INTRODUCTION

Anastomotic leakage (AL) after colorectal resection is a major complication. It is associated with significantly increased morbidity and mortality (as much as 15% or 20%) [1–3]. Next to short-term adverse events, a recent meta-analysis demonstrated that AL increased the local recurrence rate and decreased long-term overall survival, cancer-specific survival and disease-free survival [4]. Early re-intervention for AL in patients who have undergone colorectal resection can prevent mortality [5]. This implies that early diagnosis...
of possible leakage is of crucial importance. The preferred imaging modality for detecting AL is abdominal CT [6]. Alternatives include water-soluble contrast enema, plain X-ray, endoscopic examination and reoperation. Available evidence has demonstrated an overall sensitivity of 68.0%–73.0%, specificity of 84.0%–92.0%, positive predictive value (PPV) of 82.0% and negative predictive value (NPV) of 70% [3,7]. False negative rates of up to 25% of all CT scans were reported in recent studies [6]. In order to prevent delay in diagnosis and treatment of AL, the limited sensitivity and NPV should be taken into consideration [8,9]. Moreover, delayed re-intervention after false-negative CT scans leads to increased hospital stay and mortality [5]. A mortality rate of 45%–62.5% was reported in patients with false-negative CT scans, whereas mortality was only 4.2% in patients with true-positive CT scans and appropriate management [3,5]. Standard contrast-enhanced CT scans are performed with the use of oral and intravenous contrast. Several studies have shown that contrast extravasation is the most reliable and only independent variable predicting AL [10,11]. Many patients with AL also show signs of small bowel ileus, which could make it more difficult for oral contrast to reach the anastomosis [12]. With a rectal contrast enema, the likelihood of reaching the anastomosis is increased and may thereby improve the predictive value of CT for leakage. However, the evidence available in the literature is limited. This study aimed to investigate the value of rectal contrast in detecting AL after colorectal surgery.

METHOD

Study design

A retrospective cohort study was conducted from a prospectively maintained database at the Flevo Hospital in Almere, the Netherlands. This is a teaching hospital serving 200,000 inhabitants, specializing in medium-complex surgical care.

Inclusion and exclusion criteria

According to local protocol, the serum C-reactive protein (CRP) level was determined postoperatively at day 3 for all colorectal surgery patients. Routine measurement of CRP is useful for early diagnosis and early re-intervention in intra-abdominal complications such as AL [13,14]. In our practice, as a routine, patients with a colorectal anastomosis had CT imaging if their CRP level was above 150 on day 3 and/or clinical suspicion for AL was raised. All files of patients who underwent colorectal surgery (for benign and malignant conditions) with a primary anastomosis between 2009 and 2018 were reviewed. Since 2011, administration of rectal contrast has been protocolized if an AL is suspected. Before 2011 patients received contrast occasionally, depending on the requesting surgeon and radiologist. In the period between 2009 and 2018, it was found that some of our patients were scanned without rectal contrast. They were either operated on before 2011 or the wrong protocol (the standard CT-abdomen protocol instead of the AL CT protocol) was accidently used. All patients suspected to have AL and in whom a postoperative abdominal CT scan was performed within 30 days after surgery were included in this study. Patients who had CT imaging later than 30 days after surgery were excluded.

CT imaging

CT imaging was performed on a 16- and 64-sliced MDCT scanner (Philips, Netherlands), with a slice thickness of 3–5 mm with axial and coronal reconstructions. Rectal contrast was given by an experienced member of the radiology department. First, 50 ml of Telebrix Gastro was dissolved in 1 l of tepid water (1:20) in a colon bag. This bag was then placed 40 cm above the table level. A soft cannula was carefully placed rectally without inflating the balloon. The cannula was fixated when the patient turned to his or her back. A blank CT-abdomen was made. Subsequently, the contrast slowly dripped in. In the vast majority of patients the colon could fill itself with 1 l of contrast. Then the abdomen was scanned again. The radiologist has to preview the scan, before the patient leaves the CT imaging room. If the patient was scanned without rectal contrast, intravenous contrast (1 ml/kg Ultravist 300) was given. Any adverse event due to rectal, oral or intravenous contrast was documented. Six experienced radiologists reported the CT scans. The original radiology report was used for analysis, since amendments after revision of scans would be a bias in the assessment of false-negative scans. Our radiologists scored the following features to evaluate the CT scans: intra-abdominal fluid, fluid near the anastomosis, free air in the abdomen, air near the anastomosis and contrast extravasation. The CT scan was considered positive for AL if there was a combination of free fluid, free air or contrast extravasation (two out of thee). In case of an equivocal CT, clinical symptoms were leading. A diagnostic laparoscopy was performed if there was a clinical suspicion of an AL.

Variables and outcomes

Clinical and radiological outcomes were compared in groups of patients with and without the use of rectal contrast. Variables included the finding of AL, acute reactions due to contrast administration, complications, mortality, hospital stay and failure to rescue. Failure to rescue was defined as mortality among patients with serious
complications. A serious complication was defined as a complication leading to an in-hospital stay of more than 14 days, a surgical, endoscopic or radiological re-intervention, or death [15]. AL was graded according to the definition of the International Study Group of Rectal Cancer [16]. Grade C was defined as a leak requiring surgical re-intervention, a grade B leak required percutaneous re-intervention and a grade A leak required antibiotics at most. Since the indication for antibiotics was not always based on CT findings and has minimal to no clinical impact on a patient’s postoperative course, only grade B and C ALs were included in the CT-accuracy analyses.

**Statistical analysis**

Sensitivity, specificity, PPV and NPV were calculated with 95% CIs. Categorical data are shown as numbers (%) and continuous variables as mean ± SD. Values were compared using bivariate analysis. The p-values were determined by chi-square analysis or two-sided Fisher’s exact test for categorical variables. Continuous variables were compared with Student’s t-test or the Mann-Whitney U-test.

**RESULTS**

A total of 1183 records of patients who underwent colorectal resection were reviewed; 225 of these patients underwent CT-abdomen in suspicion of an AL.

The groups scanned with (n = 175) and without (n = 50) rectal contrast were similar, as presented in Table 1. There was no significant difference in patient characteristics such as age, sex and American Society of Anesthesiologists grade or location of the anastomosis.

Of the 225 patients who underwent CT imaging, 175 (77.8%) received rectal contrast. AL was found in a total of 57 patients (4.3% of all patients and 24.8% of CT-scanned patients). The overall

| TABLE 1 Patient demographics | With rectal contrast | Without rectal contrast | p-value |
|------------------------------|---------------------|------------------------|---------|
| Age (years)                  | Median 66           | 66                     | 0.206   |
|                              | Range 61.7–65.68    | 56.8–66.7              |         |
| Sex                          | Male 104            | 25                     |         |
|                              | Female 71           | 25                     | 0.259   |
| ASA grade                    | I–II 120            | 40                     | 0.207   |
|                              | III–IV 54           | 10                     |         |
| Type of surgery              | Ileocaecal resection 8 | 5                      | 0.273   |
|                              | Right colectomy     | 61                     |         |
|                              | Left colectomy      | 13                     |         |
|                              | Sigmoid resection   | 53                     |         |
|                              | Low anterior resection 22 | 3                    |         |
|                              | Subtotal colectomy  | 20                     |         |
|                              | Open 21             | 16                     | 0.005   |
|                              | Laparoscopic        | 144                    |         |
|                              | Laparoscopic conversion to open 10 | 4                 |         |
| Emergency                    | No 166              | 39                     | 0.001   |
|                              | Yes 13              | 12                     |         |
| Stoma                        | None 147            | 37                     | 0.361   |
|                              | Deviating           | 28                     |         |
| Anastomotic leak             | Grade A 4           | 1                      | 0.101   |
|                              | Grade B 3           | 3                      |         |
|                              | Grade C 35          | 16                     |         |

Abbreviation: ASA, American Society of Anesthesiologists.

aMann–Whitney U-test.

bFisher’s exact test.
sensitivity and specificity in all patients to detect AL was 68% and 93%, respectively. The PPV was 0.75 and the NPV 0.90. In the group without rectal contrast \((n = 50)\), sensitivity was 47%, specificity 88%, PPV 0.66 and NPV 0.76. The sensitivity increased to 78% with rectal contrast, the specificity to 94%, the PPV to 0.78 and the NPV 0.94.

Rectal contrast was seen at the anastomosis in 81.7% of the patients who received rectal contrast, compared with 26% of the patients who received only oral contrast \((p < 0.001)\). The sensitivity in the group of patients in whom enteral (oral or enteral) contrast reached the anastomosis increased to 93%, the specificity to 97%, the PPV to 0.88 and the NPV to 0.98 (Figure 1).

In the 17 patients with a false-negative scan, the mortality rate was 29.4% \((n = 5)\). Only 8 of these 17 patients received rectal contrast \((p = 0.004)\) and the contrast reached the anastomosis in just two patients. The average percentage failure to rescue for patients who received a CT was 11.3%; in patients who received rectal contrast it was 7.9% compared with 19.5% for the patients without contrast \((p = 0.048)\). The failure to rescue rate in the total population was 7.3%. No acute contrast reactions were observed after intravenous, enteral or rectal contrast (Table 2).

**DISCUSSION**

This study demonstrated that rectal contrast enhanced the predictive value of CT scanning for AL, resulting in a decreased percentage of failure to rescue due to a reduction in false-negative scans.

As mentioned previously, contrast extravasation has been demonstrated to be the most reliable and only independent variable predicting AL on CT scans, and thereby it is crucial that enteral contrast reaches the anastomosis.

The presumption that contrast is more likely to reach the anastomosis with rectal contrast compared with solely oral contrast seemed to be true. In the group of patients who received rectal contrast, the contrast reached the anastomosis in 81.7% of patients compared with 26.0% of patients who were given only oral contrast \((p < 0.001)\).

This study shows an increase in PPV as well as NPV of CT-abdomen for AL after giving rectal contrast.

In the group of patients who received enteral contrast but the contrast did not reach the anastomosis, the sensitivity and PPV were lower (35% and 50%, respectively) compared with the group of patients who did not receive enteral contrast (47% and 66%). A possible explanation could be that enteral contrast was given, giving a false sense of security.

In this study, no adverse effects of either intravenous or enteral contrast were seen. This seems valid given the fact that the prevalence of acute adverse reactions is very low. Contrast reactions have been observed with enteral administration; however, the vast majority of acute reactions arise from intravenous administration. The incidence of acute reaction on low- or iso-osmolar iodinated contrast is 0.15%–0.7%, with >98% being mild and self-limiting [17–20].

Our results are comparable to those of previous studies. In a cohort study \((n = 131)\), Kauv et al. demonstrated that retrograde contrast enema (rectal contrast) administered to 58 patients improved the PPV of CT for AL [11]. A recent consensus study regarding the definition of AL among 59 Dutch and 202 Chinese dedicated colorectal surgeons indicated that the leakage of contrast after rectal enema on CT was the only element with consensus [16,21]. This study also shows a lower rate of mortality and failure to rescue in the group of patients who received rectal contrast, suggesting improved outcomes due to earlier re-intervention after a true-positive CT scan.

This study is limited by its retrospective character, which resulted in an imbalance in the total number of patients. Another limitation of this study was a possible bias in time. Given the fact that more patients who did not receive rectal contrast were operated on at the
beginning of our time period (since the adjustment of the protocol concerning rectal contrast was effected in 2011) and the concept that results might improve over time due to the learning curve of the radiologists. However, as mentioned, the CTs were reviewed by six experienced radiologists, who remained consistent. The strength of this study is the inclusion of consecutive patients from a single, nonacademic, non-referral centre, which is a good reflection of daily clinical practice and the correlation of radiological findings with clinical outcome.

Despite its limitations with regard to accuracy and predictive value, CT remains an important diagnostic tool. Clinical postoperative observation of the colorectal patient is essential for early identification of AL. However, clinical signs including pelvic pain, ileus, delayed gastric emptying and tachycardia may be mild and nonspecific. Emergency laparoscopy or laparotomy in such cases of only moderate suspicion may lead to unnecessary risks for complicated recovery in the early postoperative patient, in particular for those with comorbidities [10]. Rectal contrast enema provides a safe alternative by optimizing the predictive value of CT interpretation. Besides the noninvasive nature of CT, it allows for the detection of an alternative diagnosis such as intra-abdominal abscess and, in case of leakage, the leakage severity and possible preoperative planning.

Finally, it must be recognized that a negative CT scan does not rule out AL. Even with a negative CT scan, we should remain equally alert for clinical deterioration as an argument for timely intervention [3].

**CONCLUSION**

The use of rectal contrast resulted in a significant increase in the PPV as well as NPV of CT-abdomen for AL after colorectal surgery. Rectal contrast was shown to reach the anastomosis in the majority of the patients, compared with just a quarter of the patients who received only oral contrast. No adverse events were observed after the use of rectal contrast. This suggests that rectal contrast is a safe and useful adjunct to CT-abdomen in the detection of AL.

**CONFLICT OF INTEREST**

None of the authors of this study has financial or other relationships that may cause a conflict of interest.

## DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.

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## TABLE 2: Clinically relevant effects of rectal contrast

|                      | Without rectal contrast (N = 50) | With rectal contrast (N = 175) | p-value |
|----------------------|----------------------------------|-------------------------------|---------|
| Contrast at anastomosis | 26.0% (7 out of 27)a | 81.7% (143) | <0.001b |
| False-negative scans | 18.0% (n = 9) | 4.6% (n = 8) | 0.004b |
| Mortality | 16.0% (n = 8) | 4.6% (n = 8) | 0.006b |
| Failure to rescue | 19.5% (n = 8 out of 41) | 7.9% (n = 8 out of 101) | 0.048b |

aSeven out of 27 patients who received (only) oral contrast.
bMann–Whitney U-test, chi-square test.
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