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Review Article

Long-term Neurodevelopmental and Growth Outcomes of Necrotizing Enterocolitis Among Preterm Infants: A Systematic Review

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Abstract

Background: Preterm infants with necrotizing enterocolitis (NEC) are at increased risk of mortality, severe morbidity, and adverse long-term neurodevelopmental and growth outcomes.

Objective: This systematic review aimed to identify and synthesize evidence on the long-term impact of NEC on neurodevelopmental and growth outcomes in preterm infants, including differences between medical and surgical NEC.

Methods: The review adhered to PRISMA 2020 guidelines, with literature searches conducted in ScienceDirect, Sage Journals, ProQuest, PubMed, Scopus, and Wiley for studies published between 2015 and 2025. Study quality was assessed using the Joanna Briggs Institute (JBI) critical appraisal tools. From a total of 2,055 articles identified, supplemented by citation tracking, 10 studies were included in this review.

Result: The findings indicate that NEC survivors have a higher risk of neurodevelopmental impairment, including lower cognitive, motor, and language scores, behavioral problems, and an increased risk of cerebral palsy, particularly among infants requiring surgical intervention. Regarding growth outcomes, NEC survivors demonstrated persistent deficits in weight, height, and head circumference that may extend into school age and adolescence. Several studies also reported reduced fat mass and decreased bone mineral density in early childhood. Surgical NEC was consistently associated with poorer outcomes than medical NEC.

Conclusion: The findings indicate that NEC in preterm infants has significant long-term consequences for neurodevelopment and growth. Comprehensive multidisciplinary follow-up, family empowerment, standardized developmental screening, nutritional optimization, and risk-based early intervention are crucial for improving long-term outcomes and quality of life among NEC survivors.

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Keywords
Necrotizing enterocolitis, preterm infants, neurodevelopmental outcomes, growth outcomes, long-term follow-up.

Background

Necrotizing enterocolitis (NEC) is a life-threatening gastrointestinal emergency and one of the leading causes of neonatal mortality, particularly among preterm infants. Mortality rates remain high, ranging from 15% to 45% (1). The incidence of NEC varies across countries. In the United States and Canada, NEC occurs in approximately 7–12% of all preterm births. Studies from Sweden report an incidence of 3.4 per 10,000 live births, whereas Japan reports the lowest incidence, approximately 2%, among neonates with a gestational age of less than 28 weeks. Among Very Low Birth Weight (VLBW) infants, the incidence of NEC ranges from 2% in Japan to 6–7% in the United States and 9% in Poland. These discrepancies are believed to be attributable to various environmental, dietary, and genetic predisposition factors. (2–5)

Prematurity remains the principal risk factor for NEC, with incidence inversely correlated with birth weight and gestational age. The lower the birth weight and gestational age, the greater the risk of developing NEC. Furthermore, an APGAR score ≤3 is associated with a 2.34-fold increased risk of NEC (6). Preterm infants possess an underdeveloped gastrointestinal system, which heightens their susceptibility to intestinal inflammation, leading to cellular damage, necrosis, and ultimately bowel death (7). This intestinal disease is particularly severe, as it may cause bloodstream infection, organ failure, short bowel syndrome (SBS), and prolonged parenteral nutrition dependency, all of which can impair hepatic function and result in death (8). Survivors of NEC remain at risk of significant long-term complications affecting multiple organ systems.

Beyond gastrointestinal complications, NEC is associated with a spectrum of long-term sequelae, including neurodevelopmental impairment (NDI) and growth restriction. Children who survive NEC are at considerable risk of NDI (9). The incidence of NDI in this population is approximately 40%, which is twofold higher than in children without an NEC history (10). Prospective studies assessing growth outcomes have demonstrated that growth failure is highly prevalent, particularly in infants with surgical NEC, and persists through 18–22 months of corrected age (11).

Given the high prevalence of NEC among preterm infants, its substantial mortality and morbidity burden, and its potential for serious long-term complications across multiple organ systems affecting both neurodevelopment and physical growth, a systematic and

comprehensive synthesis of current evidence is warranted. Although prior studies have addressed specific aspects of NEC outcomes, no comprehensive systematic review has synthesized recent evidence on long-term neurodevelopmental and physical growth outcomes in preterm infants with NEC. Understanding of the long-term consequences remains fragmented, rendering a holistic interpretation of NEC's impact challenging. Therefore, this systematic review aims to synthesize and provide a comprehensive overview of the long-term impact of NEC on neurodevelopment and growth in preterm infants, including the identification of differences in outcomes between medical and surgical NEC.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines (12).

Search Strategy

A comprehensive systematic literature search was performed across multiple databases, including ScienceDirect, SAGE Journals, ProQuest, PubMed, Scopus, and Wiley. The search was conducted on October 27, 2025, using the following search string: ("necrotizing enterocolitis" OR NEC) AND (preterm OR premature) AND ("long term" OR longitudinal OR cohort) AND ("neurodevelopmental impair" OR "growth"). The search results and strategy are illustrated in Figure 1. Literature was restricted to articles published within the past 10 years to ensure the relevance and currency of the included evidence.

Eligibility Criteria

The inclusion criteria were as follows: 1) preterm infants; 2) confirmed diagnosis of NEC, encompassing both medical NEC and surgical NEC; 3) studies reporting long-term outcomes related to neurodevelopmental impairment or growth restriction; and 4) articles published in English between 2015 and 2025. Studies were excluded if they were case reports, irrelevant to the research question, duplicates, unavailable in full text, or conducted in animal models.

Study Selection and Data Extraction

Search results from all databases were imported into EndNote software for deduplication. The remaining articles were screened based on PEOS criteria (Population, Exposure, Outcome, and Study design), as presented in Table 1. Each eligible study was independently evaluated by two reviewers (MM and YR) against the inclusion and exclusion criteria. Disagreements between the two reviewers were resolved through discussion with a third reviewer (MHH). The decision-making process for study inclusion was documented and presented in the PRISMA flow diagram. Data were extracted using a standardized form developed by the reviewers, capturing the following information: author(s), year of publication, country, study objective, participant characteristics, study design and measurement instruments, follow-up timepoints, and key findings (Table 4).

Table 1. Description of PEOS

Population	Premature infants
Exposure	Necrotizing Enterocolitis (NEC)
Outcomes	Long-term outcomes (neurodevelopmental and growth)
Study design	Cohort study, case-control study

Risk of Bias

The Joanna Briggs Institute (JBI) critical appraisal tools were employed to evaluate the methodological quality of all included studies, with separate tools applied to cohort studies and case-control studies, accessible at https://jbi.global/critical-appraisal-tools. Each domain question was assessed using a checklist with four response options: "Yes,"

"No," "Unclear," and "Not Applicable" (Tables 2 and 3). Total scores were converted to a percentage of the maximum score (number of "Yes" responses divided by the total number of applicable questions, multiplied by 100%). Risk of bias was classified as low when ≥70% of applicable responses were "Yes," moderate when 50–69% were "Yes," and high when fewer than 50% were "Yes". (13)

Table 2. Risk of bias assessment for cohort studies

Authors	JBI assessment tools												
	Q1[a]	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	% Yes	Risk of bias[b]
(14)	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	✓	91%	Low
(15)	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	✓	91%	Low
(10)	✓	✓	✓	✓	✓	✓	?	✓	✕	✕	✓	73%	Low
(16)	✓	✓	✓	✓	✓	✓	✓	✓	✕	✓	✓	91%	Low
(17)	✓	✓	✓	✓	✓	✓	✓	✓	✕	✓	✓	91%	Low
(18)	✓	✓	✓	✓	✓	✓	?	✓	✕	✕	✓	73%	Low
(19)	✓	✓	✓	✓	✓	✓	✓	✓	✕	✓	✓	91%	Low
(20)	✓	✓	✓	✓	✓	✓	✓	✓	✕	✕	✓	82%	Low

a Q1-Q11 indicates questions 1 to 11 based on the JBI risk assessment.

bThe risk of bias was ranked as high when the study reached up to 49% of "yes" scores, moderate when the study reached from 50 to 69% of "yes" scores, and low when the study reached more than 70% of "yes" scores. '✓' indicates yes, '✕' indicates no, '?' indicates unclear, and "-" indicates not applicable.

Table 3. Risk of bias assessment for case-control studies

Authors	JBI assessment tools											
	Q1[a]	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	% Yes	Risk of bias[b]
(21)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
(22)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	100	Low

Result and Discussion

Search Result

A database search across six electronic databases yielded 2,055 articles. After deduplication using EndNote, 239 articles were removed, leaving 1,816 for screening. The remaining records underwent additional manual deduplication and were screened based on titles and abstracts. Articles failing to meet the inclusion criteria for population, exposure, outcome, or study design were excluded. Full-text screening was then conducted on eligible

abstracts. In addition to the database search, a manual citation-tracking strategy (n=17) was used to identify additional relevant studies through reference list screening of included studies. Ultimately, 10 articles were included for analysis in this systematic review (Figure 1).

Study Characteristics

The 10 included studies were published between 2018 and 2025. Study settings were predominantly in high-income countries, with four studies conducted in the United States, four in European countries (Germany, Denmark, the United Kingdom, and Sweden), and two in Canada and South Korea. The majority of studies (n=8) employed a cohort design. The gestational age (GA) characteristics at birth were relatively homogeneous across studies, with participants being preterm infants ranging from 23 to 37 weeks GA (predominantly <29 weeks), diagnosed with either medical or surgical NEC. Birth weights ranged from approximately 700 to 1,442 grams, reflecting the highly vulnerable premature population under investigation. The follow-up periods were variable and can be categorized into three age groups: toddler age at 18–30 months, preschool and school age at 5–8 years, and adolescence to young adulthood at 10–20 years.

Standard measurement instruments for neurodevelopmental assessment included the Bayley Scales of Infant Development (BSID-II and III). Motor function and cognitive ability were assessed using the Wechsler Intelligence Scale for Children (WISC) and the Gross Motor Function Classification System (GMFCS), and behavioral problems were evaluated using the Strengths and Difficulties Questionnaire (SDQ). Growth status was predominantly assessed using CDC and Fenton growth charts. Several studies additionally employed advanced imaging modalities, including Diffusion Tensor Imaging (DTI) for assessing brain white matter microstructure (14) and Dual-energy X-ray Absorptiometry (DXA) for evaluating bone mineral density and body composition (22). Detailed characteristics of all included studies are presented in Table 4.

Neurodevelopmental Outcomes

Seven of the 10 included studies reported neurodevelopmental outcomes in preterm infants with NEC. Assessment was conducted at various follow-up timepoints, ranging from 18 months of corrected age to beyond 10 years, utilizing validated measurement instruments and structured clinical interviews. Three studies consistently reported that NEC survivors, particularly those with surgical NEC, exhibited significantly lower scores in cognitive, motor, and language domains compared to control groups (14,18, 20, 21). Allendorf et al. reported that the Mental Developmental Index (MDI) was significantly lower, with a mean of 85 versus 101 (p=0.02), and the Psychomotor Developmental Index (PDI) was significantly lower than both the medical NEC group and controls (21). These findings are consistent with a large cohort study by Zozaya et al. in Canada, which demonstrated that the NEC group had a significantly higher adjusted odds ratio (aOR 1.77) of neurodevelopmental impairment compared to the non-NEC group. (20)

A prospective cohort study employing a unique methodological approach combining neurodevelopmental assessment with neuroimaging found that infants with NEC exhibited alterations in white matter microstructure detectable using DTI. Increased Mean

Diffusivity (MD) in the Splenium of the Corpus Callosum (sCC) was negatively correlated with language outcomes (p=0.025) and motor outcomes (p=0.002) at 18 months of corrected age. These findings elucidate the neurological injury mechanism and provide neurobiological evidence of NEC survivors' vulnerability to severe motor impairment, with an exceptionally high adjusted odds ratio (aOR 58.26; 95% CI 7.80–435.12). (14)

At school age and beyond, two studies reported persistent behavioral and neurological impairments (10, 18). Hansen et al. found that children with NEC had a higher rate of abnormal SDQ scores (23.9% vs. 17.8%), and moderate-to-severe CP was three times more frequent in the NEC group compared to controls (3.1% vs. 0.9%; OR 3.67) (10). Furthermore, a study by Mondal et al. following preterm NEC survivors to a mean age of 11.2 years found that 61% experienced neurological impairment, 56% cognitive impairment, 50% learning difficulties, 22% cerebral palsy, and 17% behavioral problems. Consistently, surgical NEC patients (67%) demonstrated higher rates of impairment compared to medical NEC. (18)

In contrast, one prospective longitudinal study monitoring neurodevelopmental outcomes of extremely preterm infants up to 10 and 15 years of age found no statistically significant differences between infants with NEC (either medical or surgical) and those without NEC after adjustment for confounding variables (19). These discrepant findings may be attributed to variations in sample composition, gestational age range, and analytical methods employed to control for prematurity-related comorbidities.

Growth Outcomes

Six of the 10 included studies evaluated long-term physical growth outcomes in NEC survivors. Follow-up assessment periods extended up to 20 years of age. Growth assessment encompassed multiple indicators, including body weight, height/length, body mass index (BMI), head circumference (HC), bone mineral density (BMD), bone mineral content (BMC), and body composition.

All studies reporting growth outcomes in NEC survivors consistently found poorer growth compared to non-NEC populations, particularly in the surgical NEC group. A large prospective cohort study involving more than 100,000 participants reported that NEC survivors were at higher risk of weight-based growth failure at 18–24 months of corrected age, defined as weight below the 10th percentile. Surgical NEC was significantly associated with an increased risk of growth failure (aOR 1.58; 95% CI 1.05–2.38). Weight, length, and HC z-scores were all significantly lower in the surgical NEC group ($p<0.05$) (16). Findings related to HC growth demonstrated heterogeneity across studies. Zozaya et al. reported statistically significant HC deficits in NEC survivors persisting from 18 months to 6 years, suggesting long-term brain growth impairment (20). Hansen et al. similarly observed a trend toward smaller HC in the NEC group, although this did not reach statistical significance. (10)

Long-term growth patterns were evident from late childhood through adolescence. Vaidya et al. reported that after age 10, surgical NEC survivors demonstrated lower weight and height. Growth deficits persisted through 15 years of age, with declining weight z-scores, height z-scores, and BMI (19). In contrast, a 20-year longitudinal follow-up study

found that weight gain in NEC infants was significantly diminished over the observation period (p=0.0064), although no significant differences in linear growth (height) were observed compared to controls (p=0.09), suggesting that weight is more substantially impacted than length. (17)

Physical growth was also evaluated with respect to body composition and bone health using Dual-energy X-ray Absorptiometry (DXA) at 5 years of age. NEC survivors demonstrated significantly lower fat mass (23.4% vs. 29.1%; p=0.001), reduced BMD (355.6 g vs. 416.7 g), and lower lumbar spine bone mineral density compared to controls. Surgical NEC survivors exhibited lower weight z-scores (−1.3 SD vs. −0.7 SD; p=0.006) and were significantly shorter (p=0.002) (22). These findings indicate compromised growth quality in NEC survivors.

In severe surgical NEC (NEC totalis, residual bowel length <30 cm), clinically significant growth deficits were identified, with a median weight-for-age z-score of −0.8 (IQR −1.5 to −0.2) and height-for-age z-score of −1.6 (IQR −2.5 to −0.8), indicating a tendency toward mild stunting, while the BMI z-score was relatively preserved at +0.4 (15). Furthermore, a Canadian cohort study found that NEC was associated with significantly higher risks of growth deficit (z-score <−2) in both weight and HC. (20)

Table 5. Synthesis of long-term neurodevelopmental and growth outcomes

Outcomes Domain	Authors (References)
Neurodevelopmental	(10, 14, 15, 18–21)
Growth	(15–17, 19, 20, 22)

Overall Pattern of Findings and Heterogeneity

Disease severity is a critical determinant of long-term outcomes among NEC survivors. Across all included studies, the majority consistently reported that NEC, particularly surgical NEC, was associated with substantially worse long-term neurodevelopmental and growth outcomes. Preterm infants managed conservatively demonstrated lower severity of adverse outcomes compared to those requiring surgical intervention. This severity-dependent pattern is clinically meaningful and supports the concept that more extensive intestinal injury produces greater systemic effects on somatic growth and brain development.

This review identified considerable heterogeneity across the included studies in terms of study design (retrospective vs. prospective), follow-up duration (18 months to 20 years (14, 17), sample size (50 to over 100,000 participants (16, 22), measurement instruments, and NEC definitions applied. Despite this heterogeneity, the overall direction of findings demonstrated consistency, indicating that NEC survivors face substantially elevated risks of adverse neurodevelopmental and growth outcomes and that these risks persist well beyond the neonatal period into childhood and adolescence.

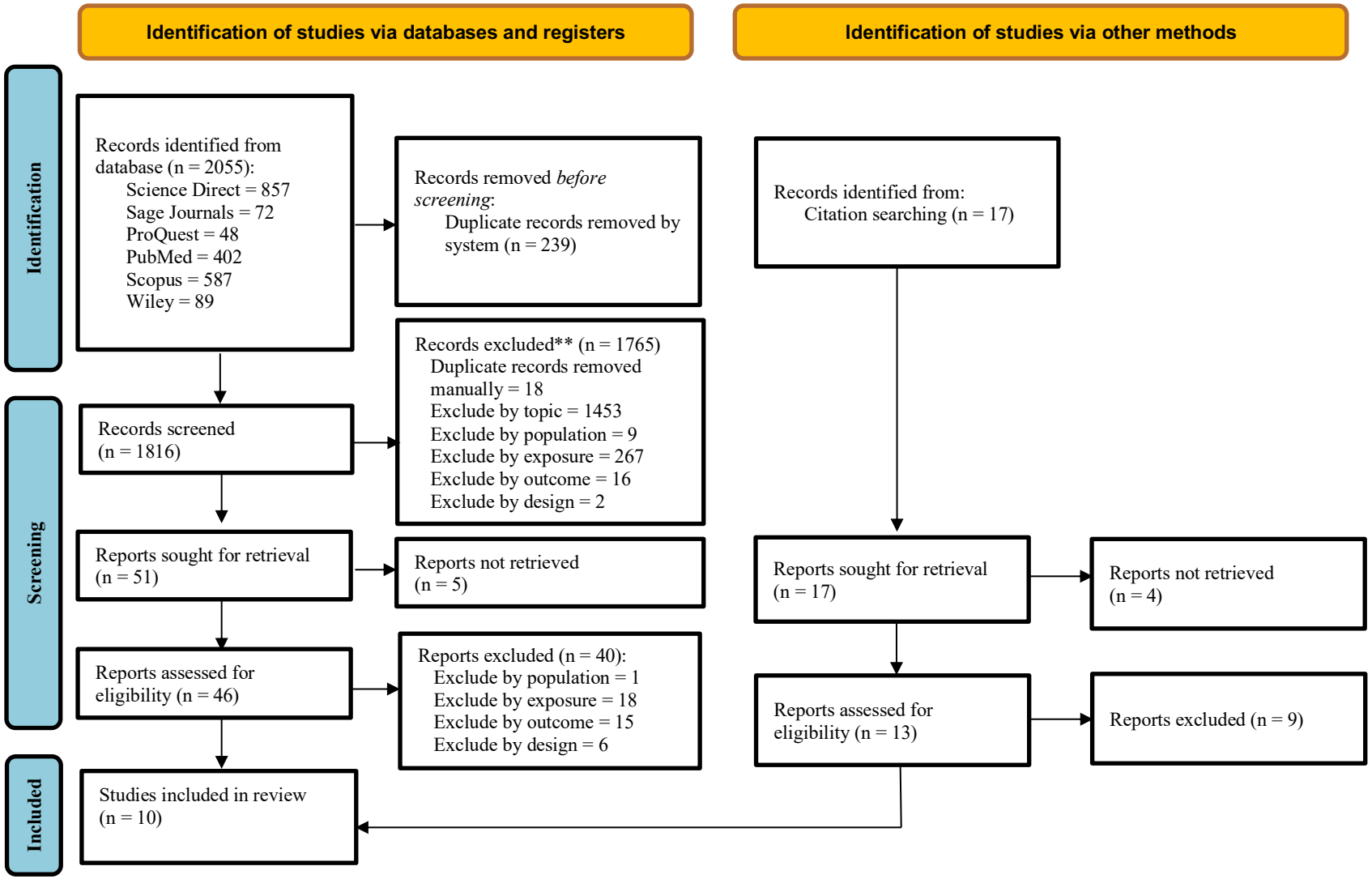


Figure 1. PRISMA Flow Chart

Table 4. Characteristic of Included Studies (N = 10)

Authors, Country	Aim	Participant characteristics	Design and Instruments	Age at Follow-up	Outcomes
(21) Germany	To investigate the long-term neurodevelopmental outcomes of preterm infants with NEC treated surgically or conservatively compared to matched controls.	Samples N: 74 Case: 37 (13 conservatively treated NEC, 24 surgical NEC) Control: 37 Characteristic - GA (mean age 27 + 6 w) - Birth weight (mean BW 1032.5 g) - APGAR-5 min (mean 7.5)	Design: Retrospective case-control study Instruments: BSID-II (Mental Developmental Index/MDI and Psychomotor Developmental Index/PDI)	At 2 years	- Surgical NEC: significantly lower MDI scores compared to controls (mean 85 vs 101; p=0.02). - Surgical NEC had significantly lower PDI (p=0.032) and MDI (p=0.020) than medical NEC. - No significant differences in medical NEC compared to controls (MDI 99 vs 100 or PDI 106 vs 109)
(14) South Korea	To assess the association between necrotizing enterocolitis and alterations in white matter microstructure, and to evaluate its correlation with neurodevelopmental disorders at 18 months of age (corrected age).	Samples N: 86 total. Case: 20. Control: 66. Characteristic - GA (mean age 27.03 w) - Birth weight (mean BW 985 g)	Design: A prospective cohort study. Instruments: - DTI) for brain microstructure. - BSID-III	At 18 months corrected age	- NEC infants had significantly lower scores in cognitive (p=0.002), language (p=0.016), and motor (p<0.001); motor impairment risk OR 58.26 (95% CI 7.80-435.12). Increased Mean Diffusivity (MD) in the Splenium of Corpus Callosum (sCC) (p=0.001) correlated with poorer language (p=0.025) and motor (p=0.002) outcomes.
(15) United States	To describe the long-term outcomes of infants with severe surgical NEC "NEC totalis" (defined as residual bowel length <30 cm), including survival, enteral	Samples N: 261 41 severe surgical NEC Characteristic - GA (median age 28 w)	Design: A retrospective cohort study Instrument: Clinical markers from the medical record (neurodevelopmental disability and growth Z-score)	At a median age of 8 years. Some participants were followed	- ≥1 marker of severe NDD in severe surgical NEC, including bilateral blindness, hearing impairment, inability to ambulate, and CP. - Severe surgical NEC survivors showed modest deficits in weight and height (weight-for-age z-score −0.8 [IQR −1.5 to −0.2]; height-for-age z-score −1.6 [IQR −2.5 to

Authors, Country	Aim	Participant characteristics	Design and Instruments	Age at Follow-up	Outcomes
	autonomy, and neurodevelopment	- Birth weight (median BW 930 g) - APGAR-1 min (median 6) - APGAR-5 min (median 8) - Residual small bowel length <30 cm		up to 16 years	−0.8]); BMI z-score relatively preserved (+0.4). A mild stunting tendency was identified.
(10) Denmark	To evaluate the school-age behavioral and neurodevelopmental impairment of neonatal necrotizing enterocolitis.	Samples N: 400 total Case: 163 Control: 237 Characteristic - GA (median age 29.7 w) - Birth weight (median BW 1442.5 g)	Design: Cohort study Instruments: - SDQ, GMFCS - Physical measurements (head circumference and height)	At a median age of 10.5 years	- Children with NEC had a higher rate of abnormal SDQ (23.9% vs 17.8%; OR 1.45, p=0.13). - Moderate/severe CP more frequent (3.1% vs 0.9%; OR 3.67, p=0.13). - Smaller HC z-score (11.8% vs 7.3%; OR 1.70, p=0.12). - Surgical NEC had the highest abnormal SDQ rate (26.4%), compared to medical NEC (20.8%).
(16) United States & Canada	To evaluate postnatal growth trajectories and identify predictors of severe growth failure at 18–24 months corrected age in survivors of necrotizing enterocolitis compared to those without NEC.	Samples N: 100.649 Case: 416 Medical NEC, 462 Surgical NEC Control: 9171 Characteristics - GA (mean age 24.5 w) - Birth Weight (700.5 g)	Design A prospective cohort study Instruments: Fenton and CDC growth charts	At 18–24 months corrected age	- NEC survivors showed a higher risk of growth failure (weight < 10th percentile) compared to non-NEC. - Surgical NEC was significantly associated with an increased risk of growth failure (aOR 1.58; 95% CI 1.05–2.38). - Weight, length, and HC z-scores were significantly lower in surgical NEC (p < 0.05).
(22) Sweden	To evaluate and compare growth, bone mineral density (BMD), bone mineral content (BMC), and	Samples N: 50 Case: 25 (11 Surgical NEC, 14 Medical NEC) Control: 25	Design Case-control study Instruments: - Standard calibrated scale and stadiometer (Weight, Height,	At 5 years	- Preterm NEC had significantly lower weight (-1.3 SD vs -0.7 SD; p=0.006) compared to controls at age 5. - Surgical NEC was significantly shorter (p=0.002). - Significantly lower fat mass (23.4% vs 29.1%;

Authors, Country	Aim	Participant characteristics	Design and Instruments	Age at Follow-up	Outcomes
	body composition between 5-year-old preterm survivors of necrotizing enterocolitis.	Characteristics - GA <37 w - Minimum NEC stage IIA	BMI) - Dual-energy X-ray absorptiometry (DXA). - DXA Calscan (with laser) - Modified Bell's Staging Criteria		p=0.001). BMC and BMD of the total body and lumbar spine decreased (355.6 g vs 416.7 g).
(17) United States	To investigate the long-term impact of neonates' growth (weight and length) with NEC over a 20-year period.	Samples N: 527 Case: 294 Control: 233 Characteristics - GA (median Age 29) - Birth weight (median 1189) - Birth length (median 7) - APGAR-1 min (median 7) - APGAR-5 min (median 8)	Design: A Retrospective cohort study Instrument: CDC growth percentile chart	At birth, 5, 10, 15 to 20 years.	- Weight gains significantly decrease in infants with NEC (p = 0.0064). - No significant difference in the change of length between NEC infants and controls (p = 0.09), suggesting weight was more severely impacted than length.
(18) United Kingdom	To assess the long-term neurodevelopmental outcomes of preterm infants who were diagnosed with necrotizing enterocolitis (NEC) over 10 years.	Samples N: 67 Case: 18 (15 Surgical NEC, 3 Medical NEC) Characteristic - GA (mean age 29 w) - Birth weight (mean BW 1216 g)	Design: A Retrospective cohort study Instruments: - EPR (Electronic Patient Record) - Structured interviews	At a mean age of 11.2 years	- Neurological impairment 61%, cognitive impairment 56%, motor impairment 33%, special education needs 56%, learning difficulty 50%, speaking difficulty 33%, cerebral palsy 22%, behavioral conditions 17%, blindness 11%, and seizures 11%. - Surgical NEC patients had a higher rate of impairment (67%) compared to medical NEC (33%).
(19) United State	To investigate long-term growth and neurodevelopmental effects of necrotizing enterocolitis (NEC) or spontaneous	Samples N: 1.660 NEC: 138 Medical NEC, 33 Surgical NEC	Design: A prospective, longitudinal study Instruments: - CDC growth charts	At 10 and 15 years	- Surgical NEC infants had lower weight and height at age 10 years. - Lower average weight z-score, lower BMI, and lower height z-score with NEC at age 15 years.

Authors, Country	Aim	Participant characteristics	Design and Instruments	Age at Follow-up	Outcomes
	intestinal perforation (SIP) in children born extremely preterm.	Characteristic GA 23-27 w	- GMFCS, DAS-II, WASI-II - ADHD symptoms CSI-4, MINI		- Deficits persisted across the school-age and adolescent periods.
(20) Canada	To assess the growth and neurodevelopmental outcomes among extremely premature infants with NEC or SIP	Samples N: 2.019 Case: 61 NEC, 115 non-perforated NEC, 39 SIP Control: 1804 Characteristic GA < 29 w	Design: A retrospective cohort study Instruments: - BSID-III, GMFCS - Growth Assessments (weight, length, and head circumference)	At 18-30 months' corrected age.	- NEC infants (aOR 1.77) had significantly higher odds of significant neurodevelopmental impairment (sNDI) compared to controls. - Mean scores in cognitive, language, and motor domains were significantly lower in NEC. - NEC was associated with higher risks of growth deficit (z-score <-2) in weight and HC. Smaller HC z-scores persisted at follow-up.

DISCUSSION

This systematic review presents a comprehensive synthesis of the long-term impact of Necrotizing enterocolitis on preterm infants, affirming that NEC is a multisystem condition that transcends acute gastrointestinal morbidity. The primary findings consistently demonstrate that preterm NEC survivors face a significantly elevated risk of neurodevelopmental impairment and persistent growth restriction extending into school age, adolescence, and even young adulthood. These findings reinforce the understanding that NEC is not merely a transient neonatal complication but a long-term risk factor for the child's future quality of life.

From a neurodevelopmental perspective, the synthesis demonstrates that the majority of studies report significant reductions in cognitive function, motor and language abilities, behavioral problems, and special educational needs, as well as an increased risk of cerebral palsy compared to non-NEC peers. These risks are most pronounced in the surgical NEC group, reflecting the relationship between disease severity and the degree of long-term disability.

The biological basis for the association between NEC and neurodevelopmental impairment can be explained through the gut-brain axis mechanism. Intestinal inflammation or injury in preterm infants with NEC directly affects the brain. Bowel injury triggers the release of inflammatory mediators, such as lipopolysaccharides (LPS), into the systemic circulation and activates Toll-like receptor 4 (TLR-4) in the intestine, leading to the release of High-Mobility Group Box 1 (HMGB1) ligands into the bloodstream (23). This cascade induces elevated pro-inflammatory cytokines (TNF-α, IL-1, IL-6) (24). These inflammatory mediators are capable of penetrating the blood-brain barrier, activating microglia—the primary immune cells in the immature preterm brain—thereby triggering neuroinflammation that causes white matter injury and hypomyelination, ultimately disrupting central nervous system structure (25, 26). Neurological impairments in NEC survivors are likely attributable to the complex interplay among systemic inflammation, prematurity, and clinical instability during the acute phase of the disease.

These findings are concordant with a meta-analysis by Wang et al., which reported that preterm infants with NEC had a 2.24-fold higher risk (OR 2.24) of neurodevelopmental impairment, a 1.69-fold higher risk of cognitive delay, a 2.21-fold higher risk of motor dysfunction, and a 1.94-fold increased risk of cerebral palsy compared to infants without NEC (27). Additional findings indicate that the most prevalent cognitive impairments among pediatric NEC survivors are learning disabilities and the need for special education. Regarding physical development, children with NEC exhibit below-average motor abilities, particularly in fine and gross motor functions. Meanwhile, neurological conditions that emerge include CP, blindness, and speech disorders. Infants who underwent surgical intervention demonstrated a higher risk of experiencing developmental delays and cognitive impairments compared to the medical NEC group. (28)

These findings reinforce the interpretation that NEC is not only a gastrointestinal complication but also a systemic condition with significant implications for brain development. Understanding this mechanism has substantial clinical consequences: interventions targeting the gut-brain axis, such as the use of probiotics and prebiotics and gut microbiome optimization, may serve as neuroprotective strategies in this high-risk population (24, 29). Furthermore, the American Academy of Pediatrics (AAP) recommends that infants with a history of NEC are highly susceptible to all forms of neurodevelopmental disability and require structured longitudinal monitoring through school age. (30)

In addition to neurological implications, this review demonstrates a consistent correlation between NEC and long-term growth restriction. Growth deficits are not only manifested through anthropometric indicators (weight, height, and HC) but also in the quality of growth, including body composition and bone health.

The biological mechanisms underlying growth restriction in NEC survivors are multifactorial, encompassing bowel length loss following surgical resection, inability to achieve adequate enteral feeding during the acute disease phase, leading to long-term parenteral nutrition dependency, and complications such as obstruction or intestinal stricture (31, 32). Additionally, elevated pro-inflammatory cytokine levels directly suppress insulin-like growth factor-1 (IGF-1) secretion and impair the function of the somatotropic axis, which regulates linear growth, thereby inhibiting somatic elongation in children. Malabsorption further contributes to deficiencies in essential micronutrients such as zinc, vitamin D, calcium, and phosphorus—all of which negatively impact bone mineralization and ultimately impair optimal growth. (33, 34)

A study by Speer et al. demonstrated that among infants with surgical NEC, growth failure is highly prevalent and persists through 18–22 months of corrected age (35). Infants with NEC, particularly surgical NEC, have been reported to exhibit persistently low length z-scores from discharge through 24 months of age (11). In infants with severe NEC (Bell's stage II/III), weight z-scores may recover to levels comparable to controls by 24 months; however, HC z-scores remain persistently lower (36). Infants who survived NEC following surgical intervention exhibited lower head circumference z-scores at 24 months of age (11). This persistent HC deficit observed across multiple studies suggests possible long-term brain growth impairment without adequate catch-up growth. Recovery of body weight does not guarantee equivalent recovery of brain volume (HC), which serves as a key indicator of brain growth. This is likely attributable to bowel length loss, malabsorption, parenteral nutrition dependency, and recurrent infectious complications. Accordingly, the consequences of NEC are both biological and nutritional in nature, necessitating an integrated long-term monitoring approach.

The impact of NEC extends beyond anthropometric measurements to affect growth quality, including body composition and bone density. An RCT measuring body composition via MRI in NEC infants born at ≤31 weeks gestation reported significant differences in weight and fat mass between medical NEC and surgical NEC groups ($p=0.001$; $p=0.043$) compared to non-NEC groups, with reduced body weight attributable

to decreased adipose tissue volume (37). The reduction in fat mass and bone mineral density at preschool age, as demonstrated in the DXA-based study by Magnusson et al., indicates that NEC survivors may face long-term health risks, including metabolic disturbances and compromised bone health (22). These findings affirm that growth monitoring in children with an NEC history should not be limited to weight and height measurements alone but should encompass a comprehensive evaluation of body composition and nutritional status.

This systematic review also consistently identified disease severity as a key determinant of long-term outcomes. Surgical NEC survivors represent a primary risk subgroup with substantially higher risks of neurodevelopmental impairment and growth restriction compared to medical NEC. This disparity is likely related to the duration of systemic infection, the extent of functional intestinal tissue loss, postoperative complications, nutritional constraints, and prolonged parenteral nutrition dependency. Studies by Garg et al. and Mutanen et al. support these findings, identifying shorter residual bowel length, longer duration of parenteral nutrition dependency, and higher frequency of recurrent infectious complications as factors significantly associated with worse long-term outcomes in surgical NEC survivors (32, 38, 39)

The differential outcomes between medical and surgical NEC underscore the importance of risk stratification in the neonatal period. Infants with surgical NEC should be prioritized within high-risk follow-up programs, with a multidisciplinary management approach applied from the period of inpatient care through sustained post-discharge follow-up. Moreover, the long-term impact of NEC not only affects the infant but also exerts a significant psychological and social burden on parents and families. Emotional support, accurate information provision, and education for parents and families regarding the potential for growth and developmental impairment and the critical importance of long-term follow-up are therefore equally essential.

In the context of nursing practice, the findings of this systematic review carry important implications and underscore the urgency of developing risk-based high-risk follow-up programs. As NEC represents one of the most significant multisystem risk factors in preterm infants, nurses occupy a pivotal role in early detection and prevention of long-term complications. The nursing role is central to the implementation of holistic developmental care during hospitalization, the administration of standardized early neurodevelopmental screening across each developmental age, periodic and continuous growth monitoring and evaluation, nutritional support optimization, and family empowerment through Family-Centered Care (FCC) approaches. Comprehensive parental education regarding long-term risks, home developmental stimulation strategies, and the importance of attending every follow-up session is paramount. Accordingly, evidence-based nursing practice, family-centered approaches, and multidisciplinary collaboration constitute key components in minimizing the long-term impact of NEC.

This review has several limitations that warrant consideration. First, the majority of included studies were retrospective in design, which may result in incomplete or missing critical data records, limiting data completeness and quality. Second, the heterogeneity in follow-up duration across studies and measurement instruments employed restricts the

capacity for direct quantitative comparisons. Third, the inevitable loss to follow-up across studies introduces a potential attrition bias. Fourth, the majority of included studies were conducted in high-income countries, limiting the generalizability of findings to low- and middle-income settings where clinical practices and resource availability may differ substantially.

Conclusion

NEC is significantly associated with long-term neurodevelopmental impairment and growth restriction in preterm infants, with more severe consequences consistently observed in cases requiring surgical intervention. This condition must be regarded as a long-term risk determinant rather than solely an acute neonatal complication.

The implementation of evidence-based, risk-stratified, multidisciplinary follow-up programs is strongly recommended, alongside integrated standardized developmental screening and systematic, continuous nutritional and growth monitoring, particularly for surgical NEC survivors, to improve the long-term quality of life for survivors. Future research should focus on targeted longitudinal studies examining the periodicity and effectiveness of early interventions in relation to long-term outcomes in children with NEC. Prospective longitudinal research with standardized methodology and the development of evidence-based nursing interventions are needed to improve the quality of long-term outcomes for this vulnerable population.

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Author Contributions

MMO: Conceptualization, Methodology, Formal analysis, Validation, Project administration, Writing-review & editing, and Original draft**;** MHH: Investigation, Supervision, Resources; YR: Investigation, Validation, Data curation; DW: Validation and Supervision of visualization.

Data Availability Statement

The dataset generated and analysed during the current study is available from the corresponding author upon reasonable request.

Declaration of the Use of AI in Scientific Writing

The authors declare that artificial intelligence (AI) tools were used solely to assist in language refinement and improving the clarity of the manuscript. The AI did not contribute to the study design, data analysis, or interpretation of results.

References

1. Duess JW, Sampah ME, Lopez CM, Tsuboi K, Scheese J, Sodhi CP, et al. Necrotizing enterocolitis, gut microbes, and sepsis. Gut Microbes. 2023;15(1):2221470.
2. Alganabi M, Lee C, Bindi E, Li B, Pierro A. Recent advances in understanding necrotizing enterocolitis. F1000Res. 2019;8(0):1–8.
3. Rich BS, Dolgin SE. Necrotizing enterocolitis. Pediatric in Review. 2017;38(12).
4. Haque KN. Necrotizing enterocolitis-Some things old and some things new: A comprehensive review. J Clin Neonatol. 2016;4:79–90.
5. Yajamanyam PK, Rasiah V, Ewer AK. Necrotizing enterocolitis: Current perspectives. Res Rep Neonatol. 2014;4:31–42.
6. Mekonnen SM, Bekele DM, Fenta FA, Wake AD. The prevalence of necrotizing enterocolitis and associated factors among enteral-fed preterm and low birth weight neonates admitted in selected public hospitals in Addis Ababa, Ethiopia: A cross-sectional study. Glob Pediatr Health. 2021;8:1–14.
7. Wu H, Guo K, Zhuo Z, Zeng R, Luo Y, Yang Q, et al. Current therapy option for necrotizing enterocolitis: Practicalities and challenges. Front Pediatr. 2022;10:1–10.
8. Markel TA, Martin CA, Chaaban H, Canvasser J, Tanner H, Denchik H, et al. New directions in necrotizing enterocolitis with early-stage investigators. Pediatr Res. 2020;88:35–40.
9. Matei A, Montalva L, Goodbaum A, Lauriti G, Zani A. Neurodevelopmental impairment in necrotising enterocolitis survivors: Systematic review and meta-analysis. Arch Dis Child Fetal Neonatal. 2020;105:F432–9.
10. Hansen LM, Jensen IV, Gregersen R, Juhl SM, Greisen G. Behavioural and neurodevelopmental impairment at school age following necrotising enterocolitis in the newborn period. PLoS One. 2019;14(4):1–11.
11. McNelis K, Goddard G, Jenkins T, Poindexter A, Wessel J, Helmrath M, et al. Delay in achieving enteral autonomy and growth outcomes in very low birth weight infants with surgical necrotizing enterocolitis. J Perinatol. 2021;41:150–6.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Bmj. 2021;372.
13. Goplen CM, Verbeek W, Kang SH, Jones CA, Voaklander DC, Churchill TA, et al. Preoperative opioid use is associated with worse patient outcomes after Total joint arthroplasty: A systematic review and meta-analysis. BMC Musculoskelet Disord. 2019;20(1):1–12.
14. Cha JH, Lim JS, Jang YH, Hwang JK, Na JY, Lee JM, et al. Altered microstructure of the splenium of corpus callosum is associated with neurodevelopmental impairment in preterm infants with necrotizing enterocolitis. Ital J Pediatr. 2022;48(6).
15. Han SM, Knell J, Henry O, Riley H, Hong CR, Staffa SJ, et al. Long-term outcomes of severe surgical necrotizing enterocolitis. J Pediatr Surg. 2020;55(5):848–51.
16. Hong CR, Fullerton BS, Mercier CE, Morrow KA, Edwards EM, Ferrelli KR, et al. Growth morbidity in extremely low birth weight survivors of necrotizing enterocolitis at discharge and two-year follow-up. J Pediatr Surg. 2018;53(6):1197–202.
17. Malek AJ, Mrdutt MM, Scrushy MG, Mallet LH, Shaver CN, Sanders EC, et al. Long-term growth outcomes in neonates diagnosed with necrotizing enterocolitis: A 20-year analysis. J Pediatr Surg. 2025;54(5):949–54.
18. Mondal A, Misra D, Al-jabir A, Hubail D, Ward T, Patel B. Necrotizing enterocolitis in neonates: Has the brain taken a hit 10 years? J Pediatr Neurosci. 2021;16:30–4.
19. Vaidya R, Yi JX, Shea TMO, Jensen ET, Joseph RM. Long-term outcome of necrotizing enterocolitis and spontaneous intestinal perforation. Pediatrics. 2022;150(5).
20. Zozaya C, Shah J, Pierro A, Zani A, Synnes A, Lee S, et al. Neurodevelopmental and growth outcomes of extremely preterm infants with necrotizing enterocolitis or spontaneous intestinal perforation. J Pediatr Surg. 2021;56(2):309–16.
21. Allendorf A, Dewitz R, Weber J, Bakthiar S, Schloesser R, Rolle U. Necrotizing enterocolitis as a prognostic factor for the neurodevelopmental outcome of preterm infants-match control study after 2 years. J Pediatr Surg. 2018;53(8):1573–7.
22. Magnusson A, Swolin-Eide D, Elfvin A. Body composition and bone mass among 5-year-old survivors of necrotizing enterocolitis. Pediatr Res. 2023;93(4):924–31.
23. Manohar K, Mesfin FM, Liu J, Shelley WC, Brokaw JP, Markel TA. Gut-Brain cross-talk: The pathogenesis of neurodevelopmental impairment in necrotizing enterocolitis. Front Pediatr. 2023;11:1–13.
24. Lu J, Martin CR, Claud EC. Neurodevelopmental outcome of infants who develop necrotizing enterocolitis: The gut-brain axis. Semin Perinatol. 2023;47(1):151694.

25. He Y, Zhang Y, Li F, Shi Y. White Matter Injury in Preterm Infants: Pathogenesis and Potential Therapy From the Aspect of the Gut–Brain Axis. Frontiers (Boulder). 2022;16:1–11.
26. Garg PM, Paschal JL, Zhang M, Pippins M, Matthews A, Adams K, et al. Brain injury in preterm infants with surgical necrotizing enterocolitis: clinical and bowel pathological correlates. Pediatr Res. 2021;91(5):1182–95.
27. Wang Y, Liu S, Lu M, Huang T, Huang L. Neurodevelopmental outcomes of preterm with necrotizing enterocolitis: a systematic review and meta-analysis. Eur J Pediatr. 2024;183(8):3147.
28. Marques BO, Gusmão ABF, Gonzaga LL, de Carvalho Laguna GG, da Silva Bragas NB, da Palma Maltez Monção C, et al. Quality of life after necrotizing enterocolitis: an integrative review. Revista Paulista de Pediatria. 2024;42.
29. Wang Y, Zhu J, Zou N, Zhang L, Wang Y, Zhang M, et al. Pathogenesis from the microbial-gut-brain axis in white matter injury in preterm infants: A review. Front Integr Neurosci. 2023;17:1–11.
30. Davis BE, Leppert MOc, German K, Lehmann CU, Adams-Chapman I. Primary care framework to monitor preterm infants for neurodevelopmental outcomes in early childhood. Pediatrics. 2023;152(1):1–17.
31. ESPGHAN Committee on Nutrition. Enteral nutrition in preterm infants: 2022 updated recommendations. Pediatr Gastroenterol Nutr. 2022. p. 248–268.
32. Garg PM, Bernieh A, Hitt MM, Kurundkar A, Adams K V., Blackshear C, et al. Incomplete resection of necrotic bowel may increase mortality in infants with necrotizing enterocolitis. Pediatr Res. 2020;89(1):163–70.
33. Faienza MF, D'Amato E, Natale MP, Grano M, Chiarito M, Brunetti G, et al. Metabolic bone disease of prematurity: Diagnosis and management. Front Pediatr. 2019;7:1–8.
34. Bozzetti V, Tagliabue P. Metabolic bone disease in preterm newborn: An update on nutritional issues. Ital J Pediatr. 2009;35(20).
35. Speer AL, Lally KP, Pedroza C, Zhang Y, Besner E, Stevenson DK, et al. Surgical necrotizing enterocolitis and spontaneous intestinal perforation lead to severe growth failure in infants: A preplanned secondary analysis of the necrotizing enterocolitis surgery trial. 2025;280(3):432–43.
36. Wang LW, Chu CH, Lin YC, Huang CC, Wang HP, Chen CC, et al. Growth outcome trends after necrotizing enterocolitis in preterm infants across changes in nutritional practices. Pediatr Res. 2025;1–8.
37. Binder C, Longford N, Gale C, Modi N, Uthaya S. Body composition following necrotising enterocolitis in preterm infants. Neonatology. 2018;113(3):242–8.
38. Garg PM, Denton MX, Talluri R, Ansari MAY, Riddick R, Ostrander MM, et al. Clinical determinants of intestinal failure and death in preterm infants with surgical necrotizing enterocolitis. J of Neonatal Med. 2023;16(4):589–96.
39. Mutanen A, Pierro A, Zani A. Perioperative complications following surgery for necrotizing enterocolitis. European Journal of Pediatric Surgery. 2018;28(2):148–51.

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