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Radiography and Ultrasonography in the Diagnosis and Monitoring of Necrotizing Enterocolitis in Neonates: A Focused Review

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ABSTRACT

Necrotizing enterocolitis (NEC) is a devastating gastrointestinal disease that predominantly affects preterm neonates and remains a major source of morbidity and mortality in neonatal intensive care units (NICUs). An early diagnosis and timely surveillance is key to optimizing the outcome of the patients. Abdominal X ray (X Ray) remains the cornerstone of the imaging of NEC with pneumatosis intestinalis, portal venous gas and pneumoperitoneum being well defined radiological signs. With the increasing role of ultrasonography (USG) in the management of NEC, the bedside evaluation of bowel thickness, vascularity, motility and the assessment of fluid collections can sometimes detect signs of NEC before they become evident on radiography. This review summarizes the role of radiography and ultrasonography in the imaging of NEC, highlights their respective merits and shortcomings, and describes the practical approaches for their use in clinical practice. It also discusses the role of contrast enhanced ultrasound, near-infrared spectroscopy and artificial intelligence in the imaging of NEC.

Keywords: necrotizing enterocolitis, neonatal imaging, abdominal radiography, ultrasonography, bowel ultrasound, contrast-enhanced ultrasound, near-infrared spectroscopy, artificial intelligence

1. Introduction

Necrotizing enterocolitis (NEC) is a catastrophic condition generally occurring in the neonatal period and is known to be the most common gastrointestinal emergency seen in neonatal intensive care units. Mortality has been reported between 10% and 50% and can reach up to 100% in cases of intestinal perforation, peritonitis, and/or sepsis. NEC commonly occurs in the second or third week of life, primarily in premature neonates with low birth weight. Clinical signs are non-specific, which often results in a late diagnosis. The clinical signs commonly reported are feeding intolerance, vomiting, lethargy, and abdominal tenderness, and it is essential to be highly suspicious of NEC, due to its non-specific presentation. Although primarily reported in preterm neonates, NEC has also been described in full-term infants, particularly after hypoxic insult. Although primarily a clinical and laboratory diagnosis, several radiographic methods like abdominal radiography, intestinal ultrasound, and newer techniques aid in the early and accurate diagnosis, management, and follow-up of NEC, which will be elaborated in the basis of the current literature, benefits, and drawbacks, and finally, their clinical implications. [1,2,3]

2. Epidemiology and Risk Factors

Prematurity and low birth weight are the most consistently recorded risk factors for NEC, with over 90% of affected infants born preterm.[1] The risk is inversely related to birthweight and gestational age, with both the incidence and fatality rates increasing in inverse proportion to these parameters. In the National Institute of Child Health and Human Development (NICHD) neonatal research network cohort (1999-2001), approximately 7% of 11,072 very low birth weight (VLBW, 1500 g) infants developed proven NEC (≥stage II), with rates of 11.5% in infants weighing 401-750 g, 9% in those 751-1000 g, 6% in those 1001-1250 g, and 4% in those 1251-1500 g. [1]

The disease occurs postnatally and is rare in infants who have never been fed, with over 90% of infants with NEC having received enteral feeds. However, feeding human milk appears to be protective, with an estimated three-fold to ten-fold risk reduction in infants fed human milk compared with those fed formula milk. Recent evidence suggests that exclusive human milk feeding may have an even greater protective effect on disease development. [2]

While NEC predominantly affects preterm infants, it can also occur in moderately preterm (28-34 weeks) and term infants, often with different risk factor profiles. Among moderately preterm infants with NEC, maternal hypertensive disorders (29%) and small for gestational age status (15%) are more common risk factors compared to extremely preterm infants. In late preterm and term infants, congenital gastrointestinal anomalies are more frequently associated with NEC development. The postnatal age at NEC onset demonstrates an inverse relationship with gestational age at birth, with more premature infants typically developing NEC later in the postnatal period. [3]

Advances in obstetric and neonatal care have improved survival rates for smaller, more immature infants, and as more VLBW preterm infants survive the early neonatal period, the population at risk for NEC continues to increase. Despite improvements in neonatal care, including advances in ventilation, nutrition, and temperature regulation, NEC remains a major cause of morbidity and mortality, with mortality rates between 10-50% and reaching up to 100% in cases with intestinal perforation, peritonitis, and/or sepsis. Infant survivors may develop significant long-term sequelae, including short bowel syndrome, cholestasis, and impaired neurodevelopment. [4]

3. Pathophysiology and Bell's Staging Criteria

The pathophysiology of NEC is multifactorial and remains incompletely understood despite decades of research. The disease is thought to develop in the premature host in the setting of bacterial colonization, often after administration of non-breast milk feeds. The premature intestinal mucosa demonstrates baseline increased reactivity to microbial ligands compared with the full-term intestinal mucosa, which leads to mucosal destruction and impaired mesenteric perfusion. This increased reactivity partly reflects an increased expression of the bacterial receptor Toll-like receptor 4 (TLR4) in the premature gut. [1,2]

Recent evidence suggests that NEC results from an altered intestinal microbiome that activates an uncontrolled proinflammatory response. In preterm infants, this proceeds briskly without adequate anti-inflammatory regulation. Prospective serial stool analysis by 16S rRNA sequencing has shown that whereas the normal premature infant gut undergoes bacterial colonization in a systematic fashion (from Bacilli to Gammaproteobacteria to Clostridia), NEC is preceded by a relative abundance of Gammaproteobacteria (facultative Gram-negative bacilli) and a paucity of strict anaerobes. [3] Additionally, impaired intestinal microcirculation

in preterm neonates compromises blood flow in response to enteral feeding, leading to localized ischemia, which initiates epithelial barrier dysfunction, exacerbates inflammatory responses, and impairs intestinal regeneration. [4]

The staging system described by Bell et al., first published in 1978 and subsequently refined, remains the cornerstone of NEC classification and guides clinical management. This system includes three stages: Stage I (suspected disease) is characterized by mild systemic signs such as apnoea, bradycardia, and temperature instability, along with mild intestinal signs including abdominal distention, gastric residuals, and bloody stools, with non-specific or normal radiological signs. Stage II (definite disease) presents with mild to moderate systemic signs, additional intestinal signs such as absent bowel sounds and abdominal tenderness, specific radiologic signs including pneumatosis intestinalis or portal venous air, and laboratory changes such as metabolic acidosis and thrombocytopenia. Stage III (advanced disease) is characterized by severe systemic illness with hypotension, striking abdominal distention and peritonitis, severe radiological signs including pneumoperitoneum, and additional laboratory changes such as metabolic and respiratory acidosis and disseminated intravascular coagulopathy. [1]

Statistical pattern analysis of clinical and radiographic variables in contemporary NEC cases has supported Bell's staging system, although the separation between NEC and spontaneous intestinal perforation still poses diagnostic challenges. The Vermont Oxford Network has developed an alternative classification system that requires one or more clinical findings (bilious gastric aspirate or emesis, abdominal distention, occult or gross blood in stool) and one or more imaging findings (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum) to establish a diagnosis of NEC.

4. Abdominal Radiography in Necrotizing Enterocolitis

Abdominal radiography (AXR) is the conventional and most commonly used imaging modality in diagnosing and managing Neonatal Enterocolitis (NEC). Since the first description of pneumatosis intestinalis by Dammann and Alfred in 1968, abdominal radiography has been at the centerpiece of the diagnosis of NEC and is therefore included in modified Bell's criteria. An AXR is a simple and widely available modality that can be performed easily in a neonatal Intensive Care Unit (ICU). It is usually done as a supine AP radiography, though an additional left lateral decubitus radiography, cross-table lateral radiography can be obtained in cases where a perforation is suspected. Serial radiographs are then taken at variable intervals ranging from

6–12 hours depending on the clinical condition of the infant. Radiography is useful for the assessment and management of the infant with suspected NEC.

Pneumatosis intestinalis is the most typical radiography sign of NEC, and is caused by intramural gas, which is considered pathognomonic for the disease. Portal venous gas is usually seen when the mucosa is severely damaged, and pneumoperitoneum is an indication of bowel perforation and usually requires an urgent surgical assessment. Other radiography signs that may be seen, and suggest the degree of disease, include dilated bowel loops, fixed or asymmetric loop positions, thickened bowel walls and, in severe cases, a gasless abdomen. [5]

Abdominal radiography is not considered a sensitive test for diagnosing early NEC. Inflammation and ischemia are said to occur before radiographic abnormalities are detectable and the test is reported to be only moderately sensitive for early NEC. The accuracy of abdominal radiography also varies with the stage of NEC and early and/or subclinical cases can be non-diagnostic. [6,7,8] Another concern is that of radiation exposure to the radiography, which is particularly a problem for preterm infants who require multiple radiography to diagnose NEC, an important consideration when using a potentially harmful radiological examination for a condition that may not be present and/or may not be a major cause of death. In an attempt to address these limitations, other studies using ultrasound have been sought to determine whether any alterations in bowel wall and/or perfusion can be seen in the abdomen of patients with early NEC. These have been successful and ultrasound has now become a regular component of the diagnostic tools for the diagnosis of NEC. [9]

5. Abdominal Ultrasonography in Necrotizing Enterocolitis

Bowel ultrasound (BUS) is a modern imaging modality, becoming more common in the early diagnosis and follow-up of NEC. It is available in all neonatal ICUs and can be done at the bedside, enabling a dynamic and non-ionizing assessment as frequently as needed in fragile preterm infants. The main ultrasound criteria include bowel wall thickness and echogenicity, peristalsis, free peritoneal fluid, intramural and portal venous gas, and intestinal doppler flow. These criteria are closely related to the early inflammatory and ischemic phases that are not yet visible with radiography. [9]

Ultrasonography has been advocated as a first line diagnostic modality for suspected NEC, since abdominal radiography has a low sensitivity for this condition, even in the optimal setting

(55-60 %). As the ultrasonogram is a functional test, it is capable of detecting early signs of NEC well before any anatomical change. The thickened bowel wall with hyperemia indicates early inflammation; as the process progresses, the bowel wall becomes thinner and there is loss of perfusion, indicating ischemia, a finding that is almost always associated with a poor outcome, occurring before necrosis. In addition, the detection of free fluid and complex ascites by bowel ultrasound enables the diagnosis of perforation earlier than is possible by radiography appearances. [10]

A number of studies have suggested that using ultrasound in clinical monitoring may help with earlier diagnosis and management of neonatal bowel abnormalities and may even aid in surgical decision making. [11] In addition to its use in evaluating potential compromise of bowel after abdominal surgery or trauma, ultrasound is increasingly recognized as an important bedside tool for providing real-time information pertinent to the safety and well-being of the neonate, including assessment of bowel vitality and perfusion, as well as early signs of inflammation. It is an important tool in the practicing physician's armamentarium and serves to improve the overall safety of neonatal care. [12]

5.1 Specific Ultrasound Parameters and Measurements

Recent studies have established specific quantitative parameters for bowel ultrasound assessment in NEC. Bowel wall thickness is a critical parameter, with studies demonstrating that bowel wall thickness greater than 2.5 mm is an independent diagnostic factor associated with NEC. Conversely, thinned bowel wall (less than 1.5 mm) has been identified as an independent diagnostic factor for definite NEC (Bell stage II), with an odds ratio of 7.081, suggesting transmural necrosis and impending perforation. The normal bowel wall in preterm neonates typically measures between 1.5-2.5 mm, and deviations from this range should prompt careful clinical correlation.

Bowel wall echogenicity provides additional diagnostic information. In early NEC, the bowel wall typically appears thickened with increased echogenicity due to inflammation and edema. As the disease progresses, the bowel wall may become hypoechoic or demonstrate a loss of normal wall stratification, indicating more severe injury. The assessment of bowel wall perfusion using color Doppler ultrasound is particularly valuable, as reduced or absent intestinal wall blood flow signal is an independent diagnostic factor for definite NEC with an odds ratio of 9.074. Color-coded Doppler ultrasound can differentiate between bowel loops with increased

perfusion (indicating inflammation) and decreased perfusion (indicating ischemia and risk for perforation).

Peristalsis assessment is another crucial parameter. Reduced or absent peristalsis has been identified as an independent diagnostic factor associated with NEC, with odds ratios ranging from 7.405 to 10.7 in different studies. Dynamic real-time assessment allows clinicians to observe bowel motility patterns that may be diminished or absent in affected segments. The presence of dilated, fluid-filled bowel loops with absent peristalsis is particularly concerning for advanced disease.

Recent literature has also identified novel sonographic features that may predict outcome in neonates with NEC. These include mesenteric thickening, hyperechogenicity of intraluminal intestinal contents, abnormalities of the abdominal wall, and poor definition of the intestinal wall. All four features were statistically significantly more frequently present in neonates with unfavorable outcomes (requiring surgery or death) compared to those with favorable outcomes. The presence of more than two of these signs was associated with significantly worse prognosis.

A logistic model combining multiple ultrasound parameters (bowel wall thickness >2.5 mm, intramural gas, portal venous gas, and reduced peristalsis) achieved an area under the receiver operating characteristic curve (AUROC) of 0.841, significantly superior to any single sonographic parameter for diagnosing NEC. Similarly, a model incorporating thinned bowel wall, reduced peristalsis, and reduced intestinal wall blood flow signal achieved an AUROC of 0.839, demonstrating superior ability in diagnosing definite NEC compared to abdominal radiography.

6. Comparison of Abdominal Radiography and Ultrasonography in NEC

Abdominal radiography has long been considered the historical imaging modality of choice for suspected NEC. It remains the first-line imaging modality in many neonatal ICUs, due to its widespread availability, standardization of interpretation and recognition of characteristic radiographic signs, including pneumatosis intestinalis, portal venous gas and pneumoperitoneum. Radiography is essential for assessment of the extent of disease, particularly for assessment of advanced disease requiring immediate surgical intervention. However, several studies have demonstrated that the radiography has poor sensitivity for early

or evolving NEC, due to the delay in the appearance of characteristic radiographic signs of NEC until significant intestinal injury has occurred. [13]

While conventional abdominal radiography can only give an impression of bowel thickening and free fluid over time, ultrasonography (USG) of the abdomen with doppler increases the information that can be obtained in real time. These include bowel wall thickness, echogenicity, peristalsis, intramural gas, free peritoneal fluid and bowel perfusion. Recent studies suggest that with ultrasonography the inflammatory changes and perfusion alterations may be seen before the development of the classical symptoms depicted on radiography. The sonographic parameters of decreased bowel wall perfusion, complex ascites or focal fluid collections have been associated with transmural necrosis and require surgery. Ultrasonography is dynamic and can be repeated as often as required, does not need to be performed in a radiology laboratory and does not involve the use of ionizing radiation, all of which makes bedside USG a worthwhile bedside tool for repeated assessment.

Currently, radiography and ultrasonography are not considered to be alternatives but rather adjuncts to each other. They are particularly useful in the settings outlined above: radiography for the acute deteriorating patient and for verifying the presence of free intraperitoneal gas. Ultrasonography can be particularly helpful in situations where the radiograph is not clear, in the case of suspected early NEC, and for assessing disease progression. All recent reviews suggest that bowel ultrasonography should be included as part of a formalized diagnostic pathway, where it can help in further clinical assessment and management of a patient, particularly for more accurate risk stratification. [13,14]

There are very few circumstances in which any imaging other than plain radiographs will be required in the diagnosis of NEC. Computer tomography and Magnetic Resonance Imaging can be avoided on account of the lack of necessity to subject the infant to irradiation and the potential of MR imaging to induce seizures, which can be catastrophic in a profoundly symptomatic neonate. Special cases that fall outside the mainstream diagnosis and management of NEC might be candidates for evaluation in a research protocol but they should not otherwise be attempted. Current practice is that plain films can provide images of established, severe, or surgical NEC, while ultrasound provides a means to diagnose NEC in an early stage, and provides detailed physiological and sequential assessment and monitoring. [15]

7. Practical Clinical Considerations and Diagnostic Algorithms

Imaging in suspected NEC should be part of a stepwise diagnostic approach based on a combination of clinical, biochemical and serial imaging assessments. [16] Clinical criteria for ultrasound include feeding intolerance, abdominal distension, and/or hematochezia, together with systemic signs of unwellness. The most common initial imaging test in these situations remains the X-ray, due to speed of availability and the potential to demonstrate pneumatosis intestinalis and/or free intraperitoneal gas. In the unstable patient radiography are repeated at intervals of usually 6 to 12 hours to assess progression of the condition in the expectation that perforation will lead to prompt clinical deterioration. [17]

Ultrasound is frequently used either as a first line adjunct to plain radiographs in situations where the clinical diagnosis remains uncertain, or as a further tool in assessment of patient risk. Bowel ultrasound may find use where there are recurrent episodes, in patients with an uncertain clinical diagnosis and radiography findings that do not adequately explain the patient's presentation, and as a tool for earlier assessment of mucosal and deeper bowel wall changes where patients are assessed as being at high-risk following episodes of moderate or severe symptoms that have completely resolved and the patient has therefore not undergone X ray examination. In these circumstances ultrasound may sometimes detect Bowel Wall Thickening, Increase Vascularity, decrease motility and minor free fluid – all symptoms that appear before the definitive radiographic signs. Doppler adds even more valuable information to assessment of an ultrasound abdomen examination. It enables a more confident decision of a patient's level of risk (which enables a patient to be treated on a more appropriate basis of conservative versus surgical – or at the very least it indicates a potential surgical intervention where the patient's bowel appears to have undergone a full thickness necrosis). Typical findings where the absence of bowel perfusion strongly suggest a need for surgical intervention comprise complex looking ascites and focal fluid collections.

Imaging findings may impact the management. [18] A suspicion of pneumoperitoneum on the radiographs always necessitates prompt surgical evaluation. Early recognition of minimal disease when suggested by subtle changes on the ultrasound or radiographs such as loss of bowel wall echogenic halo or loss of bowel wall fat shadow and absence of bowel haustra can prompt an aggressive medical management plan with bowel rest, broad spectrum antibiotics, gastric decompression and stabilization of the hemodynamic status. Monitoring the patient with

serial imaging studies is valuable in determining the effectiveness of the current therapy and planning any changes. [19]

Imaging findings should not be interpreted in isolation; rather, they should be integrated with the clinical status and laboratory markers such as metabolic acidosis and thrombocytopenia that are associated with the severity of the disease. A multimodal approach with an algorithm-based decision support tool can facilitate the early diagnosis of NEC, aid in timely surgical consultation and potentially improve the care of neonates with suspected NEC. [20]

8. Emerging Technologies in NEC Imaging

8.1 Contrast-Enhanced Ultrasound in Necrotizing Enterocolitis

Contrast-enhanced ultrasound (CEUS) represents an emerging imaging modality that has shown promise in the evaluation of NEC, particularly for assessing bowel perfusion. CEUS utilizes microbubble contrast agents that remain intravascular and provide improved real-time evaluation of both micro- and macrovascular ties of normally and abnormally perfused tissue. Unlike conventional ultrasound, which relies on Doppler techniques to assess blood flow, CEUS can visualize perfusion at the microvascular level, potentially detecting ischemic changes earlier in the disease process.

The U.S. Food and Drug Administration has approved CEUS for characterization of liver lesions and intravascular applications in children, and its use is expanding to other pediatric applications. In the context of NEC, CEUS can be used to assess bowel perfusion when problem-solving in patients with suspected disease, neonatal bowel infarction, or when conventional imaging is indeterminate. The technique provides both qualitative and quantitative information about mural and mesenteric blood flow, which is essential in determining disease activity and viability of affected bowel segments.

Case series of preterm bowel disease have explored the diagnostic utility of CEUS, and while the evidence base remains limited, initial results suggest that CEUS may enhance the precise and early detection of altered or pathological bowel wall perfusion in the initial development and course of NEC. The ability to visualize areas of decreased or absent perfusion may help identify segments of bowel at risk for necrosis before conventional imaging findings become

apparent. However, further investigation is warranted to establish standardized protocols and validate the clinical utility of CEUS in NEC diagnosis and management.

8.2 Near-Infrared Spectroscopy for NEC Detection

Near-infrared spectroscopy (NIRS) is a noninvasive, bedside technique that measures regional tissue oxygen saturation (rSO_2) and has emerged as a promising tool for early detection of NEC. NIRS technology uses near-infrared light to penetrate tissue and measure the oxygenation status of hemoglobin, providing real-time information about tissue perfusion and oxygenation. When applied to the abdomen, NIRS can measure splanchnic tissue oxygen saturation, which reflects intestinal perfusion.

Multiple studies have demonstrated that abdominal NIRS measurements are lower in preterm infants who develop NEC compared to those who do not. In a prospective cohort study of 100 preterm infants, mean abdominal tissue oxygen saturation (StO_2) during the first week of life was significantly higher in normal preterm infants compared to those who later developed NEC (77.3% ± 14.4% vs 70.7% ± 19.1%, $p = 0.002$). An StO_2 value of ≤56% identified preterm infants progressing to NEC with 86% sensitivity, 64% specificity, and 96% negative predictive value. Furthermore, infants with NEC demonstrated significantly more variation in StO_2 both during and after feeding in the first two weeks of life.

The splanchnic-cerebral oxygenation ratio (SCOR), calculated as the ratio of splanchnic rSO_2 to cerebral rSO_2, has shown particular promise as a diagnostic marker. In infants with NEC, SCOR was significantly higher (0.64 vs 0.47, $p = 0.004$) compared to infants without NEC. When adjusted for postnatal age, mechanical ventilation, and nil-per-os status, a 0.1 higher SCOR increased the likelihood of NEC diagnosis with a likelihood ratio of 1.28. Conversely, high variability of splanchnic tissue oxygen saturation (measured by coefficient of variation) may help rule out NEC when clinical suspicion arises.

Studies in premature piglet models of NEC have demonstrated that continuous abdominal NIRS monitoring can detect NEC prior to onset of clinical symptoms. In these models, NIRS values of NEC piglets remained lower throughout the study, and an A-NIRS value 75% predicted NEC with 97% sensitivity and 97% specificity. Additionally, NEC piglets demonstrated greater variability from baseline in A-NIRS compared to healthy piglets (10.1% vs 6.3%, $p=0.04$).

NIRS monitoring can also help predict the course of NEC and identify infants at risk for complicated disease. Infants with complicated NEC (Bell's stage 3B or death) demonstrated significantly lower cerebral, liver, and infraumbilical rSO_2 and higher fractional tissue oxygen extraction (FTOE) within 24 hours after onset of symptoms compared with infants with uncomplicated NEC. A continuous cerebral $rSO_2 \leq 71\%$ and liver $rSO_2 \leq 59\%$ in the first eight hours after onset of symptoms predicted complicated NEC with high sensitivity and specificity.

Recent innovations include broadband optical spectroscopy (BOS), a transcutaneous noninvasive tool that has demonstrated diagnostic specificity and early predictive power for NEC in animal models. A first-in-human pilot study of 96 premature infants demonstrated that BOS is safe and feasible for point-of-care assessment, with measurements taken during active NEC episodes being visibly different from same-infant baseline readings and identifiable with over 90% sensitivity and specificity using machine learning models. The ability to acquire reliable infrared reflectance signals from infants of all skin tones makes this technology particularly promising for diverse patient populations.

8.3 Artificial Intelligence and Machine Learning in NEC Imaging

Artificial intelligence (AI) and machine learning (ML) technologies are emerging as powerful tools to enhance the diagnostic accuracy of imaging in NEC. Deep learning models, particularly convolutional neural networks, have shown promise in recognizing subtle radiographic patterns that may be difficult for human observers to detect, especially in early-stage disease.

Several studies have demonstrated that AI models can match or exceed human expert performance in diagnosing NEC from abdominal radiographs. A deep learning feature-based model using the DenseNet121 architecture achieved an area under the receiver operating characteristic curve (AUROC) of 0.972 in the training cohort and 0.964 in external validation for identifying stage I NEC, outperforming human radiologists. This is particularly significant because characteristic features of stage I NEC are often subtle, making early diagnosis challenging for clinicians. The model's ability to identify early disease could facilitate timely intervention and potentially improve outcomes.

Another study utilizing a ResNet-50 deep convolutional neural network (DCNN) for detecting pneumatosis intestinalis achieved an AUROC of 0.918 with 87.8% accuracy, performing comparably to senior surgical residents. The study employed Gradient-weighted Class

Activation Mapping (Grad-CAM) heatmaps to visualize which regions of the radiographic images were most relevant to the neural network's decision-making process, confirming that the model was focusing on appropriate anatomical areas. This interpretability is crucial for clinical acceptance and trust in AI-based diagnostic tools.

Fine-grained visual classification approaches have also been applied to NEC diagnosis. The AIDNEC (AI Diagnosis of Necrotizing enterocolitis) system integrates Detection Transformer and Graph Convolution modules to localize discriminative areas in abdominal radiographs and formulate subtle local embeddings, which are then combined with global image features. This system achieved 79.7% accuracy in classifying NEC against no pathology, outperforming baseline models and providing meaningful discriminative regions to support classification decisions. The ability to provide visual explanations for diagnostic decisions is essential for clinical implementation, as it allows clinicians to understand and verify the AI's reasoning.

Beyond image-based diagnosis, ML algorithms are being developed to integrate multiple data streams for NEC prediction. An XGBoost machine learning algorithm trained on continuous monitoring data from 865 preterm infants delivered hourly risk predictions with 69% sensitivity for all NEC episodes and 81% sensitivity for severe episodes, with a median time gain of 10 hours compared to historical clinical diagnosis. The model maintained a low alarm rate of less than one patient alarm-day per week, making it clinically practical for implementation in busy neonatal intensive care units.

The integration of multi-omics data (genomics, proteomics, metabolomics, microbiomics) with machine learning represents a frontier in NEC biomarker discovery. Systems biology approaches analyzing "big data" could enable novel interpretations of NEC subtypes, disease progression, and potential therapeutic targets, allowing for integration with personalized medicine approaches. However, current challenges include the need for large, multicenter, multimodal datasets of high quality for model training and testing, as most published results are based on data from single institutions with limited generalizability.

Despite promising results, the clinical implementation of AI in NEC diagnosis faces several challenges. The scarcity of large, diverse, cross-institutional datasets limits the development and validation of robust AI models. Additionally, no publications with evident clinical benefits in real-world settings have been reported to date, highlighting the need for prospective clinical trials to evaluate the true potential of AI in diagnosing NEC. Standardization of imaging

protocols, validation of AI algorithms across different patient populations and imaging equipment, and integration with existing clinical workflows remain important areas for future research.

9. Conclusions

While abdominal radiography remains the first line imaging modality in the diagnosis and assessment of NEC due to widespread availability and the ability to demonstrate pathognomonic findings of pneumatosis intestinalis and pneumoperitoneum, ultrasound has become an important adjunct imaging modality allowing dynamic assessment of bowel wall echogenicity in relation echotexture changes suggestive of increased bowel wall vascular perfusion, altered bowel wall peristaltic activity, and early fluid accumulation which can often be seen before changes are apparent on a radiograph.

Combining radiography and ultrasound in the diagnostic process of suspected NEC offers a multipronged strategy that can potentially allow for earlier diagnosis, monitoring of the progression of disease and more timely and effective interventions (e.g., earlier discussion of potential need for surgery). Although there is a growing body of evidence to support the use of ultrasound, there are gaps in the literature that need to be addressed. Including standardization of the ultrasound scan, validation of additional doppler techniques and exploration of AI in ultrasonographic evaluation for the potential to improve accuracy in the diagnosis of NEC and to enhance risk assessment of those at risk for NEC.

Emerging technologies such as contrast-enhanced ultrasound, near-infrared spectroscopy, and artificial intelligence-based diagnostic tools show considerable promise in enhancing early detection and risk stratification of NEC. These modalities offer the potential for earlier identification of at-risk infants, more precise assessment of disease severity, and improved prediction of outcomes. However, further research is needed to validate these technologies in large, multicenter studies and to establish standardized protocols for their clinical implementation.

Combining the two imaging methods could provide neonatologists and pediatric radiologists with useful information for their diagnosis and treatment, hence potentially improving patient care and requiring further investigation and technological improvement. [21,22]

Disclosure

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