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ORIGINAL ARTICLE

Analysis of agreement between specialists for the evaluation of radiological findings of necrotizing enterocolitis

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Abstract

Objective: The analysis of abdominal radiography is essential for the diagnosis and management of necrotizing enterocolitis (NEC) in newborns (NB). Studies, however, show a lack of agreement among physicians in the interpretation of images. This study aims to evaluate the agreement in the radiological interpretation of the NEC between examiners from different specialties (inter-examiner analysis) and between the same examiner at different times (intraexaminer analysis).

Methods: Cross-sectional study for concordance analysis using plain radiographs of the abdomen of NB with suspected or confirmed NEC. The study included two neonatologists (Neo), two surgeons (SU), and two radiologists (RD). The participants filled out a form with questions about the radiographic findings; regarding the presence of intestinal loop distension, the specialists answered subjectively (yes or no) and objectively (calculation of the ratio between loop diameter and lumbar vertebrae measurements). Kappa coefficients were calculated for agreement analysis.

Results: A total of 90 radiological images were analyzed. For the interexaminer evaluation, the agreement was low ($\kappa < 0.4$) in 30% of the answers (Neo versus SU), 38% (Neo versus RD), and 46% (SU versus RD). In the intraexaminer evaluation, the neonatologist and the surgeon presented substantial or almost perfect agreement in 92% of the answers, and the radiologist in 77%. In the evaluation of intestinal loop distention, the greatest agreement between the specialties occurred when done objectively.

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Conclusion: The results confirmed the low intra- and interexaminer agreement in the radiological analysis of the NEC, reinforcing the importance of standardizing the methods of radiological interpretation of the disease.

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1 Introduction

2 Necrotizing enterocolitis (NEC) is a severe inflammatory disease of the gastrointestinal tract (GIT) typically found in preterm infants with very low birth weights (VLBW), especially in those younger than 28 weeks of gestational age (GA).¹⁻⁴ The incidence varies from 5 to 12% of neonates born at a VLBW, and it increases as the GA and birth weight (BW) lowers.⁵⁻¹⁰ The pathogenesis of NEC is multifactorial, and the clinical presentation is variable; its onset may be insidious, with nonspecific findings, or fulminant, in which it evolves rapidly into shock.¹¹⁻¹³

12 The diagnosis of NEC is complex and challenging. If, on the one hand, the diagnosis can be late, in advanced stages, on the other hand, "overdiagnosis" of the disease is often observed, causing unnecessary measures, such as indication of prolonged fasting, use of antibiotics, and surgical intervention.¹⁴ Although the radiological examination of the abdomen, in association with clinical findings, is an important tool for the diagnosis of the disease, divergences regarding the evaluation often occur among the professionals involved in the care, which can result in inadequate conduct, bringing consequences for the prognosis of the newborn (NB).¹⁵ Therefore, studies that evaluate the agreement between physicians involved in the management of NEC are useful to identify the main points of disagreement in the interpretation of the radiological findings, typical of NEC, and thus facilitate the elaboration of systematized protocols for this evaluation.¹⁵⁻²⁰

29 The main objective of this study is to compare the agreement between examiners from different specialties and between the same professionals at different times, in relation to the interpretation of radiological signs found in patients with suspected or confirmed NEC.

34 Methods

35 Cross-sectional study for concordance analysis, with voluntary participation of medical specialists who independently evaluated abdominal radiographs of patients suspected or confirmed for NEC, admitted to the Neonatal Intensive Care Unit of the Hospital das Clínicas of the Medical School of Botucatu, from June 2012 to July 2020. Two neonatologists, two pediatric surgeons, and two radiologists participated, all with similar experience in their respective areas of expertise and without direct involvement with the research.

44 The authors selected for this study plain radiographs of the anteroposterior (AP) view of the abdomen of patients with NEC (at any stage of the modified Bell criteria),¹³ regardless of BW and GA, that were performed no later than 24 h after the diagnostic suspicion. Radiographs of patients with NEC associated with congenital malformations of the

GIT and with technical limitations that would impair radiological analyses were excluded.

For the analysis of agreement between the participants, each of the examiners evaluated the radiological images via a form containing the following questions related to the main findings of NEC: the presence of distension of intestinal loops (diffuse or focal), air-fluid level, thickening of the intestinal wall, intestinal pneumatosis, portal venous gas, pneumoperitoneum, and ascites. For the evaluation of intestinal loop distention, the examiner, in addition to subjectively answering "yes" or "no," also performed measurements of the diameter of the most distended loop (DL), the width of the first lumbar vertebral body (L1), and the distance between the upper edge of L1 and the lower edge of the second lumbar vertebra (L2). These measurements were performed using a millimeter ruler and following the proposal of Edwards et al.²¹ The participants did not have access to information on the clinical conditions of the patients. For the intraexaminer analysis, a new evaluation of the images was performed after two months by one examiner from each specialty (a neonatologist, a pediatric surgeon, and a radiologist). The material provided to examiners is available as supplementary material 2.

The agreement values between different examiners (interexaminer agreement) and between the same examiner at different times (intraexaminer agreement) were determined.

The sample size for the analysis of interexaminer agreement was estimated according to the highest intraexaminer agreement value of 47% for the identification of intestinal pneumatosis in plain abdominal radiographs of patients with NEC, reported by Rehan et al.¹⁷ Considering a kappa value of 0.60, with a test power of 90%, to detect differences of 90% between the groups, the estimated number of radiographs was 75.²² The agreement values were determined by kappa statistics for dichotomous variables, kappa with quadratic weights (Fleiss-Kohen) for ordinal variables, and by the intraclass correlation coefficient for continuous numerical variables. The interpretation of the magnitude of the agreement estimators occurred according to the classification proposed by Landis & Koch.²³ The proportions of the results obtained by the examiner for each of the forms of interpretation of the plain radiography of the abdomen were compared by means of the binomial test. All analyses were performed with the SPSS v. 22.0 software, considering a 5% significance level.

The measurements of the DL/L1 and DL/L1-L2 ratios are presented as median and interquartile (IQR) range values. The comparisons of these measurements between suspected and confirmed cases of NEC were performed using the Mann-Whitney method.

The study was approved by the Research Ethics Committee of the Institution (CAAE: 35430220.4.0000.5411). The participants were invited to participate in the study, voluntarily, and signed the Informed Consent Form.

Table 1 Characteristics of the patient sample.

Characteristic	Total n = 72
Sex	
Female (%)	31 (43)
Male (%)	41 (57)
Gestational age (weeks)	
≥ 37 (%)	4 (6)
34–36 (%)	13 (18)
32–33 (%)	8 (11)
28–31 (%)	34 (47)
< 28 (%)	13 (18)
Type of delivery	
Normal (%)	26 (36)
Cesarean section (%)	45 (62)
Nutritional status	
AGA (%)	48 (66)
SGA (%)	23 (32)
NEC classification	
I A or B (%)	39 (54)
II A or B (%)	25 (35)
III A or B (%)	8 (11)
BW(g) – (mean ± SD)	1373 ± 604
Age at diagnosis (dl) – (median; P25-75)	6 (3–14)
Abdominal surgery (%)	23 (32)
Deaths (%)	10 (14)

AGA, appropriate for gestational age; SGA, small for gestational age; BW, birth weight; SD, standard deviation; dl, Days of life.

104 Results

105 During the evaluated period, 96 NB were identified with the
106 diagnosis of NEC, which corresponded to 0.56 % of the live
107 births. A total of 115 abdominal radiographs of these
108 patients were performed. After applying the exclusion criteria,
109 a total of 90 AP radiographs were obtained for analysis.

The sample consisted predominantly of premature NB (94%), and 54% of the patients had the diagnosis of suspected NEC (stages IA and IB) at the time of the radiography (Fig. 1 Sample selection - available as a supplementary material 1). Table 1 describes the main characteristics of the patients.

Table 2 shows the results of the analysis of agreement between the three specialties, combined into pairs. The agreement was low ($\kappa < 0.4$) in 30% of the responses between the neonatologist and the surgeon, and in 38% between the neonatologist and the radiologist. The highest frequency of low agreement occurred between the surgeon and the radiologist (46%). Regarding the diagnosis of intestinal loop distention, the greatest agreement between the specialties occurred when the analysis was made objectively when compared to the subjective evaluation of distention.

Table 3 shows the results for the comparison of the inter-examiner agreement between peers of the same specialty. The agreement was low ($\kappa < 0.40$) in 54% of the answers among neonatologists, 46% among surgeons, and 85% among radiologists.

Table 4 shows the interexaminer agreement between specialties, comparing suspected cases with confirmed cases of NEC. The degree of agreement was higher in the confirmed cases. In the comparative analyses between the neonatologist and the pediatric surgeon, the concordance category improved in 60% of the evaluations. Between the neonatologist and radiologist and between the surgeon and the radiologist, this category change occurred in 30% and 40% of the evaluations, respectively. $\kappa < 0.4$ were considered of low agreement. The detection of pneumoperitoneum demonstrated 100% concordance among suspected cases (absolute agreement to identify the absence of this radiological finding).

In the intraexaminer analysis, the neonatologist as well as the pediatric surgeon presented substantial and almost perfect agreement in 12 of 13 responses (92%). The radiologist, in turn, presented a value of 77% for substantial and almost perfect agreement. The lowest coefficients of agreement obtained by the specialists in the radiological analyses were

Table 2 Kappa values for interexaminer agreement (Neo × SU, Neo × RD, SU × RD).

Questions (n = 13)	Kappa Values		
	Neo × SU	Neo × RD	SU × RD
Intestinal loop distention	0.553	0.489	0.220
If yes, focal or fuzzy	0.180	0.369	–
DL/L1 ratio	0.633	0.778	0.455
DL/L1-L2 ratio	0.840	0.853	0.764
Air-fluid level	0.257	–	–
Thickening of the heart wall	0.367	–	0.175
Intestinal pneumatosis	0.527	0.422	0.349
Gas in the portal venous system	0.522	0.876	0.432
Pneumoperitoneum	0.709	0.788	0.903
Free fluid in the abdominal cavity	0.496	0.345	0.487
If yes, S or M or L	0.692	0.533	0.739
A lot, a little, or not suggestive for NEC	0.233	0.326	0.221
If suggestive, modified Bell rating	0.504	0.480	0.413

Neo, neonatologist; SU, pediatric surgeon; RD, radiologist; DL/L1, ratio of DL diameter to distance from L1; DL/L1-L2, ratio between DL and distance L1-L2; S, small; M, moderate; L, large; (-), null agreement.

Table 3 Kappa values for interexaminer agreement between pairs of the same specialty (Neo, SU, and RD).

Questions (n = 13)	Kappa Values		
	Neo N = 2	SU N = 2	RD N = 2
Intestinal loop distention	0.689	0.793	0.135
If yes, focal or fuzzy	0.269	0.178	–
DL/L1 ratio	0.761	0.857	0.829
DL/L1-L2 ratio	0.710	0.533	0.786
Air-fluid level	0.215	0.491	–
Thickening of the heart wall	0.352	0.579	0.173
Intestinal pneumatosis	0.517	0.390	0.245
Gas in the portal venous system	0.645	0.710	0.339
Pneumoperitoneum	–	0.313	0.347
Free fluid in the abdominal cavity	0.129	0.395	0.185
If yes, S or M or L	–	0.469	–
A lot, a little, or not suggestive for NEC	0.517	0.229	0.076
If suggestive, modified Bell rating	0.331	0.204	0.297

Neo, neonatologist; SU, pediatric surgeon; RD, radiologist; DL/L1, ratio of diameter DL to distance from L1; DL/L1-L2, ratio between DL and distance L1-L2; S, small; M, moderate; L, large; (-), null agreement.

149 the presence of free fluid in the abdominal cavity (kappa:
150 0.515; by the neonatologist) and thickening of the intestinal
151 wall (kappa: 0.665 and 0.5; by the pediatric surgeon and the
152 radiologist, respectively). The greatest agreement by the
153 neonatologist and the pediatric surgeon occurred in the
154 identification of the radiological finding of gas in the portal
155 venous system (kappa: 1.0% and 0.921%, respectively. As
156 for the radiologist, the highest agreement was in the market
157 for air-fluid level, with a kappa of 1.0.

158 Regarding the diagnosis of bowel distension, concordance
159 was performed by comparing the subjective and objective
160 assessments of the same examiner at different times. The neo-
161 natologist's diagnostic agreement was almost perfect in com-
162 parisons between the subjective assessment and the DL/L1
163 ratio measurement (kappa = 0.850) and between the objec-
164 tive assessment and the DL/L1-L2 ratio (kappa = 0.807). The
165 pediatric surgeon showed substantial agreement in these

166 comparisons (kappa = 0.739 and 0.692, respectively). The radi-
167 ologist, however, showed low agreement in both comparisons
168 (kappa = 0.261 and 0.378, respectively).

169 Considering all evaluations, the median (IQR) values of
170 the DL/L1 ratio in confirmed and suspected cases of NEC
171 were, respectively, 1.21 (1–1.5) versus 1.16 (0.93–1.40)
172 ($P = 0.089$). The median (IQR) values of the DL/L1-L2 ratio
173 were 1.13 (0.88–1.4) for suspected cases of NEC, and 1.2
174 (1.0–1.46) for confirmed cases ($P = 0.034$).

175 Discussion

176 An accurate and early diagnosis of NEC and an appropriate
177 therapeutic indication are crucially important for the prog-
178 nosis of newborns affected by the disease.²⁻⁴ Despite the
179 limitations in their interpretation, simple abdominal

Table 4 Kappa values for interexaminer agreement between specialties comparing suspected cases of NEC with confirmed cases.

Questions	Kappa Values					
	Neo × SU		Neo × RD		SU × RD	
	SC N = 44	CC N = 46	SC N = 44	CC N = 46	SC N = 44	CC N = 46
Intestinal loop distention	0.218	0.776	0.462	0.551	0.071	0.389
If yes, focal or fuzzy	0.301	–	0.201	0.637	–	–
DL/L1 ratio	0.554	0.723	0.775	0.781	0.422	0.511
DL/L1-L2 ratio	0.757	0.933	0.838	0.865	0.686	0.837
Air-fluid level	–	0.367	–	–	–	–
Thickening of the heart wall	–	0.444	0.018	0.107	0.295	0.542
Intestinal pneumatosis	–	0.642	–	0.429	–	0.498
Gas in the portal venous system	–	0.497	–	0.862	–	0.401
Pneumoperitoneum	1.0	0.631	1.0	0.726	1.0	0.877
Free fluid in the abdominal cavity	0.535	0.474	0.377	0.283	0.482	0.498

Neo, neonatologist; SU, pediatric surgeon; RD, radiologist; SC, suspected cases; CC, confirmed cases; DL/L1, ratio of diameter DL to distance from L1; DL/L1-L2, ratio between DL and distance L1-L2; (-), null agreement.

180 radiographs are, to this day, the most used imaging modality
181 in the evaluation and monitoring of NB with NEC.^{15,18-20}

182 The present study demonstrated the low agreement in
183 the analysis of abdominal radiographs of patients with sus-
184 pected or confirmed NEC among specialists involved in neo-
185 natal care. The authors found a low agreement in 30% of the
186 answers when comparing between the neonatologist and the
187 surgeon and in 38% between the neonatologist and the radi-
188 ologist. The highest frequency of disagreement occurred
189 between the surgeon and the radiologist (46%). In the calcu-
190 lation for the agreement between peers of the same spe-
191 cialty, neonatologists presented low agreement in 54%, and
192 the surgeons in 46% of the evaluations. Among radiologists,
193 low agreement occurred in 85% of the responses. These
194 results are comparable to those obtained by Markiet et al.,
195 who found a low kappa agreement of 0.259 among neonatol-
196 ogists, 0.358 among pediatric radiologists, and 0.274 among
197 radiology residents.¹⁸ In the publication by El-Kady et al.,¹⁹
198 the assessment of agreement showed a reduction in the
199 kappa coefficient when the analysis was performed between
200 different specialties. Among pediatric surgeons, the kappa
201 coefficient was 0.726 and among radiologists, 0.828; how-
202 ever, when comparing surgeons versus radiologists, the coef-
203 ficient was 0.651.

204 Notably, the degree of agreement between the exam-
205 iners was higher in the cases of confirmed NEC compared to
206 the suspected cases. This was observed by the change in the
207 magnitude of the kappa value, especially among neonatolo-
208 gists and surgeons. In this aspect, the pneumoperitoneum
209 marker stands out, of which the agreement was 100% among
210 the specialists (absolute agreement to identify the absence
211 of this radiological finding). This finding can be attributed to
212 the fact that pneumoperitoneum appears on radiographs as
213 a highly characteristic image of free air within the abdomi-
214 nal cavity. Typically, it is located below and anterior to the
215 diaphragmatic domes or between the liver and the right
216 abdominal wall, making this finding more easily identifiable
217 compared to other images found in NEC.²⁴

218 Several studies have evaluated the role of simple abdomi-
219 nal radiographs in the management of patients with NEC,
220 presenting a low agreement, both intra and interexaminers;
221 however, most did not use a standardized tool for image
222 analysis. Courtney et al., proposed a 10-point scale (Dukes
223 Abdominal Assessment Scale – DAAS) to identify radiological
224 markers and assessed the agreement between four pediatric
225 radiologists.¹⁵ In this study, the mean intraexaminer kappa
226 value was 0.792 and the mean interexaminer kappa was
227 0.665. One of the limitations of this study was that it did not
228 define the objective measure of intestinal loop distention.¹⁵
229 In this study, the authors applied a specific form with ques-
230 tions about the radiographic markers found in the NEC, and
231 the interviewees measured with a millimeter ruler the
232 parameters necessary for objective evaluation of loop dis-
233 tension (DL/L1 and DL/L1-L2 ratios).

234 Distention of the intestinal loops is a very common sign in
235 NEC and although it is nonspecific, it is often the first radio-
236 graphic manifestation and may be related to the severity of
237 the disease.²⁴⁻²⁶ The evaluation of distension, in the absence
238 of numerical data, usually uses subjective descriptions, based
239 on the concepts of the evaluator. Obtaining a more objective
240 numerical standard, using specific measurements for analyzing
241 the size of the intestinal loops allows for a more accurate and

242 reliable diagnosis. The limit of normality of the caliber of the
243 intestinal loops has already been published in adults and chil-
244 dren; however, due to the great variation in size and weight,
245 there were no defined values for NB. It was only after the pub-
246 lication of a study by Edwards et al.,²¹ in 1980, that the diame-
247 ters of the intestinal loops were compared to the width of L1
248 and the distance between L1 and L2.

249 The present results showed that, when evaluating the intes-
250 tinal loop distension using objective tools (relation to the DL/
251 L1-L2 ratio), there was an improvement in agreement, with
252 both inter- and intraexaminers. The magnitude of the agree-
253 ment between neonatologist and surgeon and between neona-
254 tologist and radiologist changed from moderate to almost
255 perfect; between surgeon and radiologist changed from low to
256 substantial agreement. In the evaluation among peers of the
257 same specialty, both neonatologists and surgeons presented
258 higher kappa values with the objective evaluation. Among
259 radiologists, the improvement in agreement was more evident,
260 which went from low agreement in the subjective evaluation
261 to a substantial and almost perfect agreement in the objective
262 analyses. These results corroborate the importance of using
263 objective and quantitative methods to define the presence of
264 intestinal loop distention. This parameter can offer diagnostic
265 and prognostic information, with a direct relationship between
266 the measurements of the intestinal loops and the complica-
267 tions of the disease, as well as for the need of surgical inter-
268 vention and a fatal evolution.^{18,27,28} Martins et al.²⁷ found that
269 NB with NEC who were submitted to surgery had a 20% higher
270 DL/L1-L2 ratio than those who did not operate; among those
271 who had complications due to the disease, this ratio was 28%
272 higher; and among the NB who died, this value was 24% higher
273 than those who survived ($p < 0.05$ for all comparisons). A simi-
274 lar result was seen in the work of Zvizdic et al.²⁸

275 Regarding the pattern of agreement in the intraexaminer
276 evaluation, the data showed substantial or almost perfect
277 agreement in more than 90% of the responses of the neona-
278 tologist and surgeon and in 77% of the responses of the radi-
279 ologist. These data were similar to those found in Courtney's
280 studies, in which radiologists had a mean intraexaminer
281 kappa of 0.792¹⁵ and both differ from those found by Markiet
282 et al.,¹⁸ which showed moderate and substantial agreement
283 among radiologists and low agreement in the evaluation of
284 neonatologists.

285 The statistical method used in the present study was the
286 quantification of the kappa coefficient, which is considered
287 to be the most appropriate and reliable way to evaluate the
288 intra- and interexaminer agreement before a given diagnosis
289 since it is able to correct any results due to chance.^{22,29}

290 An important point in the intraexaminer analysis con-
291 cerns the time elapsed between the two analyses. In gen-
292 eral, a minimum period of 14 days between the two
293 evaluations is recommended so that the interpretation of
294 the Kappa coefficient does not suffer the so-called "mem-
295 ory" bias.²⁹ In the present study, the time interval between
296 evaluations was two months, which reduced the chance of
297 similar responses in the second evaluation due to the effect
298 of the examiner's memory in relation to the first responses.

299 A limitation of this study would be the small number of
300 participating physicians. However, most studies of agree-
301 ment analysis use this methodology, considering that the
302 result is more dependent on the number of radiographs eval-
303 uated than on the number of evaluators. Notably, in this

304 study, professionals with recognized experience within their
305 specialties were chosen, reducing the chance of interfer-
306 ence of this factor in the interpretation of the results.

307 The present study brings two, thus far, unpublished analy-
308 ses to the literature. The first refers to the evaluation of
309 agreement comparing suspected cases with confirmed cases,
310 and the second refers to the analysis of intraexaminer agree-
311 ment in the objective identification of intestinal loop disten-
312 tion, showing the importance of a standardized method
313 based on the use of well-defined measures.

314 Although it is considered that radiological signs may have
315 a high positive predictive value for the diagnosis of NEC, this
316 study, in accordance with the literature, shows the limita-
317 tions of its interpretation in clinical practice.¹⁵ Thus,
318 abdominal ultrasound (US) has been recently used as an
319 important adjuvant for the diagnosis of NEC.^{25,26,30} Recent
320 studies by Muchantef and Dilli²⁰ emphasize that the two
321 imaging methods, radiography, and US, complement each
322 other and should be used together with the clinical status
323 for the evaluation and management of patients with sus-
324 pected or confirmed NEC.

325 Considering that the present study was performed at a
326 single center in a tertiary hospital, the results should be
327 analyzed with caution regarding their generalizability.
328 However, these findings were consistent with those
329 described in the literature, so it is reasonable to consider
330 its external validation.

331 Conclusion

332 The data from this study demonstrated low agreement
333 among specialists involved in the management of NEC in this
334 service. The present results underscore the importance of
335 standardizing radiological interpretation, with the adoption
336 of more objective analysis criteria, including the objective
337 assessment of intestinal loop distension through the calcula-
338 tion of the DL/L1 and DL/L1-L2 ratios. This approach aims to
339 improve communication among professionals, optimize diag-
340 nosis, and establish appropriate therapy for neonates with
341 confirmed or suspected NEC.

342 Ethics approval

343 The study was approved by the Research Ethics Committee
344 of the Institution (CAAE: 35430220.4.0000.5411). The partic-
345 ipants were invited to participate in the study, voluntarily,
346 and signed the Informed Consent Form.

347 Conflicts of interest

348 The authors declare no competing interests.

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Supplementary materials

353

Supplementary material associated with this article can be
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