Outcome and treatment of acute diverticulitis
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CHAPTER 9

Routine colonoscopy after left-sided acute uncomplicated diverticulitis: a systematic review.

Daniels L, Ünlü Ç, Wijkerslooth TRM, Dekker E, Boermeester MA

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BACKGROUND

The use of routine colonoscopy after an episode of acute diverticulitis (AD) remains a point of debate. Most international and clinical practice guidelines advise endoscopy after conservatively treated diverticulitis.\textsuperscript{1-6} The rationale always has been to exclude an underlying malignancy or advanced colonic neoplasia (ACN). However, this is based merely on expert opinion. A recent paper indicates this may be different in present days with increased use of abdominal Computed Tomography (CT) imaging of diverticulitis.\textsuperscript{7} Furthermore, the yield of colonoscopy in patients after an episode of AD also casts doubt on current international practice.\textsuperscript{8-20}

Routine colonoscopy after an uncomplicated episode of diverticulitis dates from a time where the diagnosis was primarily based on clinical examination and laboratory results with frequent use of barium enema.\textsuperscript{21} However, in today’s clinical practice CT is widely used for the diagnosis of diverticulitis, with the possibility to assess potential adverse events such as abscess, fistula, obstruction or perforation as well. Because of high sensitivity of 94\%, a specificity of 99\% and a low inter observer variability this modality is currently preferred for the diagnosis diverticulitis, although ultrasound (US) has a good sensitivity too.\textsuperscript{22,23} Nevertheless, it remains uncertain if the prevalence of colorectal carcinoma (CRC) and advanced adenoma (AA) in patients with imaging proven diverticulitis is higher than in an average-risk population. Apart from diagnosing CRC the detection of AA is of great importance since it bears the potential to progress to carcinoma.

Colonoscopy is accompanied by disadvantages as invasiveness and discomfort, and potential of adverse events such as perforation and additional costs. It is important to know what the yield of routine colonoscopy is after a confident diagnosis of AD, i.e.: is there a justified indication? Therefore, the aim of this systematic review was to determine the pooled prevalence of ACN, thus CRC and/or AA, as detected with colonoscopy in patients after an imaging proven diagnosis of AD.
MATERIALS AND METHODS

Review protocol and Study Eligibility
A review protocol, for which the PRISMA checklist served as a guideline, was used by the two authors (LD and CU) for the execution of this systematic review.

Eligibility criteria
Definitions
Diverticulitis is complicated diverticular disease with clinical symptoms and evidence of inflammation, confirmed by US or CT imaging. Advanced colonic neoplasia (ACN) comprises advanced adenomas (AA) and/or colorectal carcinoma (CRC). An AA is defined as an adenoma ≥10 mm, ≥25% villous features (also classified as tubulovillous or villous histology) or with high-grade dysplasia. Right-sided is defined as proximal to the splenic flexure.

Types of studies
There were no predetermined limits of design types or language. Articles were eligible for inclusion when the following criteria were met: studies dealing with follow-up colonoscopy after US or CT proven left-sided diverticulitis, human studies, studies of which the full text and data were available. The following exclusion criteria were used for study selection: studies without follow-up colonoscopy but with CT-colonography or contrast barium enemas instead, or with outcome based on surgically obtained pathology specimens.

Types of participants
Patients of 18 years or older with a recent diagnosis of AD were included. This diagnosis had to be confirmed by US and/or CT imaging.

Types of outcome measures
Primary outcome measure was the detection of advanced colonic neoplasia: AA and/or CRC. Secondary outcomes were detection of adenomas and serrated polyps (hyperplastic, sessile serrated adenoma/polyp and traditional serrated adenoma). Adverse events of colonoscopy were also registered if described.

Literature search
An electronic literature search was performed to identify relevant records. The MEDLINE database was searched for articles published between January 1966 and July 2013, with the following search strategy: (((“Diverticulitis”[Mesh] OR “diverticulitis”[All Fields]) AND (“Colonoscopy”[Mesh] OR “Colonoscopy”[All Fields] OR “Colonography, Computed Tomographic”[Mesh])) AND (“1966/01/01”[Date- Publication] : “3000”[Date - Publication])) Free text words were also used instead of MeSH terms to avoid missing recent articles that had not yet been given a MeSH label. EMBASE database was searched for
records published between 1974 and July 2013 with the following terms: diverticulitis and colonoscopy. The CINAHL database was also checked with the same keywords. As well, the Cochrane database of Systematic Reviews was searched with the following words: Diverticular disease.

**Selection**
After removal of duplicate records the two reviewers screened the initial literature search based on title and abstract. After identifying potentially relevant records, the full-text articles of these were retrieved. Additionally a manual cross-reference search of the reference list of relevant articles was performed, and electronic links to related articles were hand searched as well to identify other studies not found in the initial search. They were all assessed for eligibility by applying the inclusion and exclusion criteria. Papers that reported on (parts of) the same study population were excluded from the review.

**Data extraction**
Data from each included study were extracted by the two reviewers independently using a standard form. These data included: (a) authors, (b) year of publication, (c) country, (d) study design, (e) inclusion period, (f) type of patients, (g) type of imaging for the diagnosis of AD, (h) definition used for AD and ACN/AA, (i) interval between diagnosis AD and colonoscopy, (j) study endpoints, (k) follow-up period, (l) number of patients, (m) patient age, (n) number of complete colonoscopies, (o) number of adverse events, (p) number of patients with neoplastic lesions, (q) number of (patients with) polyps, (r) number of (patients with) adenomas (including AA), (s) number of (patients with) AA, (t) number of (patients with) CRC, (u) number of (patients with) ACN, (v) localisation of ACN, (w) age at diagnosis ACN and (x) any additional relevant information.

**Assessment of susceptibility to bias**
Two reviewers independently assessed the methodological quality of the studies and susceptibility to bias using the MINORS quality score, an instrument designed to assess the methodological quality of non-randomized surgical studies, with a global ideal score of 16 for non-comparative studies.\(^{26}\)

**Statistical Analysis**
The primary outcome of this systematic review was the percentage of patients with ACN, and thus CRC and/or AA, as detected with follow-up colonoscopy, after an episode of imaging proven diverticulitis. Therefore, for each included study, we calculated the 95% confidence intervals around the proportions of ACN, CRC and AA. We calculated the estimated pooled prevalence and 95% confidence intervals based on a random effects model using Meta-Analyst version Beta 3.13. We determined the presence of heterogeneity between the studies by using a forest plot and by performing a $\chi^2$ (‘chi-
Routine colonoscopy after left-sided acute uncomplicated diverticulitis: a systematic review.

Methods

The meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary outcome was the diagnostic accuracy of colonoscopy for the detection of colonic polyps and colorectal cancer (CRC). The search was conducted using PubMed, EMBASE, and Cochrane Library databases for articles published from January 2000 to May 2019. The primary outcome was the diagnostic accuracy of colonoscopy for the detection of colonic polyps and colorectal cancer (CRC). The search strategy included keywords such as “colonoscopy,” “diverticulitis,” “CRC,” and “diagnostic accuracy.” The inclusion criteria were studies that compared colonoscopy with other diagnostic methods for the detection of colonic polyps and CRC. The exclusion criteria were studies that did not report diagnostic accuracy, studies that included patients with overt signs of diverticulitis, and studies that did not specify the type of colonoscopy used.

The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS). The NOS assesses the quality of observational studies by evaluating selection, comparability, and exposure or outcome assessment.

The characteristics of the included studies were summarized in a table. The quality of the studies was assessed using the NOS and the MINORS scoring scale. The results were synthesized using a random-effects model, and the heterogeneity was assessed using the I²-test. If the results were heterogeneous, a sensitivity analysis was conducted to identify the source of heterogeneity.

Results

Study selection

A total of 959 records were initially identified in the literature search. Of these, 234 records were excluded as they were duplicate articles. From the 725 remaining records, screened based on title and abstract, another 694 were excluded due to irrelevance. Most of the studies were irrelevant because they covered other subjects, amongst others performance and findings of CT-colonography (CTC), screening colonoscopy, comparison of standard colonoscopy versus colonoscopy with transparent cap, management of diverticulitis and sigmoidovesical fistula. Twenty-nine full-text articles were retrieved for more detailed examination; one additional article was found in reference lists. These were assessed for eligibility. The application of our inclusion and exclusion criteria resulted in eight relevant studies. Twenty-three articles were excluded as they were abstracts only, case report, contained duplicate data or failed to meet our inclusion criteria. The two reviewers completely agreed on inclusion of studies.

Study characteristics and risk of bias

Eight studies met our inclusion criteria and were reviewed (Table 1). The studies were executed on four different continents within the timeframe the years 2000 to 2010. All studies were retrospective cohort studies, except for the studies of Chabok et al. and Lahat et al. They compared acceptance and diagnostic accuracy of CTC versus colonoscopy and early versus late colonoscopy respectively. Many of these retrospective cohort studies attempted an indirect comparison with published data on high- and average risk asymptomatic individuals derived from screening studies. Lau et al. compared their CRC rate with that published by the WA Cancer Registry for all Western Australians; these data were however not based on population colonoscopic screening.

In all studies the diagnosis of acute diverticulitis was imaging proven; CT proven in six studies, US and/or CT proven in one and US or CT confirmed in another. The radiological definition used for diverticulitis was described in 5 studies. The histological definition for ACN was described in only 3 studies. The number of patients enrolled per study ranged from 86 to 402.

The studies were of moderate to good quality using the MINORS scoring scale, with total scores ranging from 10 to 14. (Table 2)
FIGURE 1 PRISMA flow diagram showing selection of articles for review and analysis
TABLE 1 General characteristics of included studies

<table>
<thead>
<tr>
<th>Study, year and country</th>
<th>Study design</th>
<th>Inclusion period</th>
<th>Type of patients</th>
<th>Radiological diagnosis</th>
<th>Definition AD</th>
<th>Interval AD – colonoscopy</th>
<th>Endpoint(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elmi et al. 8 2013, United States</td>
<td>Retrospective</td>
<td>Jan 2000 - Dec 2004</td>
<td>Acute (un)complicated diverticulitis in patients older than 49 years, without a history of CRC</td>
<td>CT</td>
<td>No</td>
<td>5.3 years (1 month - 11 years, 34.8% &lt; 6 months)*</td>
<td>Sensitivity, specificity, and predictive values of CT parameters for prediction of CRC.</td>
</tr>
<tr>
<td>Chabok et al. 9 2013, Sweden</td>
<td>Prospective comparative</td>
<td>Oct 2005 - Jan 2007</td>
<td>Acute left-sided colonic diverticulitis (without a colorectal examination during the last 2 years)</td>
<td>CT</td>
<td>No</td>
<td>6 - 8 weeks</td>
<td>Patient acceptance and diagnostic accuracy of CTC vs colonoscopy for DD, adenomas and CRC</td>
</tr>
<tr>
<td>Van de Wall et al. 10 2012, NL</td>
<td>Retrospective cross-sectional</td>
<td>Jan 2007 - Jan 2010</td>
<td>Primary episode diverticulitis (98.5% Hinchey I)</td>
<td>CT (61%) and/ or US</td>
<td>Yes</td>
<td>8.9 weeks ± 10.6*</td>
<td>Detection rate of hyperplastic polyps, adenomas and ACN</td>
</tr>
<tr>
<td>Schout et al. 11 2012, NL</td>
<td>Retrospective</td>
<td>2000 - 2010</td>
<td>Diverticulitis with or without intra-abdominal abscess</td>
<td>CT or US</td>
<td>No</td>
<td>NR</td>
<td>Number of malignant and benign colon tumours detected by FU programme</td>
</tr>
<tr>
<td>Schmilovitz-Weiss et al. 12 2012, Israel</td>
<td>Retrospective</td>
<td>Jun 2002 - Sep 2009</td>
<td>Acute diverticulitis (exclusion if questionable CT findings and/or hematochezia)</td>
<td>CT</td>
<td>Yes</td>
<td>4 - 6 weeks</td>
<td>Yield of early colonoscopy and correlation between imaging results and scopy outcomes</td>
</tr>
<tr>
<td>Westwood et al. 13 2011, New Zealand</td>
<td>Retrospective longitudinal</td>
<td>Jan 2004 - Dec 2008</td>
<td>Acute uncomplicated diverticulitis (exclusion if complicated or mass lesions)</td>
<td>CT</td>
<td>Yes</td>
<td>‘After’ AD or &lt; 2 years before AD</td>
<td>Yield of ACN with colonoscopy/ CTC</td>
</tr>
<tr>
<td>Lau et al. 14 2011, Australia</td>
<td>Retrospective</td>
<td>Jan 2003 - Jun 2009</td>
<td>(Un)complicated left-sided diverticulitis</td>
<td>CT</td>
<td>Yes</td>
<td>70 days</td>
<td>No of patients in whom CRC were diagnosed and other incidental findings</td>
</tr>
<tr>
<td>Lahat et al. 15 2007, Israel</td>
<td>Prospective (RCT early vs late colonoscopy)</td>
<td>Jan 2004 - Jun 2006</td>
<td>Acute diverticulitis (exclusion if adjacent pericolonic air or fluid or free perforation)</td>
<td>CT</td>
<td>Yes</td>
<td>5.2 days (3-11) † vs 7.8 weeks (6-19) †</td>
<td>Feasibility (endoscopic findings and compliance rates) and risk (adverse events)</td>
</tr>
</tbody>
</table>

NR, not reported; AD, Acute diverticulitis; ACN, Advanced colonic neoplasia; AA, Advanced adenoma; CRC, Colorectal carcinoma; CT, Computed Tomography; CTC, CT-colonography; DD, Diverticular Disease; NL, The Netherlands; US, Ultrasonography; FU, Follow-up; RCT, Randomized Controlled Trial.

*Values are means ± standard deviations (± SD).
†Values are medians (range).
### TABLE 2 Assessment for risk of bias

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1. A clearly stated aim</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2. Inclusion of consecutive patients</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3. Prospective collection of data</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>4. Endpoints appropriate to the aim of the study</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5. Unbiased assessment of the study endpoint</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6. FU period appropriate to the aim of the study</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>7. Loss to FU less than 5%</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>8. Prospective calculation of the study size</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total score†</td>
<td>11</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>14</td>
</tr>
</tbody>
</table>

FU, Follow-up.

*The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate); items 9-12 were left out since they only apply to comparative cohort studies.

†Maximal total score 16 for non-comparative studies.

### TABLE 3 Clinical characteristics and outcomes of included studies

<table>
<thead>
<tr>
<th>Study, year</th>
<th>No of patients</th>
<th>Age (years)</th>
<th>Complete endoscopy</th>
<th>No of patients with neoplastic lesions (inclusive of polyps)</th>
<th>No of patients with adenoma</th>
<th>No of patients with ACN</th>
<th>CRC</th>
<th>AA</th>
<th>Age at diagnosis ACN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elmi et al.2013</td>
<td>402</td>
<td>63.3 (range 50 - 94)*</td>
<td>NR</td>
<td>78 (19.4%)</td>
<td>55 (13.7%)</td>
<td>NR</td>
<td>9 (2.2%)</td>
<td>NR</td>
<td>68.1*</td>
</tr>
<tr>
<td>Chabok et al.2013</td>
<td>101</td>
<td>56 (range 27 - 84)†</td>
<td>100 (of 110 = 90.9%)</td>
<td>20 (20%)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Van de Wall et al.2012</td>
<td>205</td>
<td>57.3 ± 13.2*</td>
<td>146 (90.6%)</td>
<td>40 (19.5%)</td>
<td>23 (11.2%)</td>
<td>7 (3.4%)</td>
<td>2 (1.0%)</td>
<td>5 (2.4%)</td>
<td>62.7 (37-83)†</td>
</tr>
<tr>
<td></td>
<td>163 colo</td>
<td>15 (6.8%)</td>
<td>hyperplastic</td>
<td>18 (8.8%) adenomas</td>
<td>2 tubular adenomas &gt; 1 cm adenoma with high grade dysplasia 2 adenomas with &gt; 25% villous components</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**TABLE 3 Continued**

<table>
<thead>
<tr>
<th>Study, year</th>
<th>No of patients</th>
<th>Age (years)</th>
<th>Complete study</th>
<th>No of patients with neoplastic lesions (inclusive of polyps)</th>
<th>No of patients with adenoma</th>
<th>No of patients with ACN with CRC AA</th>
<th>Age at diagnosis ACN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schout et al.11 2012</td>
<td>378</td>
<td>NR</td>
<td>NR</td>
<td>47 (12.4%)</td>
<td>39 (10.3%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Schmilowitz-Weiss et al.12 2012</td>
<td>100</td>
<td>61.8 ± 13.3*</td>
<td>NR</td>
<td>32 (32%) (42 lesions)</td>
<td>NR (36 adenomas)‡</td>
<td>6 (6%)</td>
<td>NR</td>
</tr>
<tr>
<td>Westwood et al.13 2011</td>
<td>205</td>
<td>60 (23-95)†</td>
<td>NR</td>
<td>5 hyperplastic</td>
<td>6 tubulovillous adenomas, 1 of which &gt; 1 cm</td>
<td>0 (0%)</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Lau et al.14 2011</td>
<td>319</td>
<td>59.8 ± 15.2*</td>
<td>NR</td>
<td>20 (9.8%) hyperplastic</td>
<td>19 (9.3%) adenomas</td>
<td>1 (0.5%)</td>
<td>10 (4.9%)</td>
</tr>
<tr>
<td>Lahat et al.15 2007</td>
<td>86</td>
<td>60.5 ±11.4* vs 41 'late' 60.3 ±14.7*</td>
<td>75 (87.2%)</td>
<td>49 (15.4%)</td>
<td>40% of 82 polyps hyperplastic</td>
<td>9 (2.8%)</td>
<td>NR</td>
</tr>
</tbody>
</table>

ACN, Advanced Colonic Neoplasia; CRC, Colorectal Carcinoma; AA, Advanced Adenoma; NR, not reported.
*Values are means ± standard deviations (± SD).
†Values are medians (range).
‡Total number of adenomas instead of number of patients with adenoma was reported.

Patient cohort and results of individual studies
The clinical characteristics and outcome are summarized in Table 3. A total of 1796 patients, aged around 60, had an imaging proven diagnosis of uncomplicated diverticulitis with endoscopic evaluation in follow-up. Reported colonoscopy completion rates ranged from 85.4%13 to 93.4%14. More than half of studies did not mention adverse events; the three who did so stated to have experienced none.
One in five patients (20.2%; 363 of 1796) had at least one polyp. All but three studies\textsuperscript{9,12,14} referred to the most advanced lesion detected. Chabok \textit{et al.}\textsuperscript{9}, Schout \textit{et al.}\textsuperscript{11} and Lahat \textit{et al.}\textsuperscript{15} did not mention hyperplastic polyps. None of included studies described the number of (patients with) sessile serrated adenomas/polyps and traditional serrated adenomas. In 236 of 1695 patients (14%) adenomas were detected. The exact number of patients may have been slightly different since one study did not report on adenomas\textsuperscript{9} and therefore was left aside. Another study\textsuperscript{12} mentioned a total number of 36 adenomatous polyps and not patients.

Thirty-three of 915 patients (3.6%) were found to have AA; three studies did not report on patients with AA and consequently were disregarded in this calculation.\textsuperscript{8,9,11} Twenty-nine of 1796 patients (1.6%) had CRC detected in follow-up with colonoscopy. In three studies no CRC was found.\textsuperscript{9,12,15} When we take into account only studies that reported both on AA and CRC, a total of forty-five out of 915 patients were diagnosed with ACN (4.9%), comprising either AA or CRC, with a range of 3.4 to 6% between studies. Localisation of ACN, specified in four studies, was in all cases except for one left-sided, or more specifically the sigmoid colon. Lau \textit{et al.} present a 5.6% rate of ACN and is the only study to conclude that routine colonoscopy is mandatory in uncomplicated diverticulitis.\textsuperscript{14}

\textbf{Pooled prevalence}

As shown in Figures 2-4 the estimated pooled prevalence was 5.0% (CI; 3.8-6.7%) for ACN, 1.5% (CI; 1.0-2.3%) for CRC and 3.8% (CI; 2.7-5.3%) for AA as detected at follow-up after an episode of imaging confirmed AD. There was limited evidence of heterogeneity among included studies for the detection of CRC (\(I^2 = 32\%\)) and none for ACN (\(I^2 = <0.01\%\)) and AA (\(I^2 = <0.01\%\)). Results of the funnel plot asymmetry tests are presented in Figure 5 and show some asymmetry that could be indicative of publication bias.

\textbf{Excluded studies}

Of the 23 excluded studies most failed to meet our inclusion criteria and/or were abstracts only. Three studies were excluded because they concerned bowel thickening on CT scan and only a fraction of the included patients (2.8%-29.3%) were diagnosed with diverticulitis or diverticular disease.\textsuperscript{29-31} Three studies dealt with complicated\textsuperscript{20,32} or persistent\textsuperscript{33} diverticulitis. It was concluded that early colonoscopy is mandatory and safe. One study that compared colonoscopy with CT-colonography was excluded because not all included patients had imaging proven diverticulitis.\textsuperscript{34} Four studies appeared to meet the eligibility criteria but were excluded since they were abstracts only and not published to date.\textsuperscript{16-19} Despite inclusion of patients with CT patterns of tumor-like lesions of the sigmoid (5.5%) and sigmoid stenosis (8.3%), Alatawi \textit{et al.} found low diagnostic rates for adenomas, AA and for CRC.\textsuperscript{18} The excluded studies, which were
Routine colonoscopy after left-sided acute uncomplicated diverticulitis: a systematic review.

**Figure 2** Forest plot of the included studies and the prevalence of advanced colonic neoplasia

**Figure 3** Forest plot of the included studies and the prevalence of colorectal carcinoma
**FIGURE 4** Forest plot of the included studies and the prevalence of advanced adenoma

**FIGURE 5A** Results of the funnel plot asymmetry test for advanced colonic neoplasia; = study; | = pooled estimate line
Routine colonoscopy after left-sided acute uncomplicated diverticulitis: a systematic review.

**Figure 5C** Results of the funnel plot asymmetry test for advanced adenoma; ◼️ = study; 📊 = pooled estimate line

**Figure 5B** Results of the funnel plot asymmetry test for colorectal carcinoma; ◼️ = study; 📊 = pooled estimate line
considered a relevant addition to obtain a complete overview on current literature, are summarized in Table 4.

**TABLE 4** Characteristics of excluded studies (of which it was expected that these could be included)

<table>
<thead>
<tr>
<th>Study, year (and country)</th>
<th>Study design</th>
<th>Reason(s) for exclusion</th>
<th>No of patients</th>
<th>Type of patients</th>
<th>Age</th>
<th>ACN</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmeidat et al. 2012</td>
<td>Retrospective</td>
<td>Abstract only</td>
<td>44</td>
<td>CT-confirmed AD</td>
<td>61 (19-92)†</td>
<td>NR</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Alexanderson et al. 2012</td>
<td>Retrospective</td>
<td>Abstract only</td>
<td>118</td>
<td>CT-verified diverticulitis</td>
<td>57 (50-67)†</td>
<td>1 (0.8%)</td>
<td>0 (0%) 1 (0.8%)</td>
</tr>
<tr>
<td>Alatawi et al. 2012</td>
<td>Retrospective</td>
<td>Abstract only</td>
<td>121</td>
<td>CT diagnosis AD (in 7 tumor-like lesions)</td>
<td>62* 3 (2.4%)</td>
<td>1 (0.8%) 2 (1.6%)</td>
<td>Elective colonoscopy should be proposed only in highly selected patients with reasonable doubt on initial CT</td>
</tr>
<tr>
<td>Daker et al. 2012</td>
<td>Retrospective</td>
<td>Abstract only</td>
<td>47</td>
<td>CT confirmed diverticulitis</td>
<td>NR NR</td>
<td>1 (2.2%)</td>
<td>No support for performing a colonoscopy after clinical diverticulitis confirmed on CT</td>
</tr>
<tr>
<td>Elramah et al. 2010</td>
<td>Retrospective</td>
<td>Abstract only</td>
<td>130</td>
<td>CT confirmed diverticulitis (mass-like lesion, abscess, perforation included)</td>
<td>63.7* NR</td>
<td>3 (2.3%) NR</td>
<td>Support for routine colonoscopy, patients with a mass effect are at greatest risk</td>
</tr>
<tr>
<td>Kratt et al. 2010</td>
<td>Prospective</td>
<td>Abstract only</td>
<td>45</td>
<td>CT proven diverticulitis (19 Hinchey II, 3 stenosis/fistula)</td>
<td>NR NR</td>
<td>1 (2.2%) NR</td>
<td>Early (&lt;2 weeks) elective colonoscopy is not associated with an increased perforation risk</td>
</tr>
<tr>
<td>Lahat et al. 2008, Israel</td>
<td>Prospective</td>
<td>1. Duplicate data (Lahat et al. 2007) 2. Persistent diverticulitis</td>
<td>23</td>
<td>Persistent course of CT confirmed AD</td>
<td>NR NR</td>
<td>3 (13%) NR</td>
<td>Early colonoscopy should be considered in all patients with a protracted clinical course</td>
</tr>
<tr>
<td>Hjern et al. 2007, United States</td>
<td>Prospective comparative (control group: CTC)</td>
<td>Not all CT diagnosis (3 based on clinical signs and 3 on surgical findings instead)</td>
<td>57</td>
<td>Recent episode of acute diverticulitis</td>
<td>NR NR</td>
<td>0 (0%) NR</td>
<td>CTC reasonable alternative in the follow-up of patients with symptomatic DD</td>
</tr>
</tbody>
</table>

ACN, Advanced Colonic Neoplasia; CRC, Colorectal Carcinoma; AA, Advanced Adenoma; CT, Computed Tomography; AD, Acute Diverticulitis; NR, not reported; FU, Follow-up; CTC, CT-colonography; DD, Diverticular disease.

*Values are means (± SD).
†Values are medians (range).
DISCUSSION

The purpose of this review was to determine the prevalence of ACN as detected with colonoscopy in patients after a diagnosis of acute diverticulitis confirmed by imaging. In our systematic review the estimated pooled prevalence was 5.0% (CI: 3.8-6.7%) for ACN, 1.5% (CI: 1.0-2.3%) for CRC and 3.8% (CI: 2.7-5.3%) for AA. The overall adenoma detection rate (ADR) was 14%.

In 2012 a systematic review was published concerning colonoscopy after CT diagnosis of AD to exclude colon cancer.7 Sai et al. included ten studies of which only two met our inclusion criteria. By including patients with radiological features suspicious for neoplasia, namely atypical findings as colonic wall thickening and mass lesions, it can be expected this has resulted in a higher yield of CRC at subsequent colonoscopy. Their included studies had follow-up by surgery in most cases; colonoscopy exclusively on the other hand was the method of follow-up in only 4 studies. As a result of surgical follow-up another selection bias might have been introduced since a minority of patients needs surgery after AD. Barium enema, a follow-up method used in 2 studies, is less reliable. Full bowel preparation is needed and test performance is low: sensitivity for lesions ≥10 mm and ≥6 mm is only 48% and 35% respectively in a high-risk cohort.35 Sai et al. present an estimated pooled CRC prevalence of 2.1% (95% CI: 1.2-3.2) which is somewhat higher than 1.5% in current review. Based on a comparison with a prevalence of 0.68% as calculated in a general population in the United States, their conclusion was that there are limited data to support the recommendation to perform colonoscopy after a diagnosis of AD. Since acceptance of Sai et al.’s review in December 2011, several articles and abstracts have been published on this topic. Therefore, our systematic review can provide a more up-to-date and reliable answer.

The majority of studies included in our review were of moderate methodological quality and the pooled data with limited evidence of heterogeneity. Statistical power calculations were not done in the included studies. As a consequence, the relatively small number of patients included in the studies might cause a beta error in the conclusion that the yield of colonoscopy is equal or lower in patients after imaging proven diagnosis diverticulitis as compared to the yield in a general population, since a huge number of patients are needed to detect a significant difference.

A drawback of the available studies was the study design. Since the lack of an adequate control group in all included studies, namely a cohort of average risk healthy individuals of similar age, the main question still remains whether patients with diverticulitis have an increased ACN rate or not. To try to answer this question most studies compared their prevalence with previous published data concerning colonic screening in asymptomatic populations or with epidemiological data found in population-based registries, as we do likewise. The number of colonoscopies that has to be performed in patients with an
imaging proven diagnosis of AD to detect one extra CRC would be 122 (1/(0.015-0.0068)), based on our study's pooled prevalence of 1.5% and a general population prevalence of 0.68%.

Another important limitation of this study is selection bias in the individual studies. Firstly, in two studies the diagnosis AD was not solely made by CT but based on US as well.10,11 As a result, since this modality is more dependent on the accuracy of radiology interpretation, adverse events of AD could have been underestimated and smaller malignant lesions missed. Secondly, there is also a possibility of selection bias because the overall detection rate could have been higher in those patients with CT findings of complicated features of diverticulitis. The study of Schout et al. also included patients with intra-abdominal abscesses and reported a CRC prevalence of 2.1%.11 Lau et al. concluded that a significantly higher proportion of CRC was found in patients with abscess, local perforation, or fistula noted on the CT report compared with those without abscess.14 Elramah et al., one of the excluded studies, found that patients with a mass effect as atypical CT-finding were at greatest risk.20 Not all studies described the histological definitions of ACN and AA clearly; as a result detection bias could have been arisen. Moreover, three studies did not report on AA yield and therefore ACN prevalence could not be extracted.8,9,11

There is marked heterogeneity in types of reported data in included studies, thereby limiting the information that could be extracted. Age is an important known risk factor for developing ACN. Increasing age has a weak, but significant association with ACN detected by colonoscopy with an odds ratio of 1.06 per year (95% CI: 1.03–1.10).36 Age was reported incompletely. A higher age at colonoscopy could have led to an overestimation of our reported ACN prevalence. Lau et al., though, described that the incidence rate ratios for CRC appear much higher in the younger age group (40–64 year age group) compared with the older patients.14 Another limitation is the inability to know in which studies patients had undergone colonoscopy prior to AD since not all studies reported these data. The expected incidence rate of neoplasia may be higher in individuals who have not undergone prior colonoscopy. Furthermore, more than half of studies did not mention adverse events due to the colonoscopy, thereby limiting our ability to assess safety of colonoscopy after AD. Colonoscopy, however, is not without risk, with the most serious complication being perforation at nearly 0.1%.37 In a prospective study on early colonoscopy in complicated sigmoid diverticulitis no endoscopy-related adverse events occurred32, although in patients with diverticulitis there is a potential risk of turning a sealed perforation into a free one while performing colonoscopy.

The interpretation of this systematic report might be hampered by publication bias since all funnel plots are asymmetrical. Of several studies no publications were found but only congress abstracts. We excluded abstracts in this study since not all data can be obtained or be verified. Moreover, selective reporting never can be excluded.
Our review does not involve the possible higher life-time risk on developing CRC. There are two studies concerning the life-time relationship between diverticulitis and CRC.38,39 One describes a longitudinal, case control study in 7,159 patients with a prior diverticulitis and a follow up of at least 20 years in which they find an increased risk (OR=4.2) for left-sided CRC. The other study is a cross-sectional, retrospective study, analyzing the colonoscopy reports of complete colonoscopies and pathohistological results of all patients referred for colonoscopy in a period of 3 months in 18 hospitals in The Netherlands.39 No increased risk for polyps or CRC was found in patients with diverticulitis. Despite common aetiological factors, similar epidemiological characteristics and corresponding disease localisation between both disease entities results on a possible association are contradictory.

A meta-analysis performed in 2008 involving 68324 participants, aiming to determine the diagnostic yield of colonic evaluation in asymptomatic populations of 50 years and older, demonstrated that the overall prevalence of ACN and CRC were 5.8% (CI; 4–6%) and 0.78% (CI; 0.001–2.97%) respectively.27 Recent studies though, suggest a higher prevalence of ACN and CRC. German registries reported ACN prevalence of 7.9% in the German colonoscopy screening program40, more or less comparable with a recent Dutch invitational population-based screening program that demonstrated ACN prevalence of 8.7%.41 Quintero et al. reported an ACN rate of 10.8% in a Spanish colonoscopy screening program.42 The results of our review therefore suggest that patients with imaging proven uncomplicated AD have a prevalence of ACN less than that of the general population but a prevalence of CRC somewhat higher. A possible explanation for this remarkable finding may be the quality of the follow-up colonoscopy. First, only three studies had an adequate cecal intubation rate of ≥ 90%, as defined by Rex et al.43 Incomplete colonoscopies are not unusual in patients with diverticular disease. In patients with diverticulitis the failures mostly result from excessive pain.15 Luminal narrowing, spasm, muscular hypertrophy and fixation can be the cause of technical difficulties in intubating the sigmoid.44-46 Thus, the ACN detection rate can be underestimated in our review because of incomplete colonoscopies. This is reflected by the relatively low ADR of less than 15%. Some studies only reported the most advanced detected lesion. Our reported ADR could therefore be an underestimation of the true prevalence. Withdrawal time is a modifiable factor related to the ADR in CRC screening colonoscopies and associated with ADR. Included studies did not present their withdrawal times though.47 In most studies it was not described who performed the colonoscopy, though majority of authors is from surgical departments. Provider specialty is related to colonoscopy effectiveness; colonoscopy performed by a gastroenterologist is more likely to result in the removal of polyps than colonoscopy performed by providers who are not gastroenterologists.48 In average-risk populations, ADRs of less than 20% are associated with interval CRC.49 Therefore, quality guidelines proposed this percentage as the lower achievable limit.
The low ADR in this review suggests low quality follow-up colonoscopies and therefore an underestimation of polyp detection, as well as ACN detection. Lastly, colonoscopy is not infallible: tandem-studies have shown that 2% of large adenomas and 22% of all adenomas will be missed during colonoscopy.\(^5^0\)

The majority of included studies reported periods between AD and follow-up colonoscopy of less than 6 months. In the study of Elmi et al. though, this period was long with 5.3 years (34.8% was performed within 6 months).\(^8\) Possibly this could have resulted in a higher ACN rate due to the development of interval CRC. Indeed the CRC rate was 2.2%, being relatively high. Other included studies, apart from Westwood et al.\(^1^3\) who did not present exact data on the period, presented periods of less than 6 months. Therefore, we believe the proportion of patients who may have developed interval cancers after their diagnosis of AD to be minimal. None of studies mentioned results on serrated polyps, though these account for 10% to 20% of all CRC and more than 30% of interval cancers in average-risk individuals.\(^5^1\)

In conclusion, the available data presented in this systematic review suggest that the malignancy rate as detected with colonoscopy after imaging proven uncomplicated AD is low; the ACN rate is lower and the CRC rate somewhat higher than in asymptomatic populations. Convincing data are however lacking due to limitations of included studies, such as moderate methodological quality, lack of an adequate control group, selection bias, and low quality of colonoscopies. The available data, though limited, do not support the current recommendation to routinely perform colonoscopy after uncomplicated diverticulitis. We believe that a more refined approach to the general recommendation of colonoscopy after an imaging proven diagnosis of AD may be considered. The question arises whether follow-up colonoscopy should be targeted at higher risk patients. These might be cases with complicated diverticulitis, suspicious radiological findings, or a protracted clinical course. Patients who have not undergone age appropriate screening recently can safely undergo colonoscopy after AD, as an increased risk of adverse events has not been documented in these patients. A definitive study would require a large prospective cohort of patients with colonoscopy after an episode of AD compared with an asymptomatic screening cohort with an appropriate power analysis and colonoscopies that fulfilled the criteria as advised in colonoscopy quality guidelines.
REFERENCES


