



Opinion

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Integrating point-of-care Abdominal Ultrasound, Radiographs and Advances in Multi-Omics - A Paradigm Shift in the Diagnosis of NEC



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Abbreviations: NEC: Necrotizing Enterocolitis; POCUS: Point-Of-Care Ultrasound

Introduction

Necrotizing enterocolitis (NEC) remains a diagnostic challenge in the absence of biomarkers with a disease spectrum ranging from early NEC with subtle non-specific clinical presentation to severe NEC with bowel necrosis and an acute abdomen requiring surgery for disease eradication [1]. Serious long-term complications include short-gut syndrome from intestinal failure to adverse neurodevelopmental outcomes and death [2]. Since the introduction of Bell's staging for the diagnosis of NEC in early 1970s, plain abdominal radiograph remains the gold standard primary diagnostic imaging tool [1,3]. X-ray is an excellent tool to diagnose pneumoperitoneum - a universally accepted indication for surgical intervention in NEC [1,3]. While X-ray features of pneumatosis intestinalis and / or portal venous gas define the imaging diagnosis of NEC, its limitations due to poor sensitivity in early NEC and significant inter-observer variability are well-recognized. To overcome the obvious lack of information on bowel vascularity, peristalsis, and detection of fluid within the abdominal cavity using X-rays, abdominal ultrasound emerges as a valuable adjunct and it is increasingly being adopted as a point-of-care ultrasound (POCUS) tool by the neonatal intensivist [4-6]. The complementary strengths and limitations of abdominal

radiography and ultrasound in NEC diagnosis are summarized in (Table 1), highlighting the rationale for adopting a multimodal imaging approach.

Ultrasound provides a dynamic, real-time, assessment of the bowel wall integrity, motility, and perfusion vital for a comprehensive assessment in evaluating a suspected diseased bowel state. There has been a recent surge in evidence suggesting that bowel ultrasound identifies features such as bowel wall thickening, absent peristalsis, portal venous gas, and complex peritoneal fluid more reliably than radiographs [7-9]. Doppler interrogation of the intestines is crucial to detect restrictive or absent perfusion patterns predictive of disease severity and impending perforation in infants with severe NEC [10]. In this opinion article, we share the synergistic value of using X-ray and ultrasound imaging in improving the diagnostic framework in NEC and also discuss the role of multi-omics to redefine NEC as a syndrome with multiple phenotypes rather than a single disease entity. Radiography remains the most sensitive imaging tool to detect pneumoperitoneum usually associated with advanced NEC, while ultrasound provides superior sensitivity in early NEC, has greater prognostication value, and can be safely implemented at the bedside.

Table 1: Comparison of plain abdominal radiography and ultrasound imaging in the Diagnosis of NEC.

Feature	Abdominal Radiograph (X-ray)	Abdominal Ultrasound (POCUS)
Key diagnostic strengths	Gold standard for detecting pneumoperitoneum (surgical NEC); visualizes pneumatosis and portal venous gas [1,3]	Real-time, dynamic assessment of bowel wall structure, motility, bowel vascularity, and intra- abdominal fluid [4–6]
Sensitivity in early NEC	Limited; non-specific findings in early stages [5,6,19]	superior; detects early bowel wall changes and abnormal vascularity patterns [7–10,19]
Prognostic utility	Poor correlation with disease progression [2,3]	Offers prediction for the need of surgery (e.g., absent peristalsis, bowel-wall thinning, complex fluid collection) [7–10]
Radiation exposure	Yes [1,3]	None [5,6,19]
Bedside repeatability	Restricted by radiation concerns / 24- hours availability [1,3]	Resource dependent – skills and equipment, easy bedside utility depending on resources [5–7,19]
Inter-observer variability	High [5,6]	operator dependent [6,11]
Equipment/training needs	Widely available; minimal training [1,3]	Requires high-frequency ultrasound probes and hands- on expertise [6,11,12]
Role in clinical decision-making	Confirms NEC diagnosis in advanced disease; precision in identifying advanced stages -pneumoperitoneum for immediate surgical intervention [1,3]	Greater precision in clinical decision-making pathways: medical vs. surgical management, monitoring response to therapy [7–10,19]

The evolving evidence for utilizing abdominal POCUS in the diagnosis of NEC.

In our scoping review (Diagnostics), we analyzed exactly how many studies with strong evidence showing that ultrasound outperforms plain radiography in early NEC detection [11]. Additionally, ultrasound findings of absent peristalsis, bowel-wall thinning, and complex peritoneal fluid have been correlated with progression to advanced stages of NEC predicting need for surgery [7-10]. Ultrasound is relatively radiation-safe with easy repeatability at the bedside in the hands of a skilled-operator. Thus, ultrasound is a valuable imaging tool in the management of NEC for the dynamic monitoring of disease progression, early detection of feeding intolerance with re-initiation of feeds post therapy to gauge treatment response and recovery [5,6]. The evidence of state-of-the-art findings in NEC have been well described by the radiologists two decades ago, with evolving interest in using abdomen POCUS amongst neonatal clinicians globally. However, this skill has a steep-learning curve. A, availability of high-frequency ultrasound probes and facilitation and implementation of education and training to acquire this skill given the low-incidence of NEC pose challenges in its wider acceptability and routine implementation in clinical practice [6,12]. These challenges have contributed to the slow adoption of ultrasound into routine bedside practice, despite its growing evidence of clinical advantages in NEC diagnosis. In our *Frontiers in Pediatrics* article, we describe a range of pathological bowel ultrasound findings with clinical correlations, intending to familiarize and orientate neonatal clinicians using point-of-care ultrasound to facilitate the utility of this skill as a diagnostic tool in suspected bowel dysfunction. Ultrasound is particularly valuable when radiographic findings are equivocal- situations that often heighten clinician concern yet provide little guidance in guiding clinical management pathways [12].

Integrating imaging modalities with clinical phenotypic presentations in NEC

Recent diagnostic models illustrate how ultrasound can be pragmatically integrated into neonatal diagnostic pathways. Elsayed and colleagues (202) recently classified NEC based on definite treatment interventions validating the reliability of a predominantly ultrasound integrated framework approach along with clinical and laboratory markers [13,14]. This approach provides diagnostic precision advocating for the ability of ultrasound findings in differentiating various NEC phenotypes. This structured ultrasound evaluation allows for greater diagnostic precision avoiding unnecessary interruptions in feeding, prolonged antibiotic use preventing dysbiosis, which in itself can predispose to NEC [12,15]. (Figure 1) illustrates a proposed integrated diagnostic framework, combining clinical assessment, laboratory data, imaging (radiography and ultrasound), and emerging multi-omics signals to support phenotypic classification of NEC, improving precision in diagnosis and guiding risk stratification to improve outcomes. Surveys of practice variation have highlighted the inconsistencies in NEC diagnosis and treatment addressing the need for standardized decision-making pathways for the management of NEC [12]. Integrated frameworks using multimodal evaluation of X-rays and ultrasound are therefore essential for standardization of clinical care and monitoring outcomes.

Conceptualizing NEC as a Syndrome

Advances in systems biology have challenged us to rethink and redefine the disease pathophysiology of NEC. Josef Neu and colleagues have long argued that NEC is not a single disease but rather a syndrome encompassing several overlapping entities [14]. These include classic preterm NEC, term NEC with ischemic arteriopathy secondary to hypoxic events or congenital heart

disease, food protein-induced enterocolitis. The integration of X-rays with ultrasound provides superior discriminating power to differentiate between the various phenotypes of NEC and NEC-mimics clinically. Radiographs alone are unhelpful in distinguishing these different phenotypes of what starts with suspected NEC, a major challenge in clinical management in the absence of a biomarker for this disease [14,15]. Multi-omics research provides further support for this reconceptualization. Genomic studies implicate variants in innate immune regulation,

while transcriptomic and proteomic analyses reveal altered expression of barrier and inflammatory mediators. Metabolomic profiling identifies biochemical signatures of ischemia and dysbiosis, while microbiome studies consistently report loss of protective taxa and overrepresentation of Proteobacteria before NEC-onset [15-18]. Together, these findings highlight the multi-factorial etiology in NEC guiding pathways to navigate this information in NEC diagnosis.

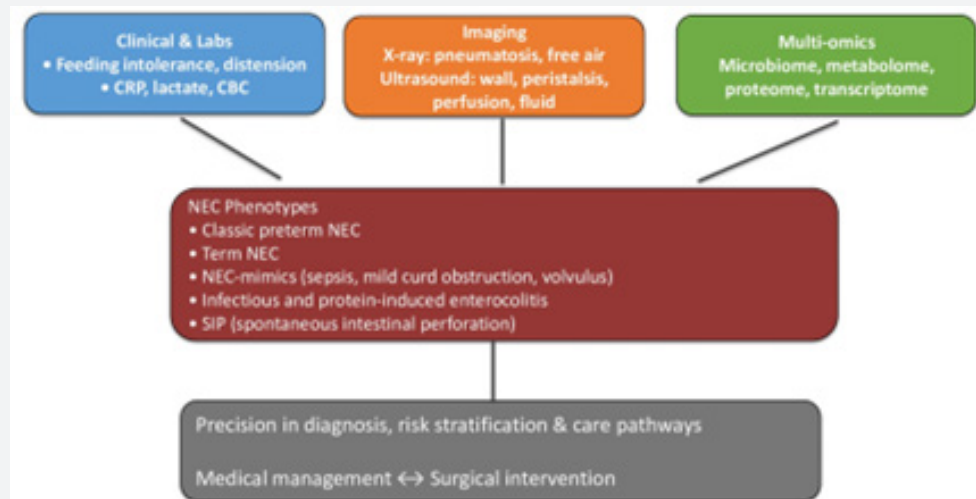


Figure 2: The Sanger sequencing results of genetic variations in the child and her parents: The patient has a heterozygous mutation of c.1996dup in the MAGEL2 gene, resulting in a frameshift change in the amino acid (p.Gln666ProfsTer47). There is no variation at this position in the parents.

Ultrasound as the Phenotypic Anchor

Within the emerging multi-omics framework, ultrasound holds a uniquely valuable role. It offers a dynamic, real-time visualization of intestinal pathophysiology- capturing vital information on bowel-wall structure, motility, perfusion, and fluid dynamics- making it an ideal tool, a phenotypic anchor for multi-omics integration. For instance, if the ultrasound reveals sluggish or absent peristalsis, bowel wall thickening, increased vascularity with characteristic NEC-associated patterns, and complex fluid collections [7-10,19]; the metabolomic profiles shows elevated inflammatory mediators and microbiome sequencing indicates a shift toward Proteobacteria dominance, the combined data-though individually insufficient can collectively be helpful to aid in assimilating a NEC profile for the correct diagnosis in the appropriate clinical setting [15-18]. The integration of imaging and multi-omics holds the potential to transform NEC diagnosis from one of uncertainty to one of precision. Recently, combining ultrasound findings with fecal calprotectin have been shown to improve sensitivity and specificity [19]. Longitudinal studies linking microbiome shifts to serial ultrasound findings are beginning to reveal patterns predictive of NEC onset [15,16].

These are early yet impactful steps towards individualized risk stratification pathways, facilitating early targeted interventions, and improving clinical outcomes in NEC [20,21].

Conclusion

Thus, the time has come for a paradigm shift by integrating the synergistic value of bowel ultrasound along with plain X-ray and utilising the advancements in multi-omics to change the diagnostic paradigm of NEC. Abdominal radiography remains a valuable primary screening tool, when integrated with abdominal POCUS, a comprehensive assessment of the bowel including assessment of vascularity, peristalsis, assessment of the intrabdominal cavity can be achieved. Ultri-omics approaches are reshaping our understanding of NEC as a heterogeneous syndrome, and ultrasound is uniquely positioned as the bridge between molecular biology and bedside care.

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