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Multicentre observational study of the natural history of left-sided acute diverticulitis $^{\!\!\!\!\!^{\pm}}$

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Abstract

Background:

The natural history of acute diverticulitis (AD) is still unclear. This study investigated the recurrence rate, and the risks of emergency surgery, associated stoma and death following initial medical or surgical treatment of AD.

Methods:

The Italian Study Group on Complicated Diverticulosis conducted a 4-year multicentre retrospective and prospective database analysis of patients admitted to hospital for medical or surgical treatment of AD and then followed for a minimum of 9 years. The persistence of symptoms, recurrent episodes of AD, new hospital admissions, medical or surgical treatment, and their outcome were recorded during follow-up.

Results:

Of 1046 patients enrolled at 17 centres, 743 were eligible for the study (407 recruited retrospectively and 336 prospectively); 242 patients (32.6 per cent) underwent emergency surgery at accrual. After a mean follow-up of 10.7 years, rates of recurrence (17.2 *versus* 5.8 per cent; P < 0.001) and emergency surgery (6.9 *versus* 1.3 per cent; P = 0.021) were higher for medically treated patients than for those treated surgically. Among patients who had initial medical treatment, age less than 40 years and a history of at least three episodes of AD were associated with an increased risk of AD recurrence. There was no association between any of the investigated parameters and subsequent emergency surgery. The risk of stoma formation was below 1 per cent and disease-related mortality was zero in this group. The disease-related mortality rate was 0.6 per cent among patients who had surgical treatment.

Conclusion:

Long-term risks of recurrent AD or emergency surgery were limited and colectomy did not fully protect against recurrence. Copyright © 2011 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd.

Introduction

Diverticulosis is common in Western industrialized countries, has a similar prevalence in both sexes, and increases with age<u>1</u>. Although most patients remain asymptomatic throughout life, up to a quarter will experience acute diverticulitis (AD)<u>2–5</u>. Following an acute episode, AD recurs in up to a third<u>5–7</u> and subsequent emergency surgery is needed in about 10 per cent<u>7–9</u>. Previous studies had limitations, including a lack of consistency in the definition of AD, mainly single-centre retrospective design, or modelled analysis of regional and national databases<u>6</u>, <u>7</u>, <u>10–12</u>. The few available prospective studies usually contained small numbers of patients accrued over long periods<u>13</u>, <u>14</u>. The natural history of AD therefore remains unclear. There has been a trend toward a more conservative approach in the past decade<u>7–9</u>, <u>15</u>. The literature has failed to show a proven benefit of sigmoid colectomy both as an elective procedure<u>16</u> and in the emergency setting, when organ-preserving surgery has now been suggested<u>17</u>.

Methods

To gather information on the natural history of complicated colonic diverticular disease, the Italian Study Group on Complicated Diverticulosis (GISDIC) was formed in 1997. This included 17 surgical units where detailed information on patients admitted to hospital for left-sided AD was recorded and sent to a central database for prospective evaluation of the rate of AD recurrence and subsequent emergency surgery, stoma formation and death. The study was approved by the ethics committee of Galliera Hospital, Genoa, Italy, and registered at ClinicalTrials.gov (NCT01276886)

To ensure expeditious collection of data from an adequate number of well documented patients, patients were recruited over 4 years (1996–1999); information on those admitted in 1996 and 1997 was accrued retrospectively from clinical records, whereas data on patients treated between 1998 and 1999 were entered into the database prospectively on admission to hospital.

Inclusion and exclusion criteria

All consecutive patients with left-sided AD diagnosed clinically by the presence of abdominal pain, associated with leucocytosis (more than 11×10^9 /l) and/or fever exceeding 38 °C, and confirmed by imaging (computed tomography (CT), ultrasonography, water-soluble contrast enema), either alone or in combination and/or by operative findings, entered the study. The CT criteria for the diagnosis included a localized thickening (at least 4 mm) of the colonic wall and signs of inflammation of the pericolic fat, with abscess and/or extraluminal air and/or extraluminal contrast. The ultrasound criteria included at least two of the following signs: bowel wall thickening (over 4 mm), diverticular inflammation, pericolic fat oedema, intramural or pericolic inflammatory mass, and intramural fistula. The diagnostic criteria for water-soluble contrast enema included segmental luminal narrowing and a tethered mucosa with or without a mass effect, or extravasation of contrast and/or the presence of extraluminal air.

Patients with inflammatory bowel disease, irritable bowel syndrome (IBS), colorectal cancer or diseases precluding adequate follow-up were excluded from the study.

Treatment

Patients were treated conservatively (antibiotics, parenteral nutrition, CT- or ultrasound-guided abscess drainage) or surgically according to the local policy of each centre.

Follow-up

The following data were collected: persistence or recurrence of chronic symptoms attributable to complicated diverticular disease, new episodes of AD, new hospital admissions for AD, type of treatment and outcome.

Recurrence was defined as a new episode of AD requiring hospital admission, which had occurred at least 2 months after complete resolution of the index episode that resulted in inclusion in the study. If surgery was performed, the timing, type of procedure, Hinchey stage and complications were recorded.

Data collection

A standardized flow sheet was used to collect data on medical history, diagnostic investigations, type of treatment and follow-up to create a dedicated database. Sex, age, date of hospital admission and discharge, diagnosis on admission and discharge, co-morbidities (diabetes mellitus, cardiovascular disease, atherosclerosis, liver or renal failure), symptoms experienced before admission and their duration, history of diverticulosis, previous AD episodes, laboratory tests, and treatment performed were recorded. Where surgery was carried out, the date and type of procedure, operative findings including Hinchey classification<u>18</u> and details of the operation (incision, extension of resection, type of anastomosis, covering stoma, drains), pathology report, and postoperative complications occurring within 30 days were all recorded.

Follow-up was obtained by contacting the patients periodically by telephone. At each contact patients were requested to report on each hospital admission for recurrent disease (date of hospital admission, treatment and post-treatment complications, if any). Patients who complained of symptoms potentially related to the diverticular disease were offered a personal consultation to investigate the clinical situation.

Endpoints

The primary endpoint was the rate of recurrence of AD requiring admission to hospital during follow-up. Additional endpoints were the risks of emergency surgery, stoma and disease-related mortality during follow-up.

Statistical analysis

Differences in proportions were compared with the χ^2 test or Fisher's test, as appropriate. The odds ratio (OR) with 95 per cent confidence interval (c.i.) was used to estimate associations between baseline characteristics (age at enrolment, sex and number of previous episodes of diverticulitis) and the risk of undergoing surgery at enrolment and of AD recurrence<u>19</u>.

Follow-up ended on 31 December 2007. Patients were followed until this date or until death or loss to follow-up, whichever occurred first. For patients who had a recurrence, the follow-up interval was censored at the time of the first recurrence.

The cumulative incidence of recurrence was determined by means of the Kaplan–Meier test<u>20</u>, and the log rank test was used to assess differences in recurrence rates between groups. A Cox regression model<u>21</u> was used to assess the effect of age, sex and number of AD episodes before enrolment on the risk of relapse and emergency surgery in medically treated patients. The model was also used to test the effect of age at enrolment, sex, treatment, cumulative number of AD episodes (including recurrences during follow-up) and co-morbidity on the risk of death. Hazard ratios (HRs) were calculated with 95 per cent c.i.

Two-sided *P* values were calculated and P < 0.050 was considered statistically significant. Data were processed using SPSS[®] statistical package release 17.0 (SPSS, Chicago, Illinois, USA).

Results

Between January 1996 and December 1999, 1046 patients were recruited of whom 303 were excluded (*Fig.1*). Of the remaining 743 eligible patients, 407 (54·8 per cent) were registered retrospectively and 336 (45·2 per cent) prospectively. Patient characteristics are shown in *Table1*. Diverticulosis was already known at the time of enrolment in 515 patients (69·3 per cent). Of these, 126 (24·5 per cent) reported at least one previous episode of AD and 92 (17·9 per cent) had been admitted to hospital for the disease. There was no significant difference in any of the investigated characteristics between the retrospectively and the prospectively enrolled cohorts.

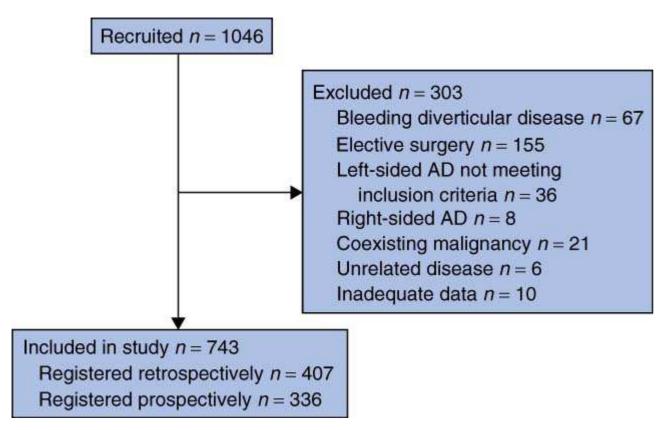


Figure 1. Flow chart for study. AD, acute diverticulitis

Table 1. Characteristics of eligible patients admitted to hospital for acute left-sided diverticulitis between 1996 and 1999

Total (<i>n</i> =	Retrospective (<i>n</i> =	Prospective (<i>n</i> =	P *
743)	407)	336)	<u>r</u> -

• Values in parentheses are percentages. AD, acute diverticulitis.

• *

χ^2 test.				
Age (years)				0.153
< 40	26 (3.5)	14 (3.4)	12 (3.6)	
40–49	67 (9.0)	40 (9.8)	27 (8.0)	
50–59	101 (13.6)	61 (15.0)	40 (11.9)	

	Total (<i>n</i> = 743)	Retrospective ($n = 407$)	Prospective (<i>n</i> = 336)	<u>P*</u>
60–69	167 (22.5)	101 (24.8)	66 (19.6)	
70–79	226 (30.4)	110 (27.0)	116 (34.5)	
≥ 80	156 (21.0)	81 (19.9)	75 (22.3)	
Sex ratio (M : F)	320:423	176 : 231	144 : 192	0.916
Diagnosis of diverticulosis				0.216
Previously unknown	228 (30.7)	134 (32.9)	94 (28.0)	
Year of enrolment	336 (45.2)	170 (41.8)	166 (49.4)	
1–5 years before enrolment	97 (13.1)	55 (13.5)	42 (12.5)	
> 5 years before enrolment	82 (11.0)	48 (11.8)	34 (10.1)	
Previous episodes of AD				0.216
None	617 (83.0)	334 (82.1)	283 (84.2)	
1	79 (10.6)	50 (12.3)	29 (8.6)	
≥ 2	47 (6.3)	23 (5.7)	24 (7.1)	
Previous hospital admissions owing to AD				0.755
None	651 (87.6)	358 (88.0)	293 (87.2)	
≥ 1	92 (12.4)	49 (12.0)	43 (12.8)	
Severe co-morbidity				0.484
Yes	168 (22.6)	96 (23.6)	72 (21.4)	
No	575 (77.4)	311 (76.4)	264 (78.6)	

 Table 1. Characteristics of eligible patients admitted to hospital for acute left-sided diverticulitis

 between 1996 and 1999

Diagnostic imaging was available for 700 patients (94·2 per cent); 183 (26·1 per cent) had CT, 385 (55·0 per cent) abdominal ultrasonography and 471 (67·3 per cent) a water-soluble contrast enema. Only an operative report was available for 43 patients.

Treatment

Medical treatment

Medical treatment (MT) was administered initially to 501 patients (67.4 per cent). The median hospital stay was 9.1 (interquartile range (i.q.r.) 6-11) days. CT- or ultrasound-guided percutaneous drainage was performed in six patients with pelvic abscess, five of whom underwent a surgical procedure during the same hospital admission. One death occurred in a 79-year-old woman 7 days after admission for sepsis.

Surgical treatment

In all, 242 patients (32.6 per cent) underwent initial surgical treatment (ST), with similar proportions in the retrospective and prospective groups. A greater number of AD episodes was the only variable associated with an increased probability of undergoing surgery. After adjustment for type of recruitment, age, sex and presence of co-morbidity, patients with two or more previous episodes of AD had twice the probability of undergoing surgery (OR 2.11, 1.15 to 3.85; P = 0.015).

Some 147 patients (60·7 per cent) had Hinchey stage 0–1, 28 (11·6 per cent) stage 2 and 67 (27·7 per cent) stage 3 or 4 disease. The Hinchey stage was more severe in patients needing surgery during their first episode of diverticulitis than in those who had experienced at least one previous episode ($\chi^2_{trend} = 7.53$; P = 0.006); 59 (88 per cent) of 67 patients with Hinchey stage 3–4 disease had their first episode of AD before entry into the study.

A stoma was created in 66 patients (27.3 per cent): 56 had an end colostomy and ten underwent resection with the anastomosis covered by a stoma; all procedures were carried out as an emergency. The remaining patients had emergency sigmoid resection and primary anastomosis without a covering stoma.

Postoperative complications occurred in 83 patients: cardiopulmonary (44), wound infection (42), intra-abdominal abscess (15), abdominal wound dehiscence (10), and anastomotic breakdown (15) with further surgery (14). The median hospital stay was 19 (i.q.r. 12–24) days.

Eleven (4.5 per cent) of 242 surgically treated patients died in hospital. All had peritonitis at laparotomy, and all but one were aged more than 65 years and had severe co-morbidity.

Follow-up data

Follow-up data were available for 474 (64·8 per cent) of 731 patients: 320 (64·0 per cent) of 500 who had initial MT and 154 (66·7 per cent) of 231 who had ST. *Table2* shows characteristics of the patients followed and those lost to follow-up. Multiple logistic regression showed that prospective manner of recruitment and age at enrolment (range 50–70 years) were the two variables significantly associated with the probability of being followed up.

Table 2. Characteristics of patients followed up and those lost to follow-up

-		-			-
Followed u	р (<i>n</i> = 4	474) Los	st to foll	ow-up $(n = 2)$	69) <u>P*</u>

- Values in parentheses are percentages. AD, acute diverticulitis.
- *

Accrual			< 0.00
Retrospective	234 (57.5)	173 (42.5)	
Prospective	240 (71.4)	96 (28.6)	
Age at enrolment (ye	ears)		< 0.00
< 40	13 (50)	13 (50)	
40–49	51 (76)	16 (24)	
50-59	81 (80.2)	20 (19.8)	
60–69	122 (73.1)	45 (26.9)	
70–79	141 (62.4)	85 (37.6)	
≥ 80	66 (42.3)	90 (57.7)	
Sex ratio (M : F)	216:258	104 : 165	0.068
Previous episodes of	AD		0.192
None	390 (63.2)	227 (36.8)	
1	57 (72)	22 (28)	
≥ 2	27 (57)	20 (43)	

Table 2. Characte	ristics of patients followed up and those lost to follow-u	ıp
	Followed up ($n = 474$) Lost to follow-up ($n = 269$)	<u>P*</u>
Severe co-morbidity		0.006

bevere co morbialty		
Yes	92 (54.8)	76 (45.2)
No	382 (66.4)	193 (33.6)

The mean actuarial follow-up was 10.7 (95 per cent c.i. 10.4 to 11.0) years.

Table<u>3</u> summarizes the outcome according to initial treatment. There was a significantly higher prevalence of persistent chronic symptoms (21.9 *versus* 16.2 per cent) among medically treated compared with surgically treated patients (P = 0.047).

Table 3. Outcome of patients followed up according to the initial treatment

	Total <u>*</u> (n = 474)	Medical <u>*</u> (<i>n</i> = 320)	Surgical <u>*</u> (<i>n</i> = 154)	Crude odds ratio <u>†</u>	<u>P¶</u>
•	Values in parentheses are *				
	percentages and				
•	Ť				
	95 per cent confidence interval	5.			

• ‡

Two patients had three hospital admissions.

• §

The risk of emergency surgery was calculated by comparing the ratio of number of surgical events to number of remaining patients in the two patient groups. AD, acute diverticulitis; NA, not applicable.

• ¶

Fisher's exact test. 315 (66.5) 195 (60.9) 120 (77.9) 1.00 (reference) Asymptomatic 1.72(1.00)**Recurrent symptoms** 95 (20.0) 70 (21.9) 25 (16.2) 0.0472.97) AD requiring hospital 3.76(1.79)< 0.001 64 (13.5) 55 (17.2) 9(5.8)admission 7.89) 3.52(1.52)0.003 1 episode 47 (9.9) 40(12.5)7(4.5)8.10) 4.61 (1.04, 0.035 \geq 2 episodes 17 (3.6) 15 (4.7)‡ $2(1\cdot 3)$ 20.54)5.61 (1.30, 22 (6.9) 0.021Emergency surgery§ 24 (5.1) $2(1\cdot 3)$ 24.17)

Table 3. Outcome of patients followed	l up according to the initial treatment
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	Total <u>*</u> (n = 474)	$\frac{\text{Medical}^*}{320} (n = $	Surgical <u>*</u> (<i>n</i> = 154)	Crude odds ratio <u>†</u>	<u> </u>
Stoma	3 (0.6)	3 (0.9)	0 (0)	NA	0.310
Disease-related death	1 (0.2)	0 (0)	1 (0.6)	NA	0.320

Recurrence

Sixty-four patients had one or more hospital admissions for recurrent AD: 55 (17·2 per cent) of 320 in the MT group and nine (5·8 per cent) of 154 in the ST group (P < 0.001). The medically treated patients had an almost fourfold higher probability of hospital admission for recurrent AD (OR 3·76, 1·79 to 7·89; P < 0.001).

In the MT group, those younger than 40 years of age at entry to the study and those with three or more previous episodes of AD had a higher risk of recurrence (*Table4*). Patients younger than 40 years had a threefold increased risk of recurrent AD compared with those aged 40 years or more (HR 3.32, 1.15 to 9.55; P = 0.026).

Table 4. Factors associated with recurrence of acute diverticulitis among patients who had initial medical therapy

Total no. of patients	No. with recurrence <u>*</u>	Hazard ratio <u>†</u>	P <u>‡</u>
Values in parentheses are			

• *

percentages and

• †

95 per cent confidence intervals. AD, acute diverticulitis;

• ‡

Wald test for significance in Cox multiple regression analysis.

Age (years)

< 40	11	4 (36)	5.01 (1.25, 20.08)	0.023
40–49	37	6 (16)	1.53 (0.44, 5.27)	0.500
50–59	51	11 (22)	1.78 (0.61, 5.20)	0.294
60–69	72	17 (24)	2.01 (0.73, 5.55)	0.177
70–79	103	12 (11.7)	1.09 (0.38, 3.14)	0.869
≥ 80	46	5 (11)	1.00 (reference)	
Sex				
Μ	143	20 (14.0)	1.00 (reference)	
F	177	35 (19.8)	1.48 (0.82, 2.63)	0.194
Episodes of AD				
1	275	39 (14.2)	1.00 (reference)	
2	31	9 (29)	1.66 (0.79, 3.49)	0.177

Table 4. Factors associated with recurrence of acute diverticulitis among patients who had initial medical therapy

	Total no. of patients	No. with recurrence*	Hazard ratio <u>†</u>	P <u>‡</u>
\geq 3	14	7 (50)	3.90 (1.69, 9.03)	0.001

The 12-year cumulative rate of recurrent AD was $21 \cdot 2$ per cent in the MT group and $11 \cdot 8$ per cent in the ST group (P < 0.001) (*Fig.<u>2a</u>*). There was no difference between patients entered retrospectively or prospectively. The extent of proximal and distal resection did not influence the risk of recurrence among patients who had initial ST.



Figure 2. **a** Cumulative rate of recurrent acute diverticulitis (AD) and **b** emergency surgery owing to recurrence of AD according to treatment at enrolment. $\mathbf{a}P < 0.001$, $\mathbf{b}P = 0.008$ (log rank test)

Subsequent surgery

During follow-up, an emergency surgical procedure was performed in 24 patients (5.1 per cent; 21 primary anastomosis and 3 end colostomy). It was fivefold more frequent among the patients who had initial MT: 22 of 320 *versus* two of 154 (age and sex-adjusted HR 5.83, 1.36 to 24.92; P = 0.017). The Hinchey stage was available for 23 of the 24 operated patients: Hinchey 0, one patient; Hinchey 1, 17; and Hinchey 3, five. Of 21 patients in the medical group, four presented with Hinchey stage 3 disease, three of whom underwent resection with end colostomy.

The 12-year cumulative proportion of patients having subsequent emergency surgery was 8.3 per cent among patients in the MT group and 1.9 per cent in the ST group (P = 0.008) (*Fig.2b*). No association was found between the risk of emergency surgery and the investigated parameters (sex, age at entry, and number of previous AD episodes) and there was no difference in the need for emergency surgery among patients entered retrospectively or prospectively. One of the 24 operated patients died shortly after surgery from sepsis (operative mortality rate 4 per cent).

During follow-up, ten patients underwent elective surgery for symptomatic diverticular disease: eight (2.5 per cent) of 320 in the MT group and two (1.3 per cent) of 154 in the ST group (P = 0.330). Four of the 154 patients in the ST group required subsequent surgery: three for incisional hernia and one for adhesions.

Mortality

In all, 85 of 474 patients died during follow-up: one after surgery (see above), 38 from cardiovascular disease, 15 from cancer and 11 from other causes; the cause of death was classified as not available but unrelated to AD in 20 patients. There were 61 deaths (19·1 per cent) among 320 patients in the MT group and 24 (15·6 per cent) among 154 patients in the ST group. The 12-year actuarial survival rates were 75·4 and 83·9 per cent respectively (P = 0.640). After adjustment for sex, age and type of treatment (MT or ST) at entry, cumulative number of AD episodes and

presence of co-morbidity, the only co-variable significantly associated with risk of death was increasing age (P < 0.001).

Discussion

At the end of the 1990s some guidelines recommended elective colectomy after a second episode of AD to prevent further recurrence and to reduce the operative risk associated with an emergency operation 22-25. Subsequent follow-up studies 26-28 questioned this management and modelled analysis studies <u>6</u>, <u>7</u>, <u>10–12</u> showed a substantial reduction in the estimated risk of recurrent AD and emergency surgery. In 2006 the American Society of Colon and Rectal Surgeons modified its previous statement, suggesting a more cautious approach to elective surgery with case-by-case evaluation <u>4</u>, as the ideal treatment was still a matter of debate because the long-term history of patients treated for AD was unclear. The published data do not support a policy of prophylactic sigmoid resection, as the majority of patients require an emergency operation at first admission <u>16</u>.

The aim of the present study was to evaluate prospectively the risk of AD recurrence and subsequent emergency surgery in a large group of patients recruited over a relatively short interval (4 years), and followed using a standard data collection protocol over a long period. To date, most published series on the natural history of AD have been retrospective, with a smaller number of patients recruited over a lengthy period and with short follow-up. Some other studies comprised a retrospective analysis of local or statewide administrative databases. The only prospective study<u>8</u> recruited 223 medically treated patients collected over a 15-year interval, with follow-up ranging between 1 and 16 years. In the present study, patient accrual was retrospective in 1996–1997 and prospective in 1998–1999. No differences in characteristics between these two cohorts were identified. Use of recent standardized retrospective data allowed analysis of almost twice the number of patients in the shortest time.

As reported elsewhere<u>8</u>, <u>15</u>, <u>29–31</u>, three of four patients in the authors' original cohort were diagnosed with diverticulosis at the time of hospital admission for AD or shortly before, indicating that an acute complication frequently presented suddenly without a previous history. It might be argued that few patients in the present study underwent CT. However, in the late 1990s CT was not a common first-line diagnostic procedure for suspected AD in Italy. First reports on the effectiveness of CT in the diagnosis and staging of AD appeared in the early 1990s, but it was only at the end of the decade that the technique was widely used in the emergency setting. At the same time ultrasonography was proposed as an equivalent diagnostic tool<u>32</u>, and more recent studies have confirmed its validity<u>33</u>, <u>34</u>. Ultrasound imaging can be used routinely in centres that do not have easy access to CT in an emergency. The use of water-soluble contrast enema has now been ruled out.

During the same hospital admission, 32.6 per cent of the present patients underwent surgery, whereas reported rates range from 13 to 20 per cent<u>6–8</u>, <u>29</u>, <u>35</u>. This suggests that an aggressive policy was pursued by surgeons at that time, as supported by the high proportion of Hinchey 0 and 1 stages (60.7 per cent) in the surgical series. Other European reports at the time of patient accrual for the present series noted a higher rate of emergency surgery for the first AD episode<u>26</u>, <u>36</u>. In the present series, surgery at first admission was associated with number of previous episodes of diverticulitis, probably following guidelines at that time. In agreement with other authors<u>37</u>, <u>38</u>, the risk of surgery was not increased in patients who were young at the time of recruitment.

The natural history of conservatively treated AD seemed quite benign. During follow-up most (60.9 per cent) of the medically treated patients remained asymptomatic. Around one in five complained of chronic persistent symptoms. The reliability of this finding is limited by the fact that IBS or

segmental colitis associated with diverticula and IBS often mimic symptoms attributable to diverticular disease<u>39–41</u>. Persistent symptoms were also reported by several patients who had ST, and the observed rate fell within the reported range of 7–25 per cent<u>40–42</u>. Persistence of symptoms after surgery can be attributed to coexisting IBS, to adhesions or to an incomplete sigmoid resection<u>42</u>. In the present study, the difference in the rate of persistent symptoms between the MT and ST groups, although statistically significant, was less than 6 per cent.

The rate of recurrent AD after MT was low: one patient in six had one or more AD episodes during follow-up. The reported recurrence rate varies between 13 and 32.5 per cent, with follow-up from 1 to 15 years 5–7, 9–11, 14, 27, 30, 31, 37, 43. In the present study, the risk was higher among young patients (aged less than 40 years at enrolment) and among those with at least three previous episodes of AD. Sex was not associated with disease severity, recurrence or subsequent surgery. The study failed to show a time interval in which most recurrences occur, such as the first 2 years 5, 44 or 5 years 27, 31 as reported in other series. Recurrences in the present series were distributed over the entire observation time.

AD recurrence did not significantly affect the likelihood of successful MT, as reported by Roberts and colleagues 22. In fact, 60.9 per cent of patients recovered after conservative treatment. Threequarters of those submitted to subsequent emergency surgery had Hinchey stage 0 or 1 disease, suggesting that an aggressive surgical policy was applied to patients who, at least in part, were probably manageable with MT.

The cumulative risk of emergency surgery in the MT group at 12 years of follow-up was 8.3 per cent, with a risk of having a stoma of less than 1 per cent and no disease-related deaths. These data are similar to those reported by Eglinton and co-workers5 and Shaikh and Krukowski8. The reported rate of emergency surgery ranges from 2 to 14 per cent, with a 0-2.3 per cent rate of stoma formation and a 0-2.7 per cent rate of related death5, 7, 8, 14. It seems that a long history of diverticulitis or an increasing number of AD episodes is not necessarily associated with a higher risk of serious complications; the frequency of Hinchey stage 3 and 4 disease did not differ substantially between patients operated on at initial observation or at recurrence after MT (27.7 *versus* 19 per cent)41, 45, 46. Perforation is more likely to occur during the first AD episode12, 15, 47, and it has been suggested that previous attacks of AD may actually protect against free perforation through adhesion of omentum or small bowel to the site of perforation<u>41</u>. Corroborating this hypothesis, a recent nationwide study of 685 390 hospital discharges following AD showed that the decline in elective surgery was not followed by an increase in the incidence of severe complicated diverticulitis<u>12</u>.

Whether young age is an independent risk factor for recurrence is still a matter of debate<u>5–9</u>, <u>14</u>, <u>36</u>, <u>48–53</u>. Similarly, the cut-off age (40 or 50 years) for identifying patients at increased risk of relapse, because of an early age at onset of the disease, is also controversial. In agreement with previous observations<u>54</u>, <u>55</u>, in the present study patients aged less than 40 years had a significantly increased risk of AD recurrence. If confirmed in larger series, this finding could be relevant in view of the growing number of very young patients (aged 18–44 years) undergoing emergency surgery for AD in recent years. However, although patients younger than 40 years had an increased risk of AD recurrence in the present study, they did not have a higher risk of subsequent emergency surgery during follow-up, as suggested previously<u>14</u>, <u>53</u>, <u>54</u>. Nevertheless, the small number of young patients followed up precludes reliable conclusions.

Compared with MT, surgery significantly reduced the cumulative risk of both recurrence (11.8 *versus* 21.2 per cent at 12 years) and subsequent surgery (1.9 *versus* 8.3 per cent), but did not eliminate the risk of future serious complications. In a historical report from the Mayo Clinic,

describing a group of 501 patients followed after bowel resection for diverticular disease, the rates of AD recurrence and emergency surgery were 10.4 and 3 per cent respectively55. Other series reported postoperative AD recurrence rates of between 1 and 10 per cent, and reoperation rates from 0 to 3 per cent<u>56</u>, <u>57</u>.

Overall, increasing age was the only parameter associated with long-term mortality in the MT group. Similarly, age was related to long-term mortality among patients in the ST group, as also reported by Vermeulen and colleagues<u>58</u>.

This study had several limitations. First, the study protocol did not specify the treatment modality according to disease severity, so it is possible that different treatment approaches to similar clinical conditions in the various participating centres may have affected the outcome. Nevertheless, this approach had the advantage that it reflected actual clinical practice. Second, the high rate of surgery even among patients with a favourable Hinchey stage at enrolment might have resulted in the selection of patients with a low risk of recurrence of AD and of emergency surgery.

Third, information after hospital discharge was not retrieved for about one-third of patients. This lack of information might have resulted from the application of different follow-up protocols in the participating centres. However, the study population was old at enrolment (median age 70 years) and about two-thirds of patients lost to follow-up were aged 70 years or more. A cross-check with the general registry of place of residence revealed that one-third of the patients lost to follow-up had died within 30 months of enrolment, and that most of them were aged over 80 years and suffered from severe co-morbidities. Finally, only AD recurrences that led to hospital admission were considered, so the true recurrence rate might have been underestimated. However, in clinical practice in Italy, patients with AD symptoms are rarely treated as outpatients; they are usually admitted to hospital for observation and treatment.

In this study, the majority of patients remained asymptomatic after MT in hospital for an acute episode of diverticulitis. Few patients developed recurrent diverticulitis, the risk of further surgery was low, and the risk of diverticular disease-related death was zero. Resection after an episode of AD did not entirely protect against recurrence, although the risk was significantly lower than that after MT. These data do not support a general policy of prophylactic colectomy, which should be advised depending on the individual patient.

Collaborators

The following GISDIC members collaborated in this study: M. Facchini (Sant'Orsola Hospital, Brescia), M. Prandi (Galliera Hospital, Genoa), P. S. Carraro and M. C. Reitano (University of Milan, Milan), G. Clerico (Colorectal Eporediensis Centre, Ivrea), L. Garibotto (Sampierdarena Hospital, Genoa), R. Aloesio (Martini Hospital, Turin), A. Sganzaroli (Abbiategrasso Hospital, Milan), M. Zanoni (San Paolo Hospital, Milan), G. Zanandrea (S. Gerardo Hospital, Monza), F. Pellegrini (Santa Maria Maddalena Hospital, Rovigo), S. Mancini (Santa Lucia Hospital, Civitanova Marche), A. Amato (Borea Hospital, San Remo), P. Barisone (Santa Croce Hospital, Mondovì), C. Bottini (S. Antonio Abate Hospital, Gallarate), D. F. Altomare (University of Bari, Bari), G. Milito (University of Rome Tor Vergata, Rome).

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