Outcome and treatment of acute diverticulitis
Ünlü, Çağdaş

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Influence of age on clinical outcome of acute diverticulitis.

Ünlü Ç, van de Wall BJ, Gerhards MF, Wiezer M, Draaisma WA, Consten EC, Boermeester MA, Vrouenraets BC.

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ABSTRACT

Objective
The controversy about the treatment of acute colonic diverticulitis in young patients continues. In this study we investigated whether an episode of acute diverticulitis at a younger age (≤ 50 years) has a higher recurrence rate or a more severe outcome.

Design
A retrospective cohort study was conducted in four teaching hospitals using hospital registry codes for diverticulitis.

Setting
Four teaching hospitals in the Netherlands participated, Sint Lucas Andreas hospital Amsterdam, Onze Lieve Vrouwe Gasthuis hospital Amsterdam, Meander Hospital Amersfoort and Sint Antonius Hospital Nieuwegein.

Patients
All patients diagnosed with acute diverticulitis between January 2004 and January 2012, confirmed by imaging, were included.

Main outcome measures
Recurrence, or complicated diverticulitis are main outcome measures.

Results
A total of 1441 consecutive patients were identified as having primary acute diverticulitis of the sigmoid colon. Four hundred and sixty-three patients (32.1%) were ≤ 50 years (group 1) and 978 patients (67.9%) were older than 50 years (group 2). Twenty patients (4.3%) needed emergency surgery, due to perforated diverticulitis, within 72 hours at first presentation in group 1 compared to 77 patients (7.8%) in group 2 (p=0.029). Recurrence rate after a median follow-up of 22 months was comparable among groups (25.6% (111 patients) in group 1 versus 23.8% (208 patients) in group 2; p=0.278). Also cumulative recurrence was comparable among groups.

Conclusions
Younger age is not associated with a more severe presentation of diverticulitis nor with a higher incidence in recurrence.
INTRODUCTION

The treatment of acute uncomplicated diverticulitis in young patients remains controversial. There is no clear consensus whether younger patients (younger than 50 years) with diverticulitis are at increased risk of complications or recurrent disease. Nevertheless, guidelines and a recent review advise elective resection in younger patients. (1-4)

In literature this debate is ongoing. Recent papers advise similar conservative treatment for younger patients as in older patients (5-9), while others advise a more aggressive approach for younger patients. (10, 11) Published studies refuting age as a risk factor for recurrence and a more severe disease course are criticized because of small numbers of young patients.

Present study aimed to determine the outcome of younger patients with acute diverticulitis in a large multicentre, retrospective cohort study.

Materials and methods

All patients with the diagnosis of acute diverticulitis were identified from the hospital patient registries using registry codes for diverticulitis. All patients presented to the out-patient clinic, emergency department and those admitted to the hospital were registered. Records from the following Dutch hospitals were searched, Sint Lucas Andreas hospital Amsterdam, Onze Lieve Vrouwe Gasthuis hospital Amsterdam, Meander Hospital Amersfoort and Sint Antonius Hospital Nieuwegein, between January 2004 and January 2012. From identified patients all records were reviewed. Inclusion for the study was firstly made on the basis of symptoms, physical examination and blood tests results. In patients suspected of having diverticulitis, the diagnosis needed to be confirmed by ultrasonography (US), computed tomography (CT), colonoscopy or pathology in case of acute resection. Exclusion criteria were right colonic diverticulitis, lower gastrointestinal bleeding due to diverticular disease, and previous episodes of acute diverticulitis prior to the study period.

The patient cohort was divided into two age groups at a 50-year cut-off level. To compare our results to previously published studies a similar cut-off was used. Patient data were stored anonymously into the study database. For this type of medical record research, approval of an institutional review board is waived in the Netherlands.

Recurrence was defined as representation with clinical symptoms, with laboratory results, similar to previous imaging proven episodes, more than 30 days after initial
presentation. When surgery was not indicated conservative treatment was given and any subsequent elective surgery was indicated according to the choice of the surgeon.

Data extracted at the time of presentation at the hospitals were age, sex, American Society of Anesthesiologists (ASA) status, nausea/vomiting, duration of symptoms, duration of hospital stay, temperature, white blood cell count, C-reactive protein (CRP) at admission, use of antibiotics, fever and imaging results. The decision to operate or give medical treatment was made by the attending surgeon. During follow-up recurrence, drainage procedures and surgical interventions were registered.

Death in hospital for diverticulitis or other causes was checked. Also recurrent disease treated as out-patient was recorded. After the episode of diverticulitis had resolved, patients treated conservatively had colonoscopy or CT colonography to rule out malignancy.

**Statistical analysis**

Continuous variables were summarized as either means with corresponding standard deviations or medians with interquartile range depending on normality. Normal distribution was assessed using Q–Q plots. Student t-test when normally distributed or else Mann Withney U test with median and interquartile range. Categorical variables were compared using Fisher’s exact test or the Chi Square test when appropriate. Multivariate logistic regression was performed to assess the risk factors for recurrence. Baseline characteristics were analyzed in univariate analysis. Variables with a univariate p<0.1 and variables of known clinical importance were entered in a multivariate regression model. Age was explored as a continuous variable and as a categorical variable. Kaplan-Meier survival curves were used for studying recurrence during follow-up period and the log-rank test for comparisons between periods. Statistical significance was defined as p<0.05. Results are presented as odds ratios with 95% confidence intervals. Statistical analysis was performed using SPSS, version 19.0 (SPSS Inc., Chicago, IL, USA).

**Results**

A total of 1441 consecutive patients were identified with the diagnosis diverticulitis. Of these patients, 463 were 50 years or younger (group 1, 32.1%) and 978 patients older than 50 years (group 2, 67.9%). The flow chart of their course of disease is depicted in Figure 1.

Patient characteristics are shown in Table 1. There were significantly more females in the older group (p=0.0001). Also the ASA classification was higher in the older age group (p=0.0001). At presentation there was no difference in body temperature (i.e., presentation with fever). Older patients were more often treated with antibiotics (p=0.03).
Influence of age on clinical outcome of acute diverticulitis.

Figure 1 Flowchart

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Age ≤ 50 years</th>
<th>Age &gt; 50 years</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=463</td>
<td>n=978</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>256 (55.2%)</td>
<td>369 (37.7%)</td>
<td>0.0001#</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>333</td>
<td>329</td>
<td>0.0001#</td>
</tr>
<tr>
<td>II</td>
<td>119</td>
<td>518</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>White blood cell count (x10^9/L) on admission*</td>
<td>12.2 (9.8-15.7)</td>
<td>11.4 (9.3-14.4)</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>CRP (mg/L) on admission*</td>
<td>77 (33.5-135)</td>
<td>80 (34-156)</td>
<td>0.45 *</td>
</tr>
<tr>
<td>Temperature (°C) $</td>
<td>37.5 (± 0.8)</td>
<td>37.5 (± 0.8)</td>
<td>0.75 $</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>71 (15.3%)</td>
<td>197 (20.1%)</td>
<td>0.03 #</td>
</tr>
<tr>
<td>Out-patient treatment</td>
<td>173 (37.3%)</td>
<td>290 (29.6%)</td>
<td>0.004 #</td>
</tr>
<tr>
<td>Duration of admission</td>
<td>4 (2-6)</td>
<td>5 (3-8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Initial treatment</td>
<td></td>
<td></td>
<td>0.029 #</td>
</tr>
<tr>
<td>Conservative</td>
<td>443</td>
<td>905</td>
<td></td>
</tr>
<tr>
<td>Early operative (≤ 72 hours)</td>
<td>20 (4.3%)</td>
<td>77 (7.3%)</td>
<td></td>
</tr>
</tbody>
</table>

# χ² test or Fisher’s Exact test if appropriate
§ Student t-test comparing means (SD)
* Mann Whitney U test (median with interquartile range)
More younger patients were treated as out-patient (p=0.004) and they had a shorter duration of admission (p<0.001).

**Treatment**

Treatment and complications per age group are summarized in table 1 and 2. Twenty patients (4.3%) underwent an emergency operation, due to perforated diverticulitis, (≤72 hours) versus 77 patients (7.8%) in the older group (p=0.029). In the first episode of diverticulitis (≤ 30 days) 29 patients (6.2%) were operated in the younger group and 104 patients (10.6%) in the older group (p=0.02).

### Table 2. Treatment in relation to age

<table>
<thead>
<tr>
<th></th>
<th>Age ≤ 50 years</th>
<th>Age &gt; 50 years</th>
<th>P (Φ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment at primary presentation (≤ 30 days)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conservative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiologic drainage</td>
<td>434 (94%)</td>
<td>875 (89%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Operative</td>
<td>2</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>Hartmann procedure</td>
<td>29</td>
<td>104</td>
<td></td>
</tr>
<tr>
<td>Primary Anastomosis</td>
<td>17</td>
<td>69</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>34</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Treatment because of recurrence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conservative</td>
<td>55 (49.5%)</td>
<td>90 (43%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Radiologic drainage</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Operative</td>
<td>58</td>
<td>118</td>
<td>0.29</td>
</tr>
<tr>
<td>Hartmann procedure</td>
<td>9</td>
<td>14</td>
<td>0.62</td>
</tr>
<tr>
<td>Primary Anastomosis</td>
<td>49</td>
<td>102</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Complications of operative treatment after primary acute diverticulitis</strong></td>
<td>n=29</td>
<td>n=104</td>
<td></td>
</tr>
<tr>
<td>Leakage</td>
<td>2 (16.7%)</td>
<td>6 (17.6%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1 (3.4%)</td>
<td>3 (2.9%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Wound infection</td>
<td>7 (24%)</td>
<td>35 (34%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Platzbauch</td>
<td>1 (3.4%)</td>
<td>7 (6.7%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>3 (10.3%)</td>
<td>10 (9.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (3.4%)</td>
<td>4 (3.8%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2 (6.9%)</td>
<td>2 (1.9%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>10 (9.6%)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Complications of operative treatment because of recurrence</strong></td>
<td>n=71</td>
<td>n=151</td>
<td></td>
</tr>
<tr>
<td>Leakage</td>
<td>2 (4.1%)</td>
<td>9 (8.8%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1 (1.4%)</td>
<td>4 (2.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Wound infection</td>
<td>9 (12.7%)</td>
<td>26 (17%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Platzbauch</td>
<td>0</td>
<td>4 (2.6%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>5 (7.0%)</td>
<td>10 (6.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>8 (5.3%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1 (1.4%)</td>
<td>10 (6.6%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>4 (2.6%)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

# χ² test or Fisher’s Exact test if appropriate
The only significant difference in postoperative complications was a higher pneumonia rate in the older group. A much higher mortality rate and two times higher leakage rate was noted in the older patient group. There was no difference in the complication rate comparing first presentation to recurrence (Table 2).

**Recurrence**

The recurrence rate in the younger group was comparable among groups (25.6% (n=111) versus 23.8% in the older group ((n=208); p=0.278)). Most patients presented with recurrence within 12 months (64.9%-63.5%; p=0.687, Table 3). In both groups the multiple recurrence rates were equal. Also cumulative recurrence was comparable among groups (Figure 2).

**Table 3.** Recurrence rate, and the recurrence rate within 12 months from initial presentation. (χ² test)

<table>
<thead>
<tr>
<th>Age ≤ 50 years (n=434)</th>
<th>Age &gt; 50 years (n=874)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence rate at median follow-up (22 months), n (%)</td>
<td>111 (25.6%)</td>
<td>208 (23.8%)</td>
</tr>
<tr>
<td>Recurrence at 12 months, n (%)</td>
<td>72 (64.9%)</td>
<td>132 (63.5%)</td>
</tr>
</tbody>
</table>

**Figure 2.** Kaplan Meier curve of cumulative recurrence in the two groups of patients. Log Rank (Mantel-Cox)
Risk factors for recurrence

Different, potentially important, baseline characteristics were entered in a multivariate logistic regression model to identify potential risk factors for recurrence. Age, gender, ASA classification, Hinchey classification and antibiotics were used in this model as potential risk factors. The independent factors significantly associated with recurrence were ASA III (1.81 (1.11-2.95)), Hinchey 1b (2.04 (1.13-3.67), Hinchey II (6.05 (2.62-13.99)) and primary conservative treated Hinchey III patients (3.82 (1.25-11.69)). Age was not a risk factor in this model. (Table 4)

Table 4. Univariate and multivariate analyses of risk factors (odds ratio) associated with recurrence.

<table>
<thead>
<tr>
<th></th>
<th>No. of patients at risk for recurrence</th>
<th>Recurrence</th>
<th>Univariate OR</th>
<th>Multivariate OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n (%)</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 years</td>
<td>434</td>
<td>100 (23%)</td>
<td>0.343</td>
<td></td>
</tr>
<tr>
<td>≥ 50 years</td>
<td>874</td>
<td>192 (22%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>575</td>
<td>115 (20%)</td>
<td>0.074</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>733</td>
<td>177 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>619</td>
<td>128 (20.7%)</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>576</td>
<td>130 (22.6%)</td>
<td>1.12 (0.85-1.47)</td>
<td>1.81 (1.11-2.95)</td>
</tr>
<tr>
<td>III</td>
<td>105</td>
<td>31 (29.5%)</td>
<td>1.61 (1.01-2.51)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>8</td>
<td>3 (37.5%)</td>
<td>2.30 (0.54-9.76)</td>
<td></td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>175</td>
<td>56 (32%)</td>
<td>0.440</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>841</td>
<td>236 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hinchey</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>1218</td>
<td>277 (22.7%)</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>52</td>
<td>20 (38.5%)</td>
<td>2.12 (1.19-3.77)</td>
<td>2.04 (1.13-3.67)</td>
</tr>
<tr>
<td>II</td>
<td>25</td>
<td>16 (64%)</td>
<td>6.0 (2.6-13.8)</td>
<td>6.05 (2.62-13.99)</td>
</tr>
<tr>
<td>III (conservative treat.)</td>
<td>13</td>
<td>7 (53.8%)</td>
<td>3.96 (1.32-11.90)</td>
<td>3.82 (1.25-11.69)</td>
</tr>
</tbody>
</table>

DISCUSSION

Present results indicate that younger patients with acute diverticulitis do not have a more aggressive presentation or course. Also the risk on recurrence is not higher compared to older patients.
Summarizing literature two different conclusions have been made with respect to age. One conclusion is that diverticulitis in younger patients has an aggressive course and significant more recurrence rate. (10, 11) The other is age makes no difference. (5-9) If we look closer to the references of these two conclusions, the first conclusion is based on two large studies. Broderick-Villa et al. studied 2366 patients followed after being treated medically for their first attack of diverticulitis. Age under 50 years and the Charlson comorbidity index were the only independent factors associated with a greater risk of recurrence. Anaya et al. studied 20,136 patients followed after being treated without surgery during their first attack. The risk of recurrent hospitalization increased with age under 50 years. These two studies, although not recent, have a large number of patients. Critically reviewing a few points can be made. Both studies do not mention if the diagnosis diverticulitis is proven by imaging. In the study of Broderick-Villa et al the recurrence rate is much lower than previously reported. Anaya et al study consists of a retrospective database between 1992-1997, and selection of study entrance is based on hospitalized patients. Moreover, patient characteristics other than age are not provided.

The second conclusion is based on multiple smaller studies (one study of 686 patients and other studies in less than 200 patients), but more recently published. All of these studies included imaging to prove the diagnosis of diverticulitis to avoid selection bias. (7, 8, 9, 13) The results of the present study with its larger sample size are in line with these conclusions.

Two studies did not primary focus on recurrence but on operative outcome. Shaikh et al. found that the incidence of subsequent surgery for the 191 patients who were discharged without resection was statistically greater for patients under 50 years of age compared with those over 50 years of age (38% versus 15%; P = 0.015). They conclude that younger patient undergo more surgery than older patients. Indication of operation is not provided and the study was conducted between 1990-2004. In a period that guidelines for elective surgery were based on the assumption that recurrent episodes (2 or more) of diverticulitis was needed and after one well-documented episode of uncomplicated diverticulitis in the younger patient (<50 years). (1) Same type of study was conducted by Biondo et al. However they conclude no difference in age-related operative outcome. Also this study was conducted between 1994-1999. Both studies provide an insight in daily practice between different countries.

The present study has limitations that need consideration. The study was observational and retrospective. Much effort was undertaken to identify any selection bias, inherent to a retrospective study, by demonstrating many clinically relevant variables.
The recurrence rate in our study varied from 23.8% to 25.6% among groups. Previous studies have reported recurrence rates of 7–42 per cent. (5-12) This large range is based on selection bias and misdiagnosis. Early studies that are hampered by serious methodological flaws suggest a more aggressive approach, not in line with recent guidelines.

The rate of emergency surgery was higher in older patients. Recent studies have shown similar results. (7, 8) Only older studies suggested a more virulent presentation for younger patients, as summarized in a recent systematic review. (13)

Recurrent diverticulitis is not age dependent, more other factors play a role. In the multivariate analysis in this study ASA III score and the occurrence of abscesses were associated with recurrence. Other studies have identified the occurrence of abscesses (14) and multiple co-morbidity (10) as potential risk factors in the occurrence of recurrence. In our study Hinchey II stage had a high recurrence rate. Such high recurrence rate has also been noted in other studies (41.2% and 45.5%). (14, 15) Another independent factor for recurrence was an initially conservative treatment in an Hinchey III patient. These are patients with free air on CT, but with mild illness and therefore treated conservatively.

Younger age is not associated with a more severe presentation of diverticulitis nor with a higher incidence in recurrence. Treatment choices do not need to be modified related to patient age.
REFERENCES


