Surgery for inflammatory bowel disease, crossing borders
Gardenbroek, T.J.

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The effect of appendectomy on the course of ulcerative colitis: a systematic review

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ABSTRACT

Background
Previous studies have shown significantly lower appendectomy rates in ulcerative colitis (UC) patients compared with healthy controls. Evidence indicating that the appendix has an immunomodulatory role in UC has been accumulating. Aim was to examine the latest evidence on the effect of appendectomy on the disease course in patients with UC.

Methods
PubMed, The Cochrane library, and EMBASE were searched. Primary end-points were number of relapses, use of steroids, number of hospital admissions and number of colectomies.

Results
The search resulted in 6 observational studies (5 case control studies and one cohort study) totalling 2532 patients. Owing to clinical heterogeneity, no meta-analysis could be conducted. One study found lower relapse rates in patients appendectomised before the onset of UC (absolute risk reduction (ARR) = 21.5%; 95% CI: 1.71% - 45.92%). Another 2 studies found a reduced requirement for immunosuppression in appendectomised patients (ARR = 20.2%; 95% CI: 9.67% - 30.46% in the first study and ARR = 21.4%; 95% CI: 10.32% - 32.97% in the second study). In addition, one study found lower colectomy rates in nonappendectomised patients (ARR = 8.7%; 95% CI: 1.29% - 18.66%), and 2 studies found lower colectomy rates in appendectomised patients (ARR = 21.4%; 95% CI: 13.17% - 28.79% in the first study and ARR = 18.7%; 95% CI: 7.50% - 29.97% in the second study).

Conclusions
There are limited and conflicting data available regarding the effect of appendectomy on the disease course of UC. Most studies suggest a beneficial effect and the minority find no, or a negative, effect.
INTRODUCTION

Ulcerative Colitis (UC) diffusely affects the colonic mucosa, and is characterized by episodes of relapse and remission. UC should be regarded as a multifactorial disease involving an interaction between genetic and environmental factors that give rise to an inappropriate immunologic response. The disease activity is confined to the colon, and almost always involves the rectum. Patients can be classified as having proctitis (disease limited to the rectum), left-sided colitis (disease activity extending to the proximal bowel but not beyond the splenic flexure), or pancolitis (disease activity extending from the rectum proximally to the cecum). Most UC patients can be treated effectively with medical therapy. When the disease is unresponsive, surgery is indicated usually in the form of restorative proctocolectomy. Up to 30%-40% of patients with UC ultimately require surgery depending on local medical culture and availability of biologic therapies. The complications of surgery have been studied in a meta-analysis.

The trigger for the development of UC is still unknown. However, cytokine imbalance and the production of inflammatory mediators by activated CD4+ T cells are considered to play an important role in the pathogenesis of UC. T-helper type 2 cells and their cytokines, particularly interleukin (IL)-4, have been suggested to enhance the development of UC. Cytokine production within the appendix has been proposed to trigger an immunological cascade in the colorectum. The appendix is therefore suggested to be a potential priming site in the development of UC.

There is growing evidence in the literature inversely linking prior appendectomy with the subsequent risk of developing ulcerative colitis. This inverse association was first reported in 1987 as an unexpected finding in a study of childhood determinants of inflammatory bowel diseases. Only when another study reported a low incidence, of 0.6%, of appendectomy in UC patients compared with an incidence of more than 25% in controls from orthopaedic clinics, did this inverse relation attract major attention. Since then, various epidemiological and case-control studies have investigated the association between appendicitis, appendectomy and the risk of developing UC.

Furthermore, a study with a T-cell receptor α-chain knockout mouse model of colitis showed that the development of inflammation was suppressed in those animals that underwent appendectomies, particularly at 3-5 weeks of age. Together with the findings that periappendiceal inflammation with a cecal patch occurs commonly as a skip lesion in UC, even in left-sided colitis, it has been suggested that the appendix is closely related to the pathogenesis of UC. The aim of this systematic review was to examine the latest evidence on the effect of appendectomy on the disease course of patients with UC.
METHODS

Search Strategy and study selection
The electronic databases PubMed, The Cochrane library, and EMBASE were searched up to 2 August 2010 by a clinical librarian. The search was performed with both keywords and MeSH terms. The search consisted of: ulcerative colitis OR colitis, ulcerative [MESH] AND (appendix OR appendectomy OR appendicectomy OR appendiceal).

Two reviewers (T.G. and E.E.) independently screened titles and abstracts for their relevance. In the event of disagreement between the two reviewers, a third reviewer (W.B.) was involved. In addition, the reference lists of all included articles were hand searched for other relevant references.

Studies designed to evaluate the effect of appendectomy on the disease course in patients with UC were included. No limits were applied to the reason for appendectomy or timing of appendectomy in UC patients. Cases were defined as patients with UC who had undergone an appendectomy at any time. Controls were defined as UC patients who had not undergone an appendectomy. Editorials and commentaries were excluded, as well as animal studies. All controlled trials and observational studies designed to investigate this effect were selected. Inclusion was not otherwise restricted by study size, language or publication type.

Outcome measures
Primary outcomes considered were the number of relapses, the number of hospital admissions, the use of steroids, and the number of colectomies. These measures were selected because of their clinical relevance. The number of relapses reflects the increase of disease activity, which can be measured in the outpatient clinic. The number of hospital admissions indicates a severe increase in activity of UC. The need for steroids is a good clinical marker for severe disease. Colectomy rates show patients with UC refractory to medical management.

Data extraction and assessment of methodological quality
Data were extracted by two reviewers independently and included the study design (cohort vs. case control), patient characteristics, total number of persons in each comparison group, disease specifications, duration of disease, medication type, potential confounders used for adjustment (e.g. smoking) and the 4 different outcome measurements compared between the appendectomised and non-appendectomised patients. Inconsistencies between the data extractions were resolved by consensus. Data reporting conformed to the Meta-Analysis of observational Studies in Epidemiology (MOOSE) group guidelines.

The methodological quality of the studies included was assessed by two reviewers independently using the Newcastle-Ottawa Scale (NOS) for assessing the quality of non-
randomised studies in meta-analyses\textsuperscript{17}, including the recruitment of cases and controls, the assessment of disease state, the description of potential confounders and other forms of potential bias. In this assessment, stars can be allocated for every item. Three broad perspectives are judged: the selection of the study groups (maximum 4 stars); the comparability of the groups (maximum 2 stars); and the ascertainment of either the exposure or outcome of interest (maximum 3 stars). The assessment of methodological quality and the data extraction was performed by two reviewers independently.

SPSS version 18.0 for Windows\textsuperscript{®} (SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis. Results for continuous data were expressed as median with range or mean $\pm$ standard deviation (SD). Results for the primary outcome measurements were expressed as absolute risk reduction (ARR) with 95\% CI.

RESULTS

A total of 359 potentially relevant titles were identified from the literature search, of which 63 were considered relevant based on title and abstract. Hereafter, 22 articles were excluded because they were commentaries, 7 articles were excluded because they did not present new data, and 23 articles were excluded because they reported on the inverse association between appendectomy and UC, not on the effect on the disease course of patients with UC.

Five articles were case reports or case series and were therefore not included in the analysis. However, the main results of these articles are shown in this review to give a complete view of all available data on this subject. One of these articles was only available in Korean; this was translated by a native speaker. A total of 6 full text articles remained for final analysis and data extraction\textsuperscript{18-23}. Details of the search are shown in Figure 1.

Description of studies

Naganuma et al.\textsuperscript{18} performed a case control study with UC patients from seven different hospitals. The studies from Radford-Smith et al.\textsuperscript{19} and Florin et al.\textsuperscript{21} collected patients with UC from a clinical database during the time-periods 1995-1999 and 1995-2002, respectively. The study of Selby et al.\textsuperscript{20} included consecutive patients from a single practice. Hallas et al.\textsuperscript{22} collected incident appendectomised UC patients from a national hospital registry during the time-period 1977-1999 and matched these patients by sex, age and age at diagnosis with UC patients who did not have had an appendectomy (controls). Each control patient was assigned an index date corresponding to the appendectomy date of the matched patient, and the disease activity of both cases and controls in the periods before and after this index date was compared. Cosnes et al.\textsuperscript{23} included a cohort of consecutive patients with UC from 1997 to 2000 and retrospectively studied the patients...
who had undergone appendectomy before disease onset and prospectively studied patients who had an appendectomy after the onset of UC.

Figure 1 Flow chart of article inclusion

Methodological quality of studies

The methodological quality of the 6 included studies is summarized in Table 1. The overall quality of the studies was moderate. Of the 6 studies, five were case-control studies and one was a cohort study. The studies varied in the selection of cases and controls. Often there was no independent validation of cases and no statement of potential selection bias. Also, differences in comparability were present. A number of studies did not report any adjustment; whereas in other studies adjustment was limited to age, sex and smoking, age, smoking status, immunosuppression and duration of disease or duration of disease alone or adjustment was extensively reported. The exposure measurement was in all studies illustrated by the statement that medical charts, national registers, interviews and/or questionnaires were used.
Table 1 Assessment of the quality of the studies using the Newcastle-Ottawa Scale (NOS)

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>Selection</th>
<th>Comparability</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naganuma et al</td>
<td>case control</td>
<td>◊</td>
<td></td>
<td>◊</td>
</tr>
<tr>
<td>Radford-Smith et al</td>
<td>case control</td>
<td>◊◊</td>
<td>◊</td>
<td>◊</td>
</tr>
<tr>
<td>Selby et al</td>
<td>case control</td>
<td>◊◊◊◊</td>
<td>◊</td>
<td>◊</td>
</tr>
<tr>
<td>Florin et al</td>
<td>case control</td>
<td>◊◊◊</td>
<td>◊</td>
<td>◊</td>
</tr>
<tr>
<td>Hallas et al</td>
<td>case control</td>
<td>◊</td>
<td>◊</td>
<td>◊</td>
</tr>
<tr>
<td>Cosnes et al</td>
<td>cohort</td>
<td>◊◊◊◊</td>
<td>◊</td>
<td>◊</td>
</tr>
</tbody>
</table>

In the assessment of methodological quality, three perspectives are judged: the selection of the study groups (maximum four points); the comparability of the groups (maximum two points); and the ascertainment of either the exposure or outcome of interest (maximum three points).

Outcome of studies

An outline of the results are shown in Table 2 and 3. Meta-analysis was not feasible because the studies were heterogeneous in terms of variation in outcome measures, timing of appendectomy and timing of measurements.

Of the four outcome measurements, Naganuma et al. studied the relapse rates of UC. In this study, a relapse was defined as hospitalization or an increase in clinical activity of UC. The study found a lower relapse rate in patients who had an appendectomy before the onset of UC (57.1%) compared with controls who had not undergone appendectomy (78.6%) (ARR = 21.5%; 95% CI: 1.71% - 45.92%).

The use of steroids in both the appendectomy and nonappendectomy patients was investigated in four of the six studies. Radford-Smith et al. and Florin et al. found a lower requirement for immunosuppression (defined as therapy with azathioprine, 6-mercaptopurine, methotrexate or mycophenolate) in the UC patients who had an appendectomy (4.8% and 5.6%, respectively) compared with the controls (25% and 27%, respectively) (ARR = 20.2%; 95% CI: 9.67% - 30.46% and ARR = 21.4%; 95% CI: 10.32%-32.97%, respectively). Selby et al. found no differences in ongoing immunosuppression requirement (defined as therapy with azathioprine, 6-mercaptopurine, or cyclosporine) between patients who had an appendectomy before onset of UC (33.3%), patients who had an appendectomy after onset of UC (12.5%) or the control group (18%). The study of Cosnes et al. found no difference in the necessity for oral steroids in the appendectomised (67%) and nonappendectomised (70%) patients.

In the study by Hallas et al., the number of hospital admissions in patients with UC before and after the appendectomy compared with hospital admissions in controls before and after the index date were reported. The number of hospital admissions in the appendectomy group was 171 before and 117 after appendectomy (a decrease of 47%). The number of admissions in the control group was 631 before and 424 after the index date (a decrease of 49%).
Table 2 Overview of included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study type</th>
<th>N patients</th>
<th>N controls</th>
<th>Appendectomy</th>
<th>Age (mean)</th>
<th>Disease localizations</th>
<th>Duration of disease</th>
<th>Medical therapy</th>
<th>Follow up</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naganuma et al.</td>
<td>Japan</td>
<td>Case-control</td>
<td>325</td>
<td>325</td>
<td>21 (6.5)</td>
<td>53 (16.3)</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Radford-Smith et al.</td>
<td>Australia</td>
<td>Case-control</td>
<td>307</td>
<td>1016</td>
<td>21 (6.8)</td>
<td>28 (8.8)</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Selby et al.</td>
<td>Australia</td>
<td>Case-control</td>
<td>259</td>
<td>280</td>
<td>12 (4.6)</td>
<td>70 (25.0)</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Florin et al.</td>
<td>Australia</td>
<td>Case-control</td>
<td>294</td>
<td>1016</td>
<td>19 (6.5)</td>
<td>275 (27.1)</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Hallas et al.</td>
<td>Denmark</td>
<td>Case-control</td>
<td>202</td>
<td>808</td>
<td>202 (8.1)</td>
<td>0</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td>19 years</td>
<td>UC patients with appendectomy after onset of UC compared to UC patients without appendectomy</td>
</tr>
<tr>
<td>Cosnes et al.</td>
<td>France</td>
<td>Cohort retrospective</td>
<td>638</td>
<td>NA</td>
<td>49 (8.0)</td>
<td>NA</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td>25 years</td>
<td>Significantly more female patients in appendectomised group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cohort prospective</td>
<td>507</td>
<td>NA</td>
<td>41 (8.1)</td>
<td>NA</td>
<td>All localizations</td>
<td>NA</td>
<td>ASA, CS, IM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are given as n, n (%) and mean ± SD. ASA, salicylates; B, biological (tumour necrosis factor-α); CS, corticosteroids; IM, immunomodulatory; NA, data not applicable. All appendectomies were performed before the onset of ulcerative colitis (UC), those with a ‡ were performed after the onset of UC.
Table 3 Outline of results of UC patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Relapse A+ patients</th>
<th>Hospital admissions A+ patients</th>
<th>Steroid use A+ patients</th>
<th>Colectomy A+ patients</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naganuma et al.</td>
<td>12 (57.1%)</td>
<td>NA</td>
<td>NA</td>
<td>1 (4.8%)</td>
<td>71 (25%)</td>
</tr>
<tr>
<td>Radford-Smith et al.</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Selby et al.</td>
<td>NA</td>
<td>NA</td>
<td>4 (33.3%)</td>
<td>43 (18.0%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Florin et al.</td>
<td>NA</td>
<td>NA</td>
<td>1 (2.5%)‡</td>
<td>74 (27%)</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Hallas et al.</td>
<td>NA</td>
<td>171/177‡</td>
<td>631/424</td>
<td>9 (4.5%)‡</td>
<td>42 (5.2%)</td>
</tr>
<tr>
<td>Cosnes et al.</td>
<td>retrospective NA</td>
<td>NA</td>
<td>NA</td>
<td>33 (67%)</td>
<td>412 (70%)</td>
</tr>
<tr>
<td></td>
<td>prospective NA</td>
<td>NA</td>
<td>NA</td>
<td>7 (14.3%)</td>
<td>33 (5.6%)</td>
</tr>
</tbody>
</table>

Data are given as n (%) unless indicated otherwise. A+, appendectomised; A-, non appendectomised; NA, data not applicable. All appendectomies were performed before the onset of UC and those with ‡ were performed after the onset of UC.
In five studies the colectomy rate was investigated. Both Selby et al.\textsuperscript{20} and Hallas et al.\textsuperscript{22} found no differences in colectomy rates between the patients who had an appendectomy before onset of UC (12.5\% and 4.5\%, respectively), patients who had an appendectomy after onset of UC (16.7\% in the study by Selby et al.) or the control group (8.8\% and 5.2\%, respectively). In the study by Cosnes et al.\textsuperscript{23} a higher proportion of appendectomised patients required colectomy (14.3\%) compared to the nonappendectomised patients (5.6\%) (ARR = 8.7\% for non-appendectomised patients; 95\% CI: 1.29\% - 18.66\%). Radford-Smith et al.\textsuperscript{19} and Florin et al.\textsuperscript{21} both found a lower colectomy rate in the appendectomy group (0\% and 5.3\%, respectively) compared to the non-appendectomy group (21.4 and 24\%, respectively) (ARR = 21.4\%: 95\% CI: 13.17\% - 28.79\% and ARR = 18.7\%: 95\% CI: 7.50\% - 29.97\%, respectively).

Case reports and case series

Two case reports and three case series have been published on the effect of appendectomy on the disease course in patients with UC (Table 4). Okazaki et al.\textsuperscript{24} described a patient with distal ulcerative colitis whose symptoms resolved after appendectomy and was asymptomatic after three years of follow up. Kim et al.\textsuperscript{25} described a patient with severe pancolitis whose symptoms decreased after appendectomy and was able to end the use of steroids.

Jarnerot et al.\textsuperscript{26} performed a pilot study on laparoscopic appendectomy in 10 patients with refractory UC. This pilot study was stopped after six patients because of the difficulties in interpreting the results caused by confounding factors. These involved difference in medication used and duration of disease. No firm conclusions were drawn by Jarnerot et al.

Jo et al.\textsuperscript{27} conducted a trial in nine patients who were compared with nine historical control patients (retrospectively matched). They found a transient decrease in the ulcerative colitis activity index (UCAI), which was only significant after 4 weeks ($P < 0.05$).

In a case series by Bolin et al.\textsuperscript{28}, 50 patients with ulcerative proctitis underwent appendectomy. The simple clinical colitis activity index (SCCAI) improved significantly from a median of nine to a median of two ($P < 0.0005$) in 40 patients (80\%). From these patients, 15 (30\%) had no need for continuing medical therapy. The SCCAI remained unchanged in 10 (20\%) of 50 patients. The initial clinical response has been maintained in 37 (93\%) of 40 patients for up to 3 years. Moreover, the appendiceal histology showed ulcerative appendicitis in 25 (50\%) patients.
### Table 4 Outline of results from case reports and case series

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>N</th>
<th>Disease localizations</th>
<th>Disease duration (range)</th>
<th>Medical therapy</th>
<th>Disease activity</th>
<th>Full resolution</th>
<th>Col.</th>
<th>FU</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okazaki et al.</td>
<td>Case report</td>
<td>1</td>
<td>Distal ulcerative colitis</td>
<td>3 years</td>
<td>None</td>
<td>Matt’s grade IV</td>
<td>1 (100)</td>
<td>0</td>
<td>3 years</td>
<td>Microscopic grade</td>
</tr>
<tr>
<td>Jamerot et al.</td>
<td>Case series</td>
<td>6</td>
<td>Refractory UC</td>
<td>Median 2.5 years (range, 4 months to 12 years)</td>
<td>ASA, CS, IM</td>
<td>NA</td>
<td>NA</td>
<td>2 (33)</td>
<td>0</td>
<td>2-4 years</td>
</tr>
<tr>
<td>Jo et al.</td>
<td>Case series</td>
<td>9</td>
<td>All localizations (mild)</td>
<td>Median 49.4 months (range, 9-168 mo.)</td>
<td>ASA, CS, T</td>
<td>UCAI 147.2 (± 29)</td>
<td>UCAI 118.8 (± 29)</td>
<td>0</td>
<td>0</td>
<td>6 months</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>Case report</td>
<td>1</td>
<td>Pancolitis</td>
<td>2 years</td>
<td>ASA, CS</td>
<td>Severe</td>
<td>Mild</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Bolin et al.</td>
<td>Case series</td>
<td>50</td>
<td>Ulcerative proctitis</td>
<td>Median 5 years (range, 8 months to 30 years)</td>
<td>ASA, CS, IM, B and T</td>
<td>SCCAI 9 (range, 7-12)</td>
<td>SCCAI 2 (range, 0-12)</td>
<td>15 (30)</td>
<td>0</td>
<td>14 months</td>
</tr>
</tbody>
</table>

Data are given as median (range), mean (± SD) or n (%). ASA, salicylates; B, biological (tumour necrosis factor-α); Col., colectomy numbers; CS, cortical steroids; FU, follow up; IM, immunomodulatory; NA, data not applicable; SCCAI, simple clinical colitis activity index; T, topical (CS or ASA); UCAI, ulcerative colitis activity index.
DISCUSSION

This review shows limited and even inconsistent data regarding the effect of appendectomy on the disease course of UC. Of the six studies, one found a lower relapse rate in patients who had an appendectomy before onset of UC. Two studies found a reduced requirement for immunosuppression in appendectomised patients. However, another 2 studies found no differences in the requirement for immunosuppression. In addition, 2 studies found no significant differences in colectomy rates between the appendectomised and nonappendectomised patients, one study actually found higher colectomy rates in appendectomised patients and 2 studies found lower colectomy rates in appendectomised patients.

The results from this systematic review show the difficulties associated with case-control and cohort studies. The methods to recruit cases and controls were different among all the studies, varying from UC cases identified in databases, consecutive UC patients from one clinic or from different hospitals, and controls from the community, from outpatient clinics or from twin databases. To establish comparability, cases and controls should be matched and/or confounders must be adjusted for in the analysis. The adjustment for confounders was insufficiently reported in all studies. Also, the median duration of follow up and median duration of disease was not always readily available.

For this review, four endpoints were chosen to identify the effect of appendectomy on the disease course of UC. At least one or more of these endpoints was investigated by the included studies. Nonetheless, the methodology was too heterogeneous and therefore it was not possible to pool the data from the studies.

Several other studies have described the effect of appendectomy on the influence of the disease course of UC. Okazaki et al. and Kim et al. both reported a case where appendectomy after UC onset beneficially influenced the clinical course of UC in a patient with distal ulcerative colitis and pancolitis, respectively. Jo et al. concluded that their period of observation was too short to conclude whether appendectomy was beneficial. They also stated that periappendiceal inflammation in UC is a consequence of UC, rather than nonspecific inflammation. This suggests that the appendix is a site possibly involved in UC. In a case series by Bolin et al., 80% of the 50 patients experienced significant improvement in clinical activity, with 30% having a complete remission of symptoms after appendectomy, without the requirement for any pharmacological treatment for up to three years of follow up. Moreover, the appendiceal histology showed ulcerative appendicitis in 25 (50%) patients. In these incident reports, one should be aware of the possible presence of publication bias because failed attempts of appendectomy as therapy for UC may not have been reported.

With the aforementioned remarks on the quality and comparability of the studies included for the review, the clinical relevance of the differences found in the studies
remains controversial. As illustrated by the prospective series published by Jarnerot et al.\textsuperscript{26} and Jo et al.\textsuperscript{27}, a major shortcoming in the studies published to date is the divergence of patients and endpoints that were analysed. The patients differed with regard to duration and localisation of the disease, the medication used and whether the appendectomy was performed before or after UC was diagnosed. In addition, different end-points were analysed in the studies, varying from histological and disease-activity end-points to the unspecific end-point of admission rate.

All these aspects make it difficult to draw conclusions, but the studies by Naganuma et al.\textsuperscript{18}, Radford-Smith et al.\textsuperscript{19}, Florin et al.\textsuperscript{21} and Bolin et al.\textsuperscript{28} do suggest that appendectomy in patients with UC may have a beneficial effect on the disease course of UC. It is evident that more rigorous and prospective data is needed. A prospective randomized trial evaluating the disease-modifying effect of appendectomy on the disease course of UC is therefore justified.
REFERENCES


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