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ORIGINAL ARTICLE

Anastomotic leaks after anterior resection for mid and low rectal cancer: survey of the Italian Society of Colorectal Surgery

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Abstract Background The aim of the survey was to assess the incidence of anastomotic leaks (AL) and to identify risk factors predicting incidence and gravity of AL after low anterior resection (LAR) for rectal cancer performed by colorectal surgeons of the Italian Society of Colorectal Surgery (SICCR). **Methods** Information about patients with rectal cancers less than 12 cm from the anal verge who underwent LAR during 2005 was collected retrospectively. AL was classified as grade I to IV according to gravity. Fifteen clinical variables were examined by univariate and multivariate analyses. Further analysis was conducted on patients with AL to identify factors correlated with gravity. **Results** There were 520 patients representing 64% of LAR for rectal cancer performed by SICCR members. The overall rate of AL was 15.2%. Mortality was 2.7% including 0.6% from AL. The incidence of AL was correlated with higher age ($p<0.05$), lower (<20 per year) centre case volume ($p<0.05$), obesity ($p<0.05$), malnutrition ($p<0.01$) and intraoperative contamination ($p<0.05$), and was lower in patients with a colonic J-pouch reservoir ($p<0.05$). In the multivariate analysis age, malnutrition and intraoperative contamination were independent predictors. The only predictor of severe (grade III/IV) AL was alcohol/smoking habits ($p<0.05$) while the absence of a diverting stoma was borderline significant ($p<0.07$). **Conclusion** Our retrospective survey identified several risk factors for AL. This survey was a necessary step to construct prospective interventional studies and to establish benchmark standards for outcome studies.

Key words Anastomotic leaks · Low anterior resection · Rectal cancer · Outcome studies

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Introduction

Anastomotic leakage (AL) is the most significant surgical complication following resection for rectal cancer [1], affecting perioperative mortality and possibly long-term survival [2, 3]. The rate of AL after anterior resection (AR) varies from 3% to 19% [4–11], being clinically significant in 2.9–15.3% of patients. Mortality following a leak may be 6.0–39.3% [12]. Most of the reports of complications after surgery for colorectal cancer come

from single institutions [1, 13–23] or are population-based outcome studies [24–30]. Only a minority of studies are nationwide multi-institutional surveys [31–33]. Comparison of complication rates between series is difficult because of the different referral patterns and different study periods, and because relatively few studies distinguish between colon and rectal site, since the incidence of AL is higher after rectal cancer surgery [5, 25].

The aim of this study was to assess the incidence and gravity of AL after surgery for rectal cancer performed by Italian colorectal surgeons, and to identify factors predicting the incidence and gravity of AL in this patient population.

Patients and methods

Study population

The study was retrospective multicentre survey, including all patients with a new diagnosis of mid or low rectal cancer who underwent sphincter saving surgery, excluding local excisions, between 1 January and 31 December 2005. All surgical centres affiliated with the Italian Society of Colorectal Surgery were contacted by e-mail and invited to participate on a voluntary basis. An online database was created and devised to maintain patient anonymity. Because of the retrospective nature of the survey approval by an ethics committee was not required.

Data included patient-related variables (sex, age, BMI greater then 30 kg/m^2, weight loss greater than 10% within 6 months, and smoking and alcohol habits), disease-related variables (stage IV) and treatment-related variables (centre case volume, type of resection, open vs. laparoscopic

approach, intraoperative contamination, anastomotic level, type of anastomosis, stoma construction, blood transfusions, and adjuvant therapy). The minimum follow-up period required was 30 days after AR or after stoma closure in those patients with a temporary stoma.

To assess the gravity of AL the classification described by Soeters et al. [34] was used which includes four progressive severity grades (Table 1). When assessing factors predicting the gravity of AL among patients with AL this classification was simplified to mild to moderate (grades 1 and 2) and severe (grades 3 and 4).

Table 1 Classification of anastomotic leaks (according Soeters-Baeten)

Grade	Type of leak
1	Limited leakage with small adjacent abscess; mild clinical signs
2	Small lateral anastomotic failure with adjacent unilocular abscess (approximately 5 cm diameter or greater)
3	Failure of half or more of the circumference of an anastomosis
4	Multilocular abscess or peritonitis

Categorical variables were evaluated using either Fisher's exact test or Pearson's chi-squared test depending on sample size. Numerical variables were evaluated using Student's *t*-test. *P* values <0.05 were considered significant. All variables which were associated with the incidence or gravity of AL in the univariate analysis were entered into a multivariate logistic regression model. Data were analysed using the STATA program (release 8.0, 2003; Stata Corporation, College Station, TX).

Results

Of 108 centres contacted, 44 (40.7%) participated. Information on 682 patients with rectal cancer who had undergone surgery was collected. Sphincter-saving surgery was performed in 579 patients (84.9%). After excluding abdominoperineal resections (*n*=100), local excisions (*n*=37), Hartmann's procedure (*n*=15) and other types of restorative (*n*=7) and nonrestorative (*n*=3) procedures, a group of 520 patients who had undergone a low AR (LAR) or coloanal anastomosis (CAA) were evaluated.

According to the Italian Network of Cancer Registries, the incidence of newly diagnosed rectal cancer in Italy in 2005 was approximately 15,000 cases [35]. According to the Society's 2005 annual report, SICCR members operated on 1,185 mid–low rectal cancers, and 815 (68.8%) of them were treated with sphincter-saving procedures [36]. Our patient sample including only anastomotic surgery represents 63.8% (520/815) of all those with mid–low rectal cancers who underwent sphincter-saving surgery performed by SICCR members.

The mean age of the patients was 65.366 years (SD 9.688 years) and 287 of the 520 patients (55.2%) were male. The number of procedures per centre ranged from 3 to 37 per year. The case volume distribution is shown in Fig. 1.

Among the surgical procedures 500 (96.15%) were LARs and 20 (3.85%) were CAAs. Of the 520 procedures, 87 (17.4%) were performed laparoscopically. Anastomoses were stapled in 459 procedures (91.8%) and hand-sewn in 61 procedures (8.2%) including 18 of the 20 CAAs (90%). Anastomoses were performed using a J-pouch in 54 of the 520 procedures (10.4%), and with a transverse coloplasty in 8 (1.5%). A diverting stoma was used in 294 procedures (56.5%) including all the CAAs.

Postoperative adjuvant radiotherapy was used in 71 of the 520 patients (13.6%) and was combined with chemotherapy in 64. Neoadjuvant radiotherapy was used

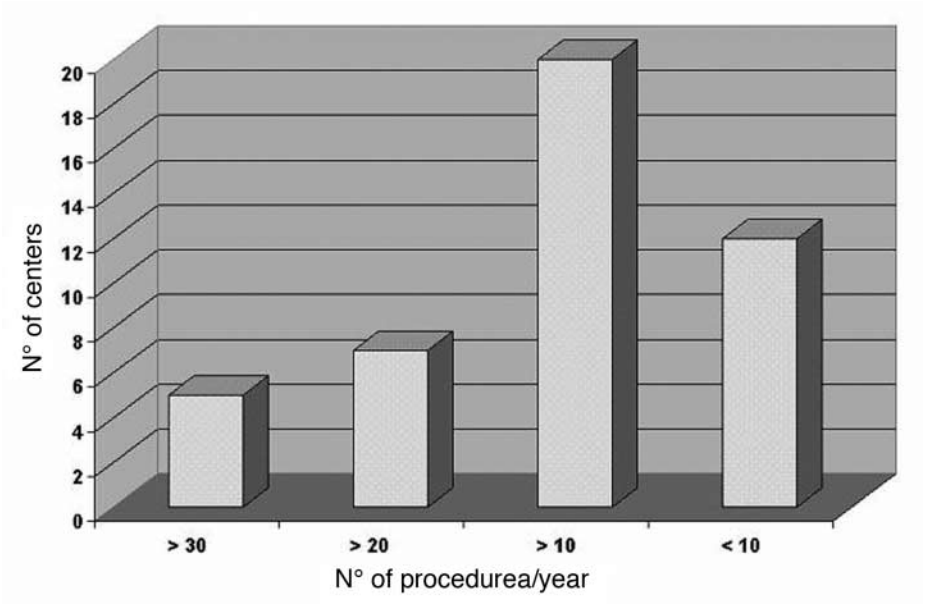

Fig. 1 Case volume distribution

in 187 patients (39.6%), and of these 187, 18 (9.6%) were done using a short-term protocol (2,000 rad over 5 days followed by immediate surgery, and 169 (90.4%) were done using a long-term protocol (4,000–4,500 rad over 5 weeks followed by a waiting period of 6–8 weeks) combined with chemotherapy in 164.

The overall incidence of AL was 15.2% (79 of 520), and 12 (2.3%) patients died within 30 days of surgery including 3 patients (0.58%) with AL. Of the 79 patients with AL, 32 (40.5%) were grade 1, 26 (32.9%) were grade 2, 17 (21.5%) were grade 3, and 4 (5.1%) were grade 4. Of the 520 patients, 22 (4.2%) underwent a routine radiographic contrast study prior to discharge from hospital and 6 of these had a small asymptomatic grade 1 leak, comprising 7.9% of all ALs.

The mean hospital stay was 12.04 days (SD 6.29). Among the 79 patients with AL, the mean hospital stay was of 14.57 days (SD 5.14) which was significantly higher than the hospital stay of patients without AL (9.433±7.440 days; $p<0.003$).

In the univariate analysis (Table 2) the occurrence of AL was correlated with higher age (68.60±11.86 years vs. 62.13±7.51 years; $p<0.014$), lower (<20 per year) centre case volume (OR 1.88, 95% CI 1.15–3.07; $p=0.011$), obesity (OR 2.03, 95% CI 1.03–4.00; $p=0.038$), malnourished state (OR 2.80, 95% CI 1.52–5.18; $p<0.001$) and intraoperative contamination (OR 3.47, 95% CI 1.32–9.12; $p=0.016$). The incidence AL was lower in patients with a colonic J-pouch reservoir (OR 0.283, 95% CI 0.086–0.928; $p=0.027$). In the multivariate analysis (Table 3) the independent predictive factors were higher age (OR 1.025, 95% CI 0.999–1.051; $p=0.057$), intraoperative contamination (OR 1.33, 95% CI 1.01–1.761; $p=0.041$) and malnourished state (OR 1.621741, 95% CI 1.238–2.122; $p=0.001$). Among the 79 patients with AL a univariate analysis was conducted to find predictors of AL gravity. Severe (grade 3 and 4) AL was correlated with alcohol and/or smoking habits (OR 13.651, 95% CI 0.775–240.43; $p=0.05$) while absence of a diverting stoma was only borderline significant (OR 0.326, 95% CI 0.106–1; $p=0.07$).

Discussion

To our knowledge this is the first Italian nationwide study on the incidence of AL among colorectal surgeons. Since the cases collected represent 64% of all rectal cancers operated on with a sphincter-saving procedure by the members of our Society in 2005 we consider the sample representative. Our AL incidence of 15.9% seems quite high compared to other studies in which it has been found to range from 2.9% to 14% [17, 28, 31, 37]. In our sample of 682 patients with rectal cancer undergoing surgery, sphincter-saving procedures were carried out in 85% of patients, which is a very high percentage. The increased AL rate may be related to the number of high-risk low rectal anastomoses [38]. Conversely our in-hospital mortality of 2.3% is in the lower range compared to a multicentre studies from Germany (2.7–3.1%) [31, 39], Sweden (1–4%) [28], Norway (3.0%) [33] and United Kingdom (7%) [25].

We found that hospital case volume correlated with a lower incidence of AL. Others have found that higher surgeon case volume is associated with lower rates of morbidity regardless of the hospital case volume [28, 32, 40]. Nevertheless, hospital case volume has been found to be a good surrogate for surgeon case volume [41]. Our

Table 2 Results of univariate analysis for incidence of anastomotic leaks (AL)

Variable	Patients with AL	Patients without AL	Odds ratio	95% CI	Chi squared or Student's *t*	*p* value
Median age (years)	68.60 (SD 11.86)	62.13 (SD 7.51)			2.521	<0.014*
Gender						
Male	44 (15.3%)	243 (84.7%)	1.024	0.633–1.659	0.009	0.922
Female	35 (15%)	198 (85%)				
Obesity						
Obese	13 (25%)	39 (75%)	2.030	1.029–4.006	4.313	<0.038*
Non-obese	66 (14.1%)	402 (85.9%)				
Nutritional status						
Malnourished	18 (30%)	42 (70%)	2.803	1.516–5.182	11.542	0.001*
Not malnourished	61 (13.3%)	399 (86.7%)				
Blood transfusion						
Yes	7 (11.9%)	25 (78.1%)	1.617	0.674–3.879	1.181	0.277
No	72 (14.8%)	416 (85.2%)				
Neoadjuvant therapy						
Yes	25 (13.4%)	162 (86.6%)	0.703	0.422–1.173	1.828	0.176
No	54 (16.2%)	279 (83.8%)				
Stage						
IV	13 (15%)	74 (85%)	0.976	0.512–1.862	0.005	0.943
I–III	66 (15.3%)	367 (84.7%)				
Smoking or alcohol habits						
Yes	13 (16.7%)	65 (83.3%)	1.139	0.594–2.183	0.154	0.694
No	66 (14.9%)	376 (85.1%)				
Centre case volume (no. per year)						
<20	49 (19.3%)	205 (80.7%)	1.880	1.150–3.073	6.475	0.011*
≥20	30 (11.3%)	236 (88.7%)				
Procedure						
Open	63 (14.9%)	359 (85.1%)	0.899	0.494–1.636	0.120	0.728
Laparoscopic	16 (16.3%)	82 (83.7%)				
Distance of anastomosis from anal verge (cm)						
<5	36 (15.7%)	194 (84.3%)	1.065	0.658–1.724	0.067	0.795
>5	43 (14.8%)	247 (85.2%)				
Technique						
Hand-sewn anastomosis	9 (12.9%)	61 (87.1%)	0.800	0.380–1.686	0.342	0.558
Stapled anastomosis	70 (15.6%)	380 (84.4%)				
J-pouch anastomosis	3 (5.3%)	54 (94.7%)	0.282	0.086–0.928	4.898	0.027*
Straight anastomosis or coloplasty	76 (16.2%)	387 (83.6%)				
Intraoperative contamination						
Yes	7 (36.9%)	12 (63.1%)	3.475	1.324–9.123	–[a]	0.016*
No	72 (14.4%)	429 (85.6%)				
Protective stoma						
No	47 (16.1%)	245 (83.9%)	1.175	0.722–1.912	0.422	0.516
Yes	32 (14%)	196 (86%)				

*p<0.05; [a]Fisher's exact test

study shows a very heterogeneous case volume distribution (Fig. 1) as is often the case for multicentre surveys. A lower incidence of ALs after J-pouch anastomosis has been previously shown [33, 42] and is confirmed by our study. Nevertheless, none of the randomized trials of J-pouch vs. straight anastomosis were adequately powered to detect a difference in ALs. A J-pouch or coloplasty was fashioned only in 11% of procedures. This despite the body of literature outlining short-term functional advantages of the J-pouch or coloplasty [43]. Our observation that malnutrition is correlated with AL confirms what others have found [32, 44] and emphasizes the need for careful preoperative assessment and the importance of pre- and postoperative diet. Also intraoperative contamination has been consistently found to be associated with AL [1, 10, 33, 45]. In the multivariate analysis higher age, malnourished state and intraoperative contamination were correlated with AL. These results are similar to those of other studies [10, 33, 46–48].

In our survey smoking/alcohol habits, while they were not correlated with incidence of AL as in other studies [47], were frequently associated with more severe leaks in the subset of patients with AL. Alcohol abusers (more than 35 drinks per week) have a significantly higher risk

Table 3 Results of the univariate analysis of the gravity of AL (grade 3 and 4) in the overall population with AL

Variable	AL grade 1–2	AL grade 3–4	Odds ratio	95% CI	Chi squared or Student's *t*	*p* value
Median age (years)	68.69 (SD 10.83)	68.42 (SD 9.25)			0.104	0.458
Gender						
Male	29 (67.4%)	14 (32.6%)	0.591	0.215–1.628	1.041	0.307
Female	28 (77.8%)	8 (12.2%)				
Obesity						
Obese	8 (61.5%)	5 (38.5%)	0.555	0.159–1.930	–§	0.269
Non-obese	49 (74.2%)	17 (25.8%)				
Nutritional status						
Malnourished	15 (83.3%)	3 (16.7%)	2.261	0.584–8.750	1.450	0.228
Not malnourished	42 (68.9%)	19 (31.1%)				
Blood transfusion						
Yes	3 (42.9%)	4 (57.1%)	0.264	0.55–1.175	–§	0.090
No	54 (75.0%)	18 (25.0%)				
Neoadjuvant therapy						
Yes	19 (73.1%)	7 (26.9%)	1.046	0.374–2.926	0.016	0.898
No	38 (71.7%)	15 (28.3%)				
Stage						
IV	8 (61.5%)	5 (38.5%)	0.546	0.164–1.819	–§	0.269
I–III	49 (74.2%)	17 (25.8%)				
Smoking or alcohol habits						
Yes	13 (100%)	0 (0%)	13.651†	0.77–24.043	–§	0.015*
No	44 (66.7%)	22 (33.3%)				
Centre case volume (no. per year)						
<20	35 (71.4%)	14 (28.6%)	0.924	0.341–2.508	0.033	0.855
>20	22 (73.3%)	8 (26.7%)				
Procedure						
Open	44 (69.8%)	19 (30.2%)	0.534	0.136–2.094	–[a]	0.535
Laparoscopic	13 (81.3%)	3 (18.7%)				
Distance of anastomosis from anal verge (cm)						
<5	34 (68.6%)	9 (11.4%)	2.135	0.784–5.811	2.247	0.134
>5	23 (63.9%)	13 (16.1%)				
Technique						
Hand-sewn anastomosis	7 (77.8%)	2 (12.2%)	1.4	0.267–7.325	–§	0.517
Stapled anastomosis	50 (71.4%)	20 (28.6%)				
J-pouch anastomosis	3 (100%)	0 (0.0%)	2.889	0.143–5.825	–§	0.556
Straight anastomosis or coloplasty	54 (71.1%)	22 (28.9%)				
Intraoperative contamination						
Yes	3 (42.8%)	4 (57.2%)	0.25	0.051–1.224	–§	0.090
No	54 (75.0%)	18 (25.0%)				
Protective stoma						
No	30 (63.8%)	17 (36.2%)	0.326	0.106–1	–§	0.072*
Yes	27 (84.4%)	5 (15.6%)				

*$p<0.05$; §Fisher's exact test; †Calculated using the approximation of Woolf

of developing AL than abstainers [49], and the causes are probably immunosuppression and decreased haemostatic function [50]. Moreover, it has been suggested that the effect of smoking in reducing collagen synthesis and oxidative killing mechanisms of neutrophils explains higher rates of AL [51]. Construction of a diverting stoma was weakly correlated with a lower AL rate. The benefit of a diverting stoma following LAR has not been unequivocally demonstrated [31] . Indeed, the use of a protective stoma seems not to decrease the leakage rate [38, 52], but it does reduce the risk of reoperation and postoperative death if leakage is present [1]. Therefore, the guidelines of the American Society of Colon and Rectal Surgeons [53] recommend creating a protective stoma for patients who show a combination of high-risk variables for AL. Finally, hospital stay was significantly longer in patients with AL. This highlights the weight of AL in terms of morbidity and of increased hospital costs.

Stapling of the anastomosis was the preferred technique being used in 92% of procedures. The percentage of CAAs was low (2.9%) which may have been due to the known poor functional results and quality of life reported after this procedure [53, 54]. A laparoscopic approach was used in 18% of patients which is similar to the per-

centage of laparoscopic colorectal surgery procedures in other international studies [55, 56]. Laparoscopic total mesorectal excision appears to have clinically measurable short-term advantages in patients with primary resectable rectal cancer [57], although long-term oncological results are awaited from large on-going randomized trials [42].

The incidence of AL has been determined in national and multicentre surveys [31–33]. A limitation of these studies is that they included heterogeneous types of procedures. The Norwegian national audit on complications following rectal cancer excision rapresents to our knowledge the only attempt to standardize the surgical procedure variable [23, 30, 58].

There is a recognized lack of a universally accepted definition of AL. Indeed, a systematic review reported 29 different definitions of AL among 49 studies [59]. This may have been due to factors such as subjective interpretation of clinical signs or to whether a water-soluble enema was routinely used. In our survey we adopted the classification proposed by Soeters et al. which allows discrimination between clinically relevant severe AL (grade III–IV) usually requiring surgical intervention and small leaks which may respond to conservative treatment.

The limitation of our study is in its retrospective nature since retrospective collection of risk factors may be subject to bias. The aim of the survey was to provide preliminary data on the incidence and gravity of ALs among Italian colorectal surgeons. The risk factors identified should now be prospectively studied. The protective effect of the colonic J-pouch on ALs should be investigated with adequately powered randomized trials. In order to establish a useful benchmark standard for outcome studies, a prospective study should be carried out to standardize surgical variables such as stoma construction including only high-volume centres.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this article.

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