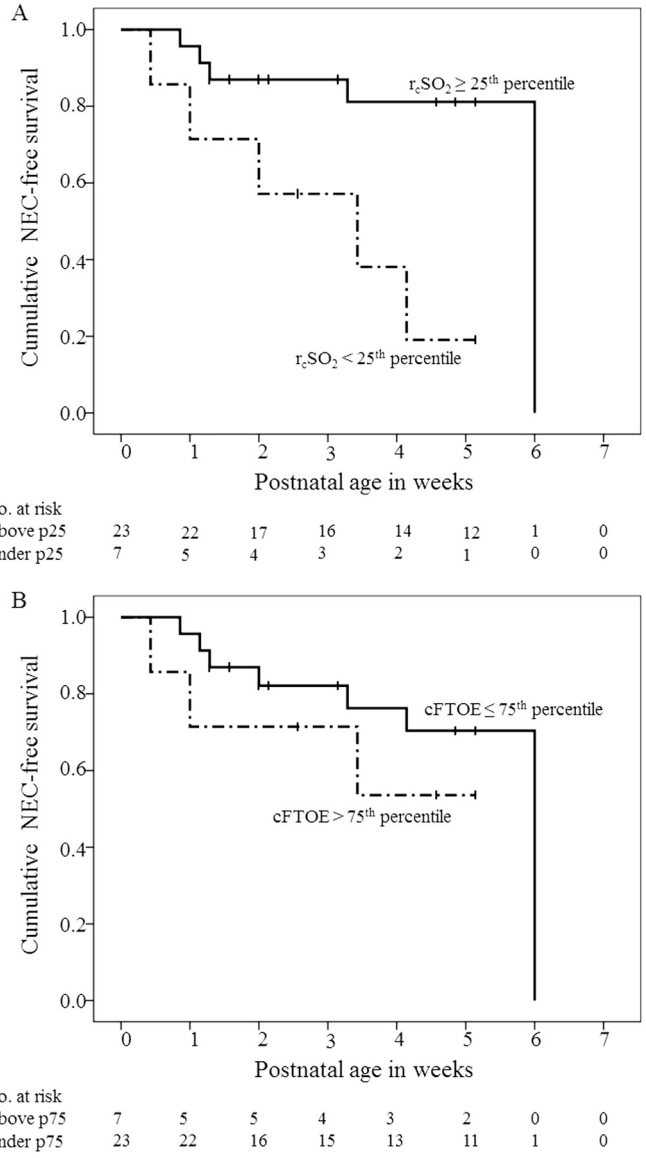

Fig. 2. Kaplan-Meier plots illustrating the occurrence of NEC in infants with r_cSO_2 values below (– · –) and above (——) the 25th percentile (A) and infants with cFTOE values below (——) and above (– · –) the 75th percentile (B) on the first measurement on day one or two.

Table 2
Logistic regression analysis (NEC dependent variable).

	Odds ratio (95% confidence interval)
r_cSO_2 < 70% (unadjusted)	9.0 (1.3–61.1)*
r_cSO_2 < 70% (adjusted for gestational age)	8.8 (1.3–60.2)*
r_cSO_2 < 70% (adjusted for birth weight)	9.9 (1.4–70.3)*
r_cSO_2 < 70% (adjusted for IUGR)	9.3 (1.3–64.7)*

* *P*-value < .05.

cerebral and intestinal rSO_2 was not different between cases and controls (Table 3).

4. Discussion

In this study, we found that r_cSO_2 values within the first days after birth are associated with increased risk of NEC development later on in preterm infants. The probability of developing NEC was nine-fold

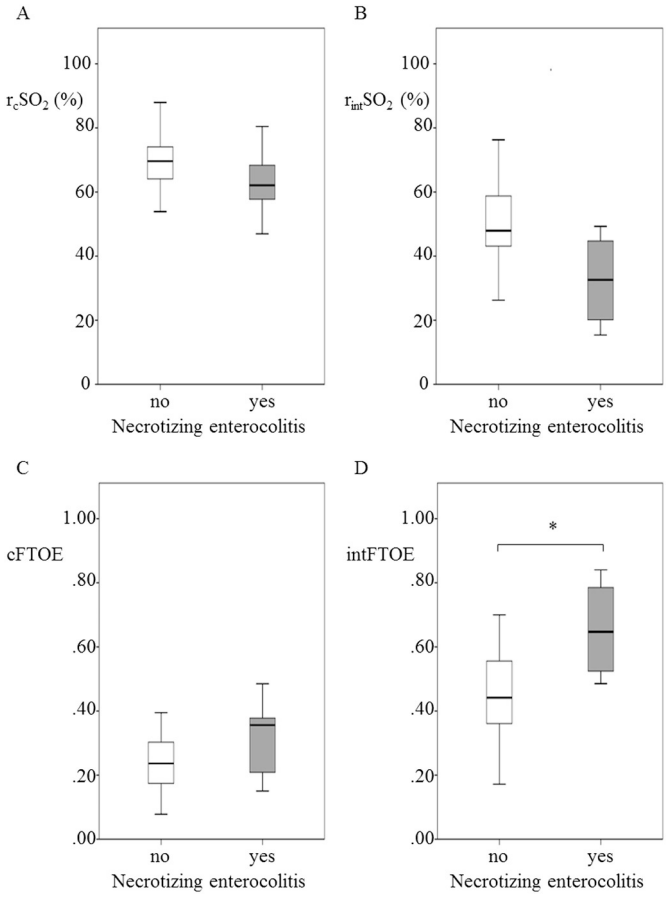

Fig. 3. Median values of r_cSO_2 (A), $r_{int}SO_2$ (B), cFTOE (C), and intFTOE (D) of the last NIRS measurement prior to NEC onset in infants who developed NEC and their controls. Data are shown in box and whisker plots. * Indicates $P < .05$.

Table 3
Cerebral and intestinal variability (CoVar) after birth and before NEC onset.

	NEC cases (n = 10)	Controls (n = 20)	Difference (95% CI)
First 48 h			
r_cSO_2	6.7 (3.5–9.9)	4.6 (3.6–7.2)	2.1 (−7.5–59.0)
$r_{int}SO_2$	23.0 (15–31)	10.7 (2.7–44.0)	12.3 (−39.0–31.0)
Last measurement before onset of NEC or same day of life for controls			
r_cSO_2	8.0 (2.9–12.1)	7.5 (2.9–19.6)	0.5 (−2.6–3.6)
$r_{int}SO_2$	23.0 (16–58.6)	16.0 (7.8–36.2)	7.0 (−67.0–38.0)

Data are presented as median (range) of CoVar (%).There were no significant differences between NEC cases and controls. CoVar, coefficient of variation; NEC, necrotizing enterocolitis; r_cSO_2, regional cerebral tissue oxygen saturation; $r_{int}SO_2$, regional intestinal tissue oxygen saturation; CI, confidence interval.

higher in infants with r_cSO_2 values < 70% within the first two days after birth compared to infants with r_cSO_2 values ≥70%. Furthermore, we found significantly higher intestinal FTOE values in the week prior to NEC development in preterm infants who developed NEC compared to matched controls. The variability of cerebral and intestinal oxygenation did not differ between the groups.

Our findings suggest that infants who go on to develop NEC often have impaired cerebral oxygenation as early as the first 48 h after birth. We offer several explanations for this finding. First, low r_cSO_2 values might be caused by low SpO_2 values as it was recently found that low SpO_2 values were associated with NEC development [22]. However, we did not find that SpO_2 values were lower in cases than in controls. Nonetheless, since we only measured 2 h daily, we might have missed episodes in which infants were in the lower SpO_2 range. Secondly, low rcSO2 values might be the result of a low systemic perfusion, which has shown to contribute to NEC development [10,11]. Because several clinical factors such as mechanical ventilation and presence of PDA were not different between cases and controls, we believe that lower rcSO2 values cannot be explained by these factors. Still, infants who go on to develop NEC may be relatively underperfused immediately following birth resulting in a detectable lower rcSO2, for example due to inflammation, maternal medication, low blood pressure, a more pronounced left to right flow across the PDA, or a combination of these circumstances. The subtle changes in hemodynamics can go unnoticed when only clinical signs and conventional monitoring are considered, but they are reflected in changes of tissue oxygenation. Recently it was reported that changes in tissue oxygenation measured using NIRS preceded changes in conventional hemodynamic monitoring in children with congenital heart disease who unexpectedly deteriorated and needed resuscitation [23]. In our study, the r_cSO_2 may therefore be a first and sensitive sign indicating imminent impaired systemic perfusion, inciting the chain of events leading to development of NEC. It is striking that this already occurs during the first days after birth, suggesting that the set-off of the development towards NEC lies in the period before, during and/or just after birth. Further research in a larger patient population is warranted to investigate this hypothesis.

As opposed to r_cSO_2 values, $r_{int}SO_2$ values within the first days after birth were not associated with NEC development later on. We were, however, only able to measure $r_{int}SO_2$ for 31% of the time. In the very preterm and small-for-gestational age infants space was lacking for adequate sensor placement. The resultant small sample size will have limited our ability to detect significant differences in intestinal oxygenation values between the two groups.

Patel et al. demonstrated that $r_{int}SO_2$ values were lower in the first week after birth in infants who later developed NEC compared to infants who did not [18]. We did not find such a difference, perhaps because of our small sample size. In the study of Patel et al. infants with NEC were also of lower GAs and had lower BWs than their controls [18], whilst our cases were matched and therefore comparable with controls. It has been reported that intestinal rSO_2 measurements might be GA-dependent [24].

With regard to the last NIRS measurement prior to NEC onset, we found approximately one and a half times higher intFTOE values in preterm infants with NEC than in controls. This finding supports the hypothesis that infants who develop NEC have decreased intestinal perfusion several days prior to the development of clinical NEC [16,17]. As a predictor of NEC in individual infants this measurement is clinically not useful, because of the large intra-individual range of the intFTOE values. However, it provides insight into the role of intestinal perfusion in the pathophysiology of NEC. Further studies are needed to investigate the possibility of using intestinal oxygenation values to predict the onset of NEC.

With regard to the variability measurements, we did not find significant differences between infants with NEC and their matched controls. However, intestinal variability tended to be higher in infants developing NEC, both directly after birth, and the last measurement before NEC onset. Possibly, the two-hour measurements may be rather long for variability assessment [25]. Controversy exists on the pathophysiological role of variability of intestinal oxygenation measured by NIRS in relation to NEC development. In line with our finding, higher variability has been described in piglets before developing NEC [13]. Cortez et al., however, suggested that loss of variability pointed towards the development of NEC [19], which we also recently found in infants developing blood transfusion associated NEC [26]. Further research is warranted to assess the usefulness of using variability in intestinal oxygenation for detecting an infant at risk for developing NEC.

The strength of this study is that we prospectively collected the data, and matched the infants who developed NEC to controls, based on GA,

BW, and presence of hemodynamically significant PDA [27]. A limitation is that we were not able to apply the infraumbilical sensor in every infant due to lack of space, mainly due to the common practice at our NICU to tape the umbilical catheter to the infra-umbilical skin, which we were not able to change in time for this study. As a result, we were unable to obtain $r_{int}SO_2$ values in the smallest infants, which could have biased our results. Moreover, the small number of infants will have reduced the power to disregard abdominal oxygen saturation measurement in the process of NEC prediction. Also, suboptimal precision of the current NIRS measurement technique [28] hampers individual risk assessment of NEC development. In addition, $r_{int}SO_2$ values might be affected by air, stool or a full bladder [29,30]. Therefore, results should be interpreted with caution. Of note, since there are different NIRS devices, each with their own algorithm, our results are representative for the INVOS 5100C device with neonatal sensors [31,32]. Unfortunately we were not able to reliably register FiO_2 values, nor did we correct for potential influence of enteral feeding, which may have affected our measurements. Finally, multiple testing may have led to low *P*-values by chance. We deliberately chose not to adjust the p-value, because of the explorative nature of this study.

In conclusion, cerebral rSO_2 values in the first two days after birth might be useful in the risk assessment of NEC development later on in preterm infants with a GA of < 32 weeks. The cause for this phenomenon is as yet unknown. Although impaired intestinal perfusion is possibly present before the onset of NEC, the usefulness of monitoring intestinal oxygenation values to predict the onset of NEC needs to be investigated further.

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Conflict of interest

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