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## ORIGINAL ARTICLE



Is proctoscopy sufficient for the evaluation of colorectal anastomosis prior to ileostomy reversal? A nationwide retrospective analysis of the Italian Society of Surgical Oncology Colorectal Cancer Network Collaborative group (SICO-CCN)

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#### Abstract

**Aim:** Several methods for assessing anastomotic integrity have been proposed, but the best is yet to be defined. The aim of this study was to compare the different methods to assess the integrity of colorectal anastomosis prior to ileostomy reversal.

**Method:** A retrospective cohort analysis on patients between 1 January 2010 and 31 December 2020 with a defunctioning stoma for middle and low rectal anterior resection was performed. A propensity score matching comparison between patients who underwent proctoscopy alone and patients who underwent proctoscopy plus any other preoperative method to assess the integrity of colorectal anastomosis prior to ileostomy reversal (transanal water-soluble contrast enema via conventional radiology, transanal water-soluble contrast enema via CT, and magnetic resonance) was performed.

**Results:** The analysis involved 1045 patients from 26 Italian referral colorectal centres. The comparison between proctoscopy alone versus proctoscopy plus any other preoperative tool showed no significant differences in terms of stenoses (p=0.217) or leakages (p=0.103) prior to ileostomy reversal, as well as no differences in terms of misdiagnosed stenoses (p=0.302) or leakages (p=0.509). Interestingly, in the group that underwent proctoscopy and transanal water-soluble contrast enema the comparison between the two procedures demonstrated no significant differences in detecting stenoses (2 vs. 0, p=0.98), while there was a significant difference in detecting leakages in favour of transanal water-soluble contrast enema via CT (3 vs. 12, p=0.03).

**Conclusions:** We can confirm that proctoscopy alone should be considered sufficient prior to ileostomy reversal. However, in cases in which the results of proctoscopy are not completely clear or the surgeon remains suspicious of an anastomotic leakage, transanal water-soluble contrast enema via CT could guarantee its detection.

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SICO-CCN Collaborative Group: the members of the Italian Society of Surgical Oncology Colorectal Cancer Network Collaborative Group are listed in the Appendix.

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KEYWORDS contrast enema, ileostomy, leakage, proctoscopy, reversal

## INTRODUCTION

Anastomotic leakage (AL) after low rectal resection represents one of the most troublesome complications, being associated with shortand long-term consequences and increased postoperative morbidity and mortality [1, 2]. For this reason, and in accordance with current clinical practice guidelines, a defunctioning stoma should be performed after low anterior resection to reduce the risk of serious postoperative conditions, i.e. pelvic abscess or sepsis [3–5]. Nevertheless, it is important to underline that the presence of a defunctioning stoma does not reduce the overall rate of AL, thus the evaluation of anastomotic integrity prior to reversal remains mandatory.

Several methods for assessing anastomotic integrity have been proposed, but the best is yet to be defined [6–9]. The most commonly adopted methods are digital rectal examination (DRE), an endoscopic procedure (proctoscopy) and transanal water-soluble contrast enema (ta-WSCE) via either conventional radiology or CT, and magnetic resonance (MR).

A recent systematic review [10] tried to analyse the sensitivity and specificity of the adoption of contrast enema for the detection of asymptomatic AL, comparing it with DRE or proctoscopy. The authors showed comparable value among the three procedures, although proctoscopy and contrast enema radiology was associated with greater patient discomfort and higher radiation doses. The authors concluded that there were too few studies to give definitive conclusions, and considered the overall evidence of their review fragile.

The aim of the present study was to compare the different methods for assessing the integrity of colorectal anastomosis prior to ileostomy reversal after anterior resection for middle and low rectal cancers.

## METHOD

This was a retrospective cohort study of patients with a defunctioning stoma for middle and low rectal cancer resection, in which anastomotic integrity prior to ileostomy reversal was assessed by several preoperative tools. The eligible cohort were patients in 26 tertiary Italian referral centres for colorectal surgery between 1 January 2010 and 31 December 2020. All consecutive ileostomy reversals were included in our analyses.

The study was approved by the institutional review board of all participating centres. All items required by the STROBE checklist for reports of observational studies have been included [11].

The aim of the study was to establish if proctoscopy alone was sufficient to detect anastomotic complications prior to ileostomy reversal.

### What does this paper add to the literature?

This is the largest series to compare the different methods for assessing the integrity of colorectal anastomosis prior to ileostomy reversal. Furthermore, our study introduces an important concept: when the surgeon remains suspicious of an anastomotic leakage after preoperative proctoscopy, transanal water-soluble contrast enema via CT could guarantee its detection.

Patients who underwent a DRE performed by the operating surgeon, a proctoscopy, a transanal water-soluble contrast enema via CT (taCT-WSCE), a transanal water-soluble contrast enema via conventional radiology (ta-WSCE) or magnetic resonance (MR) were included. However, in order to evaluate the validity of proctoscopy alone or in combination with any other preoperative tool, patients who did not undergo proctoscopy were excluded from the final analysis (Figure 1).

A comparison between patients who underwent proctoscopy alone and patients who underwent proctoscopy plus any other preoperative method for assessing the integrity of colorectal anastomosis prior to ileostomy reversal (ta-WSCE, taCT-WSCE and MR) was performed. Furthermore, subgroup analysis included a one-to-one comparison between patients who underwent proctoscopy alone and patients who underwent proctoscopy plus ta-WSCE, taCT-WSCE or MR. Finally, an intra-group analysis was performed in the groups in which patients underwent proctoscopy plus one of preoperative methods (ta-WSCE, taCT-WSCE and MR), adopting each patient as his or her own control.

All preoperative images were reviewed and validated by radiologists with more than 10 years of experience. Proctoscopy was performed by rigid or flexible endoscopy by the operating surgeon or by an endoscopist, inserting the instrument in the anus for few centimetres, with the aim of assessing the integrity of the colorectal anastomosis and to exclude stenoses. The choice between rigid or flexible endoscopy was according to the physician's preference. All the WSCEs were performed by gastrointestinal radiologists or surgeons with insertion of a Foley (various sizes) in the anus, with dilute iodine contrast agent.

Collected data were gender, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, mean distance of the tumour from the anal verge in centimetres, preoperative tools used, assessment of the presence of AL or stenoses prior to reversal and their treatment, and misdiagnosed AL or stenoses and their treatment after closure of the diverting stoma.

AL was defined as a condition of clinical or radiological anastomotic dehiscence that either needed or did not need surgical **FIGURE 1** STROBE flowchart of the included patients (ASA, American Society of Anesthesiologists; BMI, body mass index; ta-WSCE, transanal water-soluble contrast enema).



revision. Specifically, AL was classified as grade A if it resulted in no change to a patient's management, grade B if it required active therapeutic intervention but not surgical intervention or grade C when a surgical reoperation was needed [12]. Stenoses were defined clinically as the impossibility of passing through the colorectal anastomosis with a paediatric endoscope.

Statistical analysis was performed using the SPSS 27 system (SPSS Inc., Chicago, IL, USA). Continuous data are expressed as mean  $\pm$  SD, while categorical variables are expressed as percentages. Continuous variables were compared by an independent sample *t*-test. The Wilcoxon test for paired samples was employed as a nonparametric test similar to the paired samples *t*-test used for continuous variables. Categorical data were analysed by the chi-square test. Fisher's exact test was adopted when the minimum expected value was <5. All the results are presented as two-tailed values with statistical significance of *p* < 0.05.

A predicted probability of the adoption of each preoperative procedure was estimated by a multivariate logistic regression model of procedures based on age, sex, BMI and ASA score. However, the groups were entirely matched for the analysed characteristics and no propensity matching was needed for the analysis.

The agreement between the diagnostic methods in patients who underwent proctoscopy and any other preoperative assessment tool was calculated using the weighted Cohen  $\kappa$  statistic. The  $\kappa$  values were considered as follows: 0–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1 almost perfect agreement.

#### RESULTS

The entire cohort included 2043 patients from 26 Italian referral colorectal centres. However, after excluding patients who underwent only DRE, ta-WSCE or MR without proctoscopy, the final analysis involved 1045 patients, of whom 634 were men (60.7%) and 411 women (39.3%). A STROBE flowchart of patient selection is presented in Figure 1.

The mean patient age was  $67.13 \pm 12.02$  years, the mean BMI was  $25.74 \pm 3.76$  kg/m<sup>2</sup>, the mean ASA score was  $2.2 \pm 0.69$  and the mean distance of the tumour from the anal verge was  $8.2 \pm 3.3$  cm. A misdiagnosed stenosis after reversal of ileostomy occurred in 18 patients (1.7%), of which one (5.5%) was detected by DRE, 10 (55.5%) by proctoscopy, two (11.1%) by ta-WSCE and two (11.1%) by taCT-WSCE; these data were not reported in three cases (16.7%). Regarding the required treatment, two stenoses (11.1%) were resolved by rectal corticosteroid treatment, 12 (66.6%) were resolved by endoscopic dilation and four (22.3%) were resolved by a new surgical procedure.

A misdiagnosed leakage after reversal ileostomy occurred in 10 patients (1%), of which four were grade A (40%), four grade B (40%) and two grade C (20%). No leakage was detected by DRE (0%), three by proctoscopy (30%), none by ta-WSCE, four by taCT-WSCE (40%)



and three by CT of the abdomen (30%). Regarding the treatment, six patients required no additional treatment (60%), two required radiological drainage (20%) and two a surgical reintervention (20%) (one reileostomy one Hartmann's procedure). All data are shown in Table 1.

# Proctoscopy alone versus proctoscopy and any other preoperative method (ta-WSCE, taCT-WSCE or MR)

The comparison performed between proctoscopy alone versus proctoscopy and any other preoperative tool included the entire sample (722 in the proctoscopy alone group and 323 in the proctoscopy and other preoperative tools group). The two groups did not significantly differ in terms of gender (p=0.682), age ( $67.07\pm12.5$  years vs.  $67.29\pm10.89$  years; p=0.781), BMI ( $25.69\pm3.85$ kg/m<sup>2</sup> vs.  $25.85\pm3.61$ kg/m<sup>2</sup>; p=0.537), ASA score ( $2.24\pm0.74$  vs.  $2.26\pm0.59$ ; p=0.667) and mean difference of the tumour from the anal verge ( $8.3\pm3.6$  cm vs.  $8.1\pm2.7$  cm; p=0.473). No significant differences were found in the two groups in terms of stenoses (41 in 722 patients vs. 25 in 323; p=0.217) and leakages (49 in 722 patients vs. 32 in 323; p=0.103) prior to ileostomy reversal or in terms of misdiagnosed stenoses (15 in 722 patients vs. 3 in 323; p=0.302) or leakages (6 in 722 patients vs. 4 in 323; p=0.509). The results of this comparison are shown in Figure 2.

## Sub-group analyses

### Proctoscopy alone versus proctoscopy and ta-WSCE

The comparison between proctoscopy alone versus proctoscopy and ta-WSCE involved 849 patients (722 and 127, respectively). In the group in which proctoscopy and ta-WSCE were performed, more stenoses were detected prior to ileostomy reversal (41 in 722 patients vs. 21 in 127; p < 0.0001) as well more ALs (49 in 722 patients vs. 18 in 127;

**TABLE 1** (A) Characteristics of the patients who underwent proctoscopy alone. (B) Characteristics of the patients who underwent proctoscopy and any other method. (C) Characteristics of the patients who underwent proctoscopy and transanal water-soluble contrast enema (ta-WSCE) via conventional radiology. (D) Characteristics of the patients who underwent proctoscopy and ta-WSCE with CT (taCT-WSCE).

(A) Characteristics	All patients (n = 1045)	Proctoscopy alone ( $n = 722$ )
 Male gender	634 (60.7)	441 (61.08)
Age (years)	$67.13 \pm 12.02$	67.07±12.5
BMI (kg/m <sup>2</sup> )	$25.74 \pm 3.76$	25.69±3.85
ASA score	2.2±0.69	$2.24 \pm 0.74$
Distance of the tumour from the anal verge (cm)	8.2±3.3	8.3±3.6
(B) Characteristics	All patients ( $n = 1045$ )	Proctoscopy and other method (ta- WSCE, taCT-WSCE or MR) (n=323)
Male gender	634 (60.7)	193 (59.75)
Age (years)	67.13±12.02	67.29±10.89
BMI (kg/m <sup>2</sup> )	25.74±3.76	$25.85 \pm 3.61$
ASA score	2.2±0.69	2.26±0.59
Distance of the tumour from the anal verge (cm)	8.2±3.3	$8.1 \pm 2.7$
(C) Characteristics	All patients (n = 1045)	Proctoscopy and ta-WSCE ( $n = 127$ )
(C) Characteristics Male gender	All patients (n = 1045) 634 (60.7)	Proctoscopy and ta-WSCE (n = 127) 87 (68.5)
(C) Characteristics Male gender Age (years)	All patients (n = 1045) 634 (60.7) 67.13 ± 12.02	Proctoscopy and ta-WSCE (n = 127) 87 (68.5) 66.60±10.08
(C) Characteristics Male gender Age (years) BMI (kg/m <sup>2</sup> )	All patients (n = 1045) 634 (60.7) 67.13 ± 12.02 25.74 ± 3.76	Proctoscopy and ta-WSCE (n = 127) 87 (68.5) 66.60±10.08 24.91±3.65
(C) Characteristics Male gender Age (years) BMI (kg/m <sup>2</sup> ) ASA score	All patients (n = 1045) $634$ (60.7) $67.13 \pm 12.02$ $25.74 \pm 3.76$ $2.2 \pm 0.69$	Proctoscopy and ta-WSCE (n = 127) 87 (68.5) 66.60±10.08 24.91±3.65 2.23±0.65
(C) Characteristics Male gender Age (years) BMI (kg/m <sup>2</sup> ) ASA score Distance of the tumour from the anal verge (cm)	All patients ( $n = 1045$ )634 (60.7)67.13 $\pm$ 12.0225.74 $\pm$ 3.762.2 $\pm$ 0.698.2 $\pm$ 3.3	Proctoscopy and ta-WSCE (n = 127) 87 (68.5) 66.60±10.08 24.91±3.65 2.23±0.65 7.5±3.19
(C) Characteristics Male gender Age (years) BMI (kg/m <sup>2</sup> ) ASA score Distance of the tumour from the anal verge (cm) (D) Characteristics	All patients (n = 1045) 634 (60.7) 67.13 ± 12.02 25.74 ± 3.76 2.2 ± 0.69 8.2 ± 3.3 All patients (n = 1045)	Proctoscopy and ta-WSCE (n = 127) 87 (68.5) 66.60±10.08 24.91±3.65 2.23±0.65 7.5±3.19 Proctoscopy and taCT-WSCE (n = 183)
(C) Characteristics         Male gender         Age (years)         BMI (kg/m <sup>2</sup> )         ASA score         Distance of the tumour from the anal verge (cm)         (D) Characteristics         Male gender	All patients ( $n = 1045$ )         634 (60.7)         67.13 ± 12.02         25.74 ± 3.76         2.2 ± 0.69         8.2 ± 3.3         All patients ( $n = 1045$ )         634 (60.7)	Proctoscopy and ta-WSCE (n = 127)           87 (68.5)           66.60±10.08           24.91±3.65           2.23±0.65           7.5±3.19           Proctoscopy and taCT-WSCE (n = 183)           101 (55.2)
(C) Characteristics         Male gender         Age (years)         BMI (kg/m²)         ASA score         Distance of the tumour from the anal verge (cm)         (D) Characteristics         Male gender         Age (years)	All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$ $25.74 \pm 3.76$ $2.2 \pm 0.69$ $8.2 \pm 3.3$ All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$	Proctoscopy and ta-WSCE (n = 127)           87 (68.5)           66.60±10.08           24.91±3.65           2.23±0.65           7.5±3.19           Proctoscopy and taCT-WSCE (n = 183)           101 (55.2)           67.87±11.24
(C) Characteristics         Male gender         Age (years)         BMI (kg/m²)         ASA score         Distance of the tumour from the anal verge (cm)         (D) Characteristics         Male gender         Age (years)         BMI (kg/m²)	All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$ $25.74 \pm 3.76$ $2.2 \pm 0.69$ $8.2 \pm 3.3$ All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$ $25.74 \pm 3.76$	Proctoscopy and ta-WSCE (n = 127)           87 (68.5)           66.60±10.08           24.91±3.65           2.23±0.65           7.5±3.19           Proctoscopy and taCT-WSCE (n = 183)           101 (55.2)           67.87±11.24           26.48±3.46
(C) Characteristics         Male gender         Age (years)         BMI (kg/m <sup>2</sup> )         ASA score         Distance of the tumour from the anal verge (cm)         (D) Characteristics         Male gender         Age (years)         BMI (kg/m <sup>2</sup> )         ASA score	All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$ $25.74 \pm 3.76$ $2.2 \pm 0.69$ $8.2 \pm 3.3$ All patients (n = 1045) $634 (60.7)$ $67.13 \pm 12.02$ $25.74 \pm 3.76$ $2.2 \pm 0.69$	Proctoscopy and ta-WSCE (n = 127)           87 (68.5)           66.60 $\pm$ 10.08           24.91 $\pm$ 3.65           2.23 $\pm$ 0.65           7.5 $\pm$ 3.19           Proctoscopy and taCT-WSCE (n = 183)           101 (55.2)           67.87 $\pm$ 11.24           26.48 $\pm$ 3.46           2.26 $\pm$ 0.55

Note: Categorical variables are express as number (percentage), continuous variables as mean  $\pm$  SD.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; MR, magnetic resonance.



**FIGURE 2** Results of the comparison between proctoscopy alone versus proctoscopy and any other preoperative method (transanal water-soluble contrast enema, transanal water-soluble contrast enema via CT, or MR).

Characteristics	Proctoscopy alone (n = 722)	Proctoscopy and ta-WSCE ( $n = 127$ )	p-value
Male gender	441 (61.08)	87 (68.5)	0.114
Age (years)	67.07±12.5	$66.60 \pm 10.08$	0.645
BMI (kg/m²)	$25.69 \pm 3.85$	24.91±3.65	0.05
ASA score	$2.24 \pm 0.74$	$2.23 \pm 0.65$	0.905
Prereversal stenoses	41 (5.7)	21 (16.5)	<0.0001
Prereversal leakages	49 (6.8)	18 (14.2)	0.007
Misdiagnosed stenoses	15 (2)	2 (1.6)	1.000
Misdiagnosed leakages	6 (0.8)	4 (3.1)	0.048

 TABLE 2
 Comparison between proctoscopy alone and proctoscopy with transanal water-soluble contrast enema (ta-WSCE).

*Note*: Categorical variables are express as number (percentage), continuous variables as mean $\pm$ SD. Bold values indicate statistically significancy (p < 0.05). Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.

p=0.007). The comparison between the two groups showed no significant difference in terms of misdiagnosed stenoses (15 in 722 patients vs. 2 in 127; p=1.000), but a significant difference in terms of misdiagnosed leakages in favour of proctoscopy alone (6 in 722 patients vs. 4 in 127; p=0.048). The results of the comparison between proctoscopy alone versus proctoscopy and ta-WSCE are shown in Table 2.

# Proctoscopy alone versus proctoscopy and taCT-WSCE

This analysis included 905 patients, 722 in the proctoscopy group and 183 in the proctoscopy + taCT-WSCE group. The proctoscopy

group showed more stenoses detected prior to ileostomy reversal (41 in 722 patients vs. 2 in 183; p=0.006) and a similar number of leakages (49 in 722 patients vs. 12 in 183; p=1.000). No differences were shown in terms of misdiagnosed stenoses (15 in 722 patients vs. 0 in 183; p=0.051) and leakages (6 in 722 patients vs. 0 in 183; p=0.607). Results of the comparison between proctoscopy alone and the combination of proctoscopy and taCT-WSCE are summarized in Table 3.

#### Proctoscopy alone versus proctoscopy and MR

The comparison between proctoscopy alone versus proctoscopy and MR included 735 patients (groups of 722 and 13, respectively). No

TABLE 3 Comparison between proctoscopy alone and proctoscopy with transanal water-soluble contrast enema via CT (taCT-WSCE).

Characteristics	Proctoscopy alone (n=722)	Proctoscopy and taCT-WSCE (n = 183)	p-value
Male gender	441 (61.08)	101 (55.2)	0.152
Age (years)	$67.07 \pm 12.5$	67.87±11.24	0.398
BMI (kg/m <sup>2</sup> )	25.69±3.85	$26.48 \pm 3.46$	0.075
ASA score	$2.24 \pm 0.74$	2.26±0.55	0.700
Prereversal stenoses	41 (5.7)	2 (1.1)	0.006
Prereversal leakages	49 (6.8)	12 (6.5)	1.000
Misdiagnosed stenoses	15 (2)	O (O)	0.051
Misdiagnosed leakages	6 (0.8)	O (O)	0.607

Note: Categorical variables are express as number (percentage), continuous variables as mean  $\pm$  SD. Bold values indicate statistically significancy (p < 0.05).

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.



**FIGURE 3** Results of the intra-group analyses: (A) comparison between proctoscopy and transanal water-soluble contrast enema (ta-WSCE); (B) comparison between proctoscopy and ta-WSCE with CT (taCT-WSCE); (C) comparison between proctoscopy and MR.

differences were found in terms of detected stenoses and leakages prior to ileostomy reversal [41 in 722 patients vs. 2 in 13 (p=0.173) and 49 in 722 vs. 2 in 13 (p=0.226), respectively] or in terms of misdiagnosed stenoses and leakages after reversal ileostomy [15 in 722 patients vs. 1 in 13 (p=0.251) and 6 in 722 vs. 0 in 13 (p=1.000), respectively].

#### Intra-group analyses

#### Comparison between proctoscopy and ta-WSCE

In the group that underwent proctoscopy and ta-WSCE the concordance between the two preoperative tools in detecting stenoses and leakages was 61.9% (13/21;  $\kappa$ =0.742, moderate agreement) and 55.5% (10/18;  $\kappa$ =0.679, moderate agreement), respectively (Figure 3). However, the comparison between the two methods showed no significant differences in detecting stenoses (6 vs. 2, p=0.20) or leakages (3 vs. 6, p=0.33). The stenoses were treated by waiting, by endoscopic dilation and by reintervention in 1, 11 and 2 cases, respectively, while no data were recorded about the remaining cases. The leakages were treated by waiting, by drainage, by transanal closure, by endoscopic treatment and by surgical procedure in nine, three, four, two and zero cases, respectively. The results of the comparison between ta-WSCE and proctoscopy are shown in Figure 3A. The agreement between the two procedures was high.

#### Comparison between proctoscopy and taCT-WSCE

In the group that underwent proctoscopy and ta-WSCE the concordance in detecting stenoses was 0% (in both cases the stenosis was detected by proctoscopy;  $\kappa$ =0.000, no agreement), while it was 25% (3/12;  $\kappa$ =0.480, fair agreement) for detection of AL. Specifically, the comparison between the two procedures demonstrated no significant differences in detecting stenoses (2 vs. 0, p=0.98), but there is a significant difference in detecting AL in favour of taCT-WSCE (3 vs. 12, p=0.03). The two stenoses were both treated with endoscopic dilation prior to ileostomy reversal, while the leakages were treated by waiting, by drainage, by transanal closure, by endoscopic treatment and by surgical procedure in six, one, two, three and zero cases, respectively. The results of the comparison between taCT-WSCE and proctoscopy are shown in Figure 3B.

#### Comparison between proctoscopy and MR

In the group that underwent proctoscopy and MR, the concordance in detecting stenoses and AL was 100% for both. In fact, in the 13 analysed patients both proctoscopy and MR detected two stenoses and two leakages in the same patients (p = 1.000 in both comparisons;  $\kappa = 1.000$ , perfect agreement). The results of the comparison between MR and proctoscopy are shown in Figure 3C.

#### DISCUSSION

AL after anterior rectal resection for rectal cancer is considered to be the most troublesome complication, with an incidence varying from 0% to 36%. Although some series showed a very low rate of AL, in some cases its magnitude cannot be considered negligible and it is associated with various short- and long-term outcomes [1, 2, 13, 14]. For this reason, it is recommended that concurrent faecal diversion is done by performing a temporary ileostomy [15, 16].

However, it must be remembered that a defunctioning stoma is useful for preventing leakage-related symptoms but does not have any impact on the incidence of leakage [17, 18]. Thus, before ileostomy reversal, the integrity of the colorectal anastomosis must be investigated to avoid a misdiagnosed asymptomatic leakage that could cause abdominal complications after the restoration of ileal continuity [7, 8, 19-22]. Several methods for this have been proposed during the last years, but no consensus on the best preoperative tool has been reached [5].

In a systematic review with meta-analysis on 11 articles and 1142 WSCEs prior to ileostomy reversal, Habib et al. [21] found that WSCE had a high specificity (95.4%) and negative predictive value (98.4%) and a moderate sensitivity (79.9%) and positive predictive value (64.6%) for the detection of clinically significant anastomotic problems. Furthermore, occult radiological leakages were visible at WSCE in 5.7% of cases, and the correlation between WSCE and rectal examination findings was 96.7%. The obtained results led Habib et al. to conclude that WSCE was effective in excluding clinically significant anastomotic problems, while it was unclear what additional information could be provided by this method.

On the contrary, recent studies have demonstrated that endoscopy prior to ileostomy reversal could be considered sufficient to assess AL. In a retrospective analysis on 312 patients, Shalabi et al. [9] compared the findings of DRE and rigid proctoscopy with those of water-soluble enema. They obtained that the sensitivity of DRE and proctoscopy for the diagnosis of strictures was 100%, and watersoluble contrast enema provided no additional information.

Similarly, Lindner et al. [6] performed a retrospective analysis to assess the overall sensitivity and specificity of endoscopy and contrast enema in detecting AL before ileostomy closure. Their results showed that the overall sensitivity for the detection of AL was 76% and 60%, respectively, while the specificity was 100% in both groups.

From a clinical point of view, results of a comparison by Farzaneh et al. [22] between endoscopy alone and endoscopy plus contrast evaluation showed no differences between the groups in terms of postoperative anastomotic complications. According to their results, Farzaneh et al. independently concluded that the adoption of WSCE could be considered superfluous before ileostomy reversal. Based on the current literature, we decided to perform a comparison between proctoscopy alone and proctoscopy associated with other methods to detect anastomotic complications prior to ileostomy reversal, with the aim of assessing if proctoscopy could be considered sufficient prior to ileostomy closure. In this setting, our results confirm that endoscopy can be considered sufficient in most cases. In fact, in the comparison between proctoscopy alone and proctoscopy combined with ta-WSCE, taCT-WSCE or MR, no differences were found in terms of stenoses (15 in 722 patients vs. 3 in 323; p=0.302) and leakages (6 in 722 vs. 4 in 323; p=0.509) detected after ileostomy closure.

Our secondary aim was to assess if there could be a different tool that would be useful for assessing any anastomotic complications prior to ileostomy reversal. For this reason, we performed subgroup analyses comparing proctoscopy alone versus proctoscopy and ta-WSCE, proctoscopy and taCT-WSCE, and proctoscopy and MR, respectively. Our results confirmed the results obtained in the main analysis, demonstrating that endoscopy alone can be considered sufficient prior to ileostomy reversal.

The comparison between proctoscopy alone versus proctoscopy and ta-WSCE resulted in no differences in terms of misdiagnosed stenoses (15 in 722 patients vs. 2 in 127; p = 1.000), but a significant difference in terms of misdiagnosed leakages in favour of proctoscopy alone (6 in 722 vs. 4 in 127; p = 0.048).

Similarly, comparing the proctoscopy alone group and the proctoscopy and taCT-WSCE group, no differences were found in terms of misdiagnosed stenoses (15 in 722 patients vs. 0 in 183; p=0.051) or leakages (6 in 722 vs. 0 in 183; p=0.607) or in the comparison between the proctoscopy alone group and the proctoscopy and MR group [misdiagnosed stenoses and leakages after reversal ileostomy: 15 in 722 patients vs. 1 in 13 (p=0.251) and 6 in 722 vs. 0 in 13 (p=1.000), respectively]. Thus, by pooling together 1043 patients with a defunctioning stoma for middle and low rectal cancer resection we can confirm that proctoscopy alone should be considered sufficient prior to ileostomy reversal.

However, to better evaluate the validity of each preoperative method for the detection of anastomotic complications prior to ileostomy reversal, we decided to compare the different adopted procedures in patients who were treated with more than one preoperative tool. The results of these analyses were interesting. In fact, although detection of anastomotic complications was similar between proctoscopy and ta-WSCE or MR, taCT-WSCE seemed to be more useful for detecting AL. In this setting, the concordance between proctoscopy and ta-WSCE in detecting stenoses and leakages was 61.9% (13/21) and 55.5% (10/18), respectively, and the comparison showed no significant differences in detecting stenoses (6 vs. 2, p=0.20) or leakages (3 vs. 6, p=0.33). In the group that underwent proctoscopy and MR, the concordance in detecting stenoses and leakage was 100% in both cases.

Differently, the comparison between proctoscopy and taCT-WSCE showed no concordance (0%) and low concordance (25%) in detecting leakages and stenoses, respectively. Specifically, the comparison between the two procedures demonstrated no significant



differences in detecting stenoses (2 vs. 0, p = 0.98) but a significant difference in detecting leakages in favour of taCT-WSCE (3 vs. 12, p = 0.03).

Based on these results, we can introduce another concept: in cases where the results of proctoscopy are not completely clear or the surgeon remains suspicious of an AL, taCT-WSCE could guarantee its detection.

Although the strength of this study is its large sample size, some limitations should be addressed: first, the retrospective design is associated with some inherent bias; then, each surgeon chose a different method for assessing anastomotic complications prior to ileostomy closure in accordance with his/her own preference; finally, the absence of some clinicopathological data (i.e. anastomotic height, neoadjuvant or adjuvant radio- or chemotherapy and tumoural TNM score) made it impossible to analyse any relation between those aspects and the real diagnostic power of the different assessment tools. In this setting, this study could be the stimulus for performing future ad hoc randomized studies on this topic.

#### AUTHOR CONTRIBUTIONS

Michele Manigrasso: Investigation; writing - original draft; validation; methodology; writing - review and editing; formal analysis; data curation. Maurizio Degiuli: Writing - original draft; validation; writing - review and editing; visualization. Francesco Maione: Writing - original draft; writing - review and editing; methodology; validation. Pietro Venetucci: Methodology; formal analysis; writing original draft; writing - review and editing. Franco Roviello: Writing - original draft; validation; writing - review and editing; visualization. GIOVANNI DOMENICO De Palma: Writing - original draft: validation; writing - review and editing; supervision. Marco Milone: Supervision; writing – original draft; validation; writing – review and editing; conceptualization. Pietro Anoldo: Validation; writing - review and editing; writing - original draft. Sara Vertaldi: Validation; writing - review and editing; writing - original draft. Mario Quarantelli: Validation; writing - review and editing; writing - original draft. Rossella Reddavid: Validation; writing - review and editing; writing - original draft. Nicoletta Petronio: Validation; writing - review and editing; writing - original draft. Gianluca Rizzo: Validation; writing - review and editing; writing - original draft. Claudio Coco: Validation; writing - review and editing; writing - original draft. LUCA EMANUELE Emanuele AMODIO: Validation; writing - review and editing; writing - original draft. Gaetano Gallo: Validation; writing - review and editing; writing - original draft. Giuseppe Sena: Validation; writing - review and editing; writing - original draft. Giuseppe Sammarco: Validation; writing - review and editing; writing - original draft. Giuseppe Sica: Validation; writing - review and editing; writing - original draft. Leandro Siragusa: Validation; writing - review and editing; writing - original draft. Vittoria Bellato: Validation; writing - review and editing; writing - original draft. Francesco Bianco: Validation; writing - review and editing; writing original draft. Simona Gili: Validation; writing - review and editing; writing - original draft. Paola Incollingo: Validation; writing - review

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#### CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

#### DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

#### ETHICS STATEMENT

The study was approved by the Ethical Committee of the "Federico II" University of Naples.

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#### APPENDIX

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