Effects of appendicectomy on the course of ulcerative colitis

J Cosnes, F Carbonnel, L Beaugerie, A Blain, D Reijasse, J-P Gendre

Background: Appendicectomy reduces the risk of having ulcerative colitis. However, its effect on the natural history of ulcerative colitis remains uncertain.

Aim: To determine whether appendicectomy reduces the overall severity of ulcerative colitis.

Patients and methods: Appendicectomy status and smoking habits were specified by direct interview in 638 patients seen consecutively between 1997 and 2000. Severity of ulcerative colitis was assessed by reviewing therapeutic needs from the onset of colitis. Additionally, the annual incidence of flare up was assessed prospectively between 1997 and 2000 in patients who had not been colectomised.

Results: The 10 year risk of colectomy was 16 (7)% in previously appendicectomised patients (n=49) compared with 33 (2)% in non-appendicectomised patients (n=589, p=0.05). Cox regression showed that previous appendicectomy and current smoking were independent factors protecting against colectomy (adjusted hazard ratio and 95% confidence intervals: 0.40 (0.20–0.78) and 0.60 (0.40–0.95), respectively). The respective proportions of appendicectomised and non-appendicectomised patients who required oral steroids and immunosuppressive therapy were not significantly different (67% v 70% and 27% v 19%, respectively). Between 1997 and 2000, ulcerative colitis was active for 48% of the time in appendicectomised patients (47 of 98 patient years) and for 62% of the time in non-appendicectomised patients (631 of 1024 patient years; p<0.01).

Conclusion: Previous appendicectomy is associated with a less severe course of ulcerative colitis. The beneficial effect of appendicectomy on the risk of colectomy is additive to that of current smoking.

METHODS

Patient population

From January 1997 to December 2000, all consecutive patients with ulcerative colitis who attended our unit were included prospectively in the study. The diagnostic criteria for ulcerative colitis were based on the presence of at least three or four criteria after previous exclusion of infectious and neoplastic disease: typical case history with diarrhoea and/or blood and/or pus in the stools for more than a week in repeated episodes; typical findings on sigmoidoscopy with granulated friable mucosa with or without ulcerations of the mucosa; histological and/or cytological signs of inflammation of the mucosa; and radiological or colonoscopic signs of inflammation with a spiculated granulated inner surface of the colon proximal to the rectum and/or frank ulcerations.

Appendicectomy status and smoking habits

Appendicectomy and smoking status were specified during direct interview of the patient. Patients were classified as previously appendicectomised if appendicectomy had been performed prior to the diagnosis of colitis. They were classified as current smokers if they were smoking more than seven cigarettes per week for at least six months when ulcerative colitis was diagnosed.

Characteristics of colitis

The characteristics of colitis were completed according to retrospective analysis of medical charts. The onset of colitis, designated as the time of diagnosis, was defined as the date of first detection of unequivocal inflammatory abnormalities of the rectum, as assessed by endoscopic observations. The initial extent of colitis was determined by colonoscopy in most patients seen after 1975 whereas a few patients had only barium enema initially. After diagnosis, patients were followed clinically with 3–4 visits per year, and only investigated again in case of flare up or development of new symptoms. Morphological investigations included proctosigmoidoscopy, colonoscopy, and barium enema. The cumulative extent of colitis was established from the results of the latest colonoscopy performed from 1997. Isolated perianal inflammatory changes were not considered as a marker of extensive disease.

Treatment policy

Therapy was based on the principles of maintenance treatment with sulphasalazine or mesalamine, and treatment of flare up episodes with mesalamine or prednisolone enemas, increased oral mesalamine or sulphasalazine, or systemic glucocorticoids starting at 1 mg/kg/day prednisolone for 3–4 weeks, tapering off over a period of 1–2 months, and then withheld for a few weeks. When the flare up was severe or could not be controlled by this regimen, patients received...
intensive intravenous treatment according to Truelove and Jewell. Indications for colectomy were failure of intensive intravenous treatment, protracted dependence on oral steroids, and cancer or dysplasia detected during colonoscopic surveillance. Immunosuppressive therapy was rarely prescribed before 1995. Since then, cyclosporin has been used in some cases after failure of intensive intravenous treatment and azathioprine has been proposed in some patients who had a severe attack which responded to cyclosporin and in those who were steroid dependent.

Severity of ulcerative colitis

Overall severity of disease was assessed in several ways. Firstly, the colectomy rate, the time from diagnosis to colectomy, need for systemic steroids, and need for immunosuppressive therapy were assessed prospectively. Secondly, patients who were steroid dependent. A severe attack which responded to cyclosporin and in those who had undergone appendicectomy before the age of 20 years. As median age of 11 years (range 6–43). Thirty five patients had undergone appendicectomy after diagnosis were included in the non-appendicectomised at diagnosis. Patients who were appendicectomised after diagnosis were included in the non-appendicectomised group until the time when they underwent appendicectomy. When analysing the respective effects of appendicectomy and current smoking, current smokers at diagnosis were included in the smokers group until the time when they stopped smoking, and non-smokers or former smokers were included in the non-smokers group until the time when they started or resumed smoking. For actuarial analysis, the Kaplan-Meier model was used, with the date of diagnosis as the starting point. The curves were compared using the log rank test. Multivariate analyses were performed with Cox proportional hazards regression to adjust for confounding. All baseline variables suspected as possible predictors of colectomy (young age (<20 years), old age (>40 years), sex, ethnicity (Caucasian or not), diagnosis after 1995, familial history, extraintestinal manifestations, initial extent of colitis, smoking status, and previous appendicectomy) were entered into the model. Diagnosis after 1995 was retained as a variable because the use of immunosuppressive therapy became widespread only after this date. Results of analysis are presented as hazard ratios with 95% confidence intervals (CIs). Calculations were performed using GB-stat statistical software.

RESULTS

Effect of previous appendicectomy

Among 638 patients with ulcerative colitis, 49 patients (8%) had undergone appendicectomy before disease onset. Appendicectomy had been performed one month to 66 years (median 17 years) before diagnosis of ulcerative colitis, at a median age of 11 years (range 6–43). Thirty five patients had undergone appendicectomy before the age of 20 years. As
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Figure 1 Cumulative percentage of patients requiring colectomy according to previous appendicectomy. Numbers above the curve indicate the number of patients at risk at the various intervals.

Figure 2 Cumulative percentage of patients requiring colectomy, according to current smoking and previous appendicectomy. Numbers above the curve indicate the number of patients at risk at the various intervals.

Table 4 Predictors of colectomy according to multivariate Cox analysis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Adjusted relative risk</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>0.60</td>
<td>0.40–0.95</td>
<td>0.03</td>
</tr>
<tr>
<td>Previous appendicectomy</td>
<td>0.40</td>
<td>0.20–0.78</td>
<td>0.01</td>
</tr>
<tr>
<td>Left colon lesions</td>
<td>2.41</td>
<td>1.69–3.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sigmoid lesions</td>
<td>1.69</td>
<td>1.05–2.70</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 5 Effect of previous appendicectomy and current smoking on medical therapeutic needs during the course of ulcerative colitis

<table>
<thead>
<tr>
<th></th>
<th>Non-appendicectomised</th>
<th>Appendicectomised</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-smokers</td>
<td>Smokers</td>
</tr>
<tr>
<td>Duration of disease (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.8(8.1)</td>
<td>7.7(7.7)</td>
<td>9.7(7.0)</td>
</tr>
<tr>
<td>No requiring oral glucocorticoids</td>
<td>345</td>
<td>65</td>
</tr>
<tr>
<td>Relative risk</td>
<td>0.88</td>
<td>0.98</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.75–1.03</td>
<td>0.80–1.20</td>
</tr>
<tr>
<td>No requiring intensive intravenous treatment</td>
<td>44</td>
<td>47</td>
</tr>
<tr>
<td>Relative risk</td>
<td>0.66</td>
<td>1.07</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.48–0.91</td>
<td>0.76–1.50</td>
</tr>
<tr>
<td>No requiring immunosuppressive therapy</td>
<td>101</td>
<td>9</td>
</tr>
<tr>
<td>Relative risk</td>
<td>0.42</td>
<td>1.23</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.22–0.79</td>
<td>0.72–2.10</td>
</tr>
</tbody>
</table>

*Significantly different (p<0.05) from non-appendicectomised non-smoker group.
patient years) compared with 62% in non-appendicectomised patients (631 of 1024 patient years; p<0.01).

DISCUSSION

The present results show that previous appendicectomy has a beneficial effect on the course of ulcerative colitis. Appendicectomy patients had a less marked year by year disease activity and a decreased risk of colectomy. This effect was independent of confounding factors and additive to that of current smoking.

We believe that retrospective collection of data did not alter the results of our study. Selection bias was minimal as we did not use a postal questionnaire but included prospectively all consecutive patients seen over a four year period. The criteria used to assess the severity of disease were objective and based on therapeutic needs. In particular, the main outcome measure was colectomy, which is an unequivocal marker of the severity of ulcerative colitis, even retrospectively. The recent introduction of immunosuppressive therapy may not have influenced the results because it was used with a similar frequency in appendicectomised and non-appendicectomised patients. Likewise, the decreased colectomy rate we observed in appendicectomised patients was not a result of differences in cumulative extension of colitis which did not differ significantly in the two groups, a finding similar to that of Reif and colleagues. Finally, the proportion of our patients who had undergone appendicectomy previously to ulcerative colitis onset was relatively high compared with other series but it must be kept in mind that, for unknown reasons, the frequency of appendicectomy in childhood is especially high in France. In a recent case controlled study, Uzan and colleagues reported an appendicectomy rate of 8% in ulcerative colitis patients, similar to that of the present series and significantly less than 31% in age and sex matched controls.

The beneficial effect of previous appendicectomy on the course of ulcerative colitis was somewhat expected. The protective effect of appendicectomy on the development of ulcerative colitis is well documented and the appendix is recognised as a possible important site for priming of the cells involved in the development of ulcerative colitis. Appendiceal inflammation is observed in half of colectomy specimens from involved in the development of ulcerative colitis. Appendiceal inflammation is observed in half of colectomy specimens from involved in the development of ulcerative colitis. Appendiceal inflammation is observed in half of colectomy specimens from involved in the development of ulcerative colitis. Appendixes with ulcerative colitis are more frequently associated with acute appendicitis and the appendix is recognised as a possible important site for priming of the cells involved in the development of ulcerative colitis, even retrospectively. The recent introduction of immunosuppressive therapy may not have influenced the results because it was used with a similar frequency in appendicectomised and non-appendicectomised patients. Likewise, the decreased colectomy rate we observed in appendicectomised patients was not a result of differences in cumulative extension of colitis which did not differ significantly in the two groups, a finding similar to that of Reif and colleagues. Finally, the proportion of our patients who had undergone appendicectomy previously to ulcerative colitis onset was relatively high compared with other series but it must be kept in mind that, for unknown reasons, the frequency of appendicectomy in childhood is especially high in France. In a recent case controlled study, Uzan and colleagues reported an appendicectomy rate of 8% in ulcerative colitis patients, similar to that of the present series and significantly less than 31% in age and sex matched controls.

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Gut 2002 51: 803-807
doi: 10.1136/gut.51.6.803

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