Efficacy of hydrostatic balloon dilatation of anastomotic Crohn’s disease strictures

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Introduction
The cumulative risk of a first surgical procedure five years after diagnosis of Crohn’s disease is to the order of 50% [1-3]. After surgery, there is also a risk of postoperative recurrence. Endoscopic recurrence is noted early and precedes symptomatic recurrence and surgical recurrence: prospective studies have shown that the rate of endoscopic recurrence is to the order of 77%-85% three years after surgical resection considered curative [4, 5]. Recurrence is generally observed at the anastomosis or in the pre-anastomotic ileum after ileocolonic anastomosis, it can also occur above the anastomosis in patients with colocolonic anastomosis [6]. After a postoperative follow-up of three years or more, 50% of patients present anastomotic stricture [6]. The cumulative rate of revision surgery for postoperative recurrence, principally because of anastomotic stricture, is about 20% at five years [7-10]. Hydrostatic dilatation (HD) has been used for about fifteen years as an alternative to surgical treatment of anastomotic stricture in Crohn’s disease [11]. Data are however scarce on long-term outcome and the usefulness of associating medical treatment of Crohn’s disease with HD [12-21]. The purpose of this retrospective analysis was to evaluate the effects of HD associated with medical treatment in Crohn’s disease patients with symptomatic anastomotic stricture.

Patients and methods

Inclusion criteria
The diagnosis of anastomotic stricture of Crohn’s disease was established at endoscopy performed in patients with symptoms of intestinal obstruction: acute abdominal pain, Koeing syndrome, obstructive syndrome, associated with radiological signs of intestinal stricture (air levels, stricture on barium study). Endoscopic stenosis was defined as a narrow portion of the intestinal lumen which could not be crossed with the endoscope. Standard 13.6 mm endoscopes were used.

Results — HD failed in 3 patients (19%). Thirty-two HD are performed in the other 13 (1 HD: 6; 2 HD: 2; > 2 HD: 5). No severe complication was observed. Eight patients received immunosuppressive treatment started before the first HD in 4 cases or following the second HD in 4 cases. Based on actuarial analysis, clinical and surgical recurrence rates were 39% and 0% at 1 year and 73% and 12% at 2 years, respectively. Time between the first and the second HD were not statistically different (P = 0.24) for HD performed with (11.5 ± 8.8 months; range: 5-30) or without (8.0 ± 6.9 months; range: 2-17) immunosuppressive treatment.

Conclusion — HD delays the surgical timing for anastomotic Crohn’s disease strictures. Medical treatment associated with HD does not seem to modify the duration of the clinical remission.

Between September 1997 and June 2002, 16 patients (8 men, 8 women, mean age 44 years) underwent at least one attempted HD of an anastomotic stricture of Crohn’s disease. Patient characteristics are presented in table 1. In 11 of the 16 patients, the indication for surgery was fistulizing Crohn’s disease. Initial resection of Crohn’s disease lesions was completed in all patients who all presented endoscopic signs of recurrence. Twelve of the 16 patients presented ulceration of the colonic portion of the anastomosis. Four patients free of colonic ulceration presented intestinal ulcerations distant from the anastomosis.

Hydrostatic dilatation technique
HD was performed under general anesthesia (Diprivan®) in all patients after preparation with polyethylene glycol given orally. The stenosis was catheterized with a Microvasive Rigiflex TTS® balloon (Boston Scientific) measuring 15 or 20 mm in diameter. The balloon was inflated with water under manometric control. A guidewire was used to facilitate catheterization if needed. A 20-mm balloon measuring 5 to 8 mm in length was used for most of the patients. Maximal pressure was maintained for two periods with a total duration of 2 to 3 minutes. HD was considered successful if the balloon could be inserted and dilated to a diameter greater than or equal to 10 mm, whether the endoscope could pass through or not. If the stenosis could not be catheterized, HD was considered to have failed. The patient was discharged the evening of the procedure or the next morning unless there were complications.

Medical treatment associated with HD
Immunosuppressor treatment could be continued or instituted at the first HD in the event of early postoperative recurrence or steroid independence if steroid resistance had developed since surgery. Immunosuppressor treatment was given systematically if the patient underwent a second HD; treatments were adapted to efficacy and tolerance of prior immunosuppressors. Corticosteroid treatment (prednisone, budesonide, or bethametasone for patients with intestinal obstruction) was generally prescribed before the first HD and generally continued for 4 to 8 weeks after the first HD independently of the endoscopic findings. Corticosteroid treatment was not usually proposed in association with subsequent HD.

Patient follow-up
All patients were seen 1 to 2 months after HD, then as needed for routine care. HD was considered effective if the clinical signs of obstruction resolved. In the event of clinical recurrence, defined as resumption of the initial clinical signs after a symptom-free period, a new endoscopy

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Summary
Objectives — To estimate the efficacy of hydrostatic balloon dilatation (HD) of anastomotic stricture of Crohn’s disease and the impact of medical treatment on the duration of HD effects.

Methods — Sixteen patients with anastomotic stricture (average length: 4.7 cm) were treated by HD and followed-up for a median duration of 24 months. Immunosuppressive treatment was given when a second HD was necessary.

Results — HD failed in 3 patients (19%). Thirty-two HD are performed in the other 13 (1 HD: 6; 2 HD: 2; > 2 HD: 5). No severe complication was observed. Eight patients received immunosuppressive treatment started before the first HD in 4 cases or following the second HD in 4 cases. Based on actuarial analysis, clinical and surgical recurrence rates were 39% and 0% at 1 year and 73% and 12% at 2 years, respectively. Time between the first and the second HD were not statistically different (P = 0.24) for HD performed with (11.5 ± 8.8 months; range: 5-30) or without (8.0 ± 6.9 months; range: 2-17) immunosuppressive treatment.

Conclusion — HD delays the surgical timing for anastomotic Crohn’s disease strictures. Medical treatment associated with HD does not seem to modify the duration of the clinical remission.

The full text of this article is available in English on the web on www.e2med.com
was proposed for a second HD procedure if the patient presented anasto-
omatic stricture. We noted time to clinical recurrence and time to surgi-
cal recurrence (defined as surgical resection of the stenosis) from data
collected at consultation or by telephone interview. Data collection was
terminated in June 2002.

Statistical analysis

Kaplan-Meier survival curves were calculated for time to clinical
recurrence and time to surgical recurrence. The effect of associated
medical treatment was evaluated with Student’s t test comparing times to
recurrence and time to surgical recurrence. The effect of associated
immunosuppressor treatment. Results are expressed as mean ±
standard deviation.

Results

HD could not be performed in three patients (19%) (patients
n° 12, 13, 14) because the stenosis could not be catheterized or
the balloon could not be introduced. The anastomosis was ulcer-
ated in one of these three patients who all underwent intestinal
resection. The characteristic features of the 13 patients who had
at least one HD are summarized in table II. Mean length of the
anastomotic stricture was 4.7 cm. These 13 patients underwent
32 HD procedures (mean 2.5 per patient, range 1-8). Six
patients (46%) had one HD, 2 (15%) had two, and 5 (39%) had
more than two. One patient (n° 12) underwent two HD of supple-
mentary strictures situated above the anastomosis. After HD, the
endoscope passed through correctly in 30 of 32 attempts
(93.7%). There were no complications (perforation, hemor-
rhage). One patient developed a painful abdomen with no signs of
peritoneal involvement which resolved 24 hours after the HD.

Among the 13 patients who had at least one HD, recurrent
symptoms were observed in 39% and 73% one and two years
after the first HD (figure 1). The rate of technical efficacy, defined
as the absence of surgical treatment during the follow-up period,
was 100% at one year and 88% at two years (figure 1). One
patient (n° 4) underwent surgery 21 months after a first HD for
an ulcerated stricture of an ileocolonic anastomosis.

Eight patients started immunosuppressor treatment before or
after the first HD (N = 4 patients) or second HD (N = 4 patients).
Drugs used were azathioprine (2 mg/kg/d, N = 7 patients), later
replaced by mofetil mycophenolate (1 g/d) in one and by meth-
otrexate (25 mg/week) in another. Among the five patients who
were not given immunosuppressor treatment, four had had one
HD and the fifth (n° 10) was given successively azathioprine,
methotrexate, and ciclosporin, with no effect. Globally, 19 of the
32 HD were performed in association with immunosuppressor
treatment (azathioprine, N = 17). Time between the first and sec-
ond HD was not statistically different (P = 0.24) between patients
undergoing HD with or without immunosuppressor treatment
(11.5 ± 8.8 months, range 5-30 versus 8.0 ± 6.9 months, range
2-17).

Discussion

With the exception of two studies [14, 16], all reports on HD
of strictures in Crohn’s disease patients have been retrospective
analyses. Like our study, most reports have included a small
number of patients [11-21]. We limited our analysis to anasto-
omatic strictures diagnosed in patients with symptoms suggestive of
intestinal obstruction which did not respond to short-term corti-
coesteroid therapy; this type of patient would appear to be the best
candidate for HD [14]. We considered that Crohn’s disease was

Table 1. – Patient characteristics.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Number of operations</th>
<th>Time from diagnosis to surgery (months)</th>
<th>Type of surgery</th>
<th>Indication for surgery</th>
<th>Site of stricture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>M</td>
<td>1</td>
<td>72</td>
<td>Ileocolic</td>
<td>Peritonitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>M</td>
<td>1</td>
<td>10</td>
<td>Ileocolic</td>
<td>Peritonitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>F</td>
<td>1</td>
<td>96</td>
<td>Subtotal ileocolonectomy</td>
<td>Abscess</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>F</td>
<td>1</td>
<td>4</td>
<td>Ileocolic</td>
<td>Small bowel obstruction</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>F</td>
<td>1</td>
<td>48</td>
<td>Total ileocolonectomy</td>
<td>Resistant to medical treatment</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>6</td>
<td>77</td>
<td>M</td>
<td>1</td>
<td>36</td>
<td>Rectosigmoidectomy</td>
<td>Sigmoid ileal fistula</td>
<td>Colorectal</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>F</td>
<td>1</td>
<td>0</td>
<td>Right ileocolonectomy</td>
<td>Appendicitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>8</td>
<td>45</td>
<td>F</td>
<td>1</td>
<td>214</td>
<td>Left colectomy</td>
<td>Resistant to medical treatment</td>
<td>Colorectal</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>M</td>
<td>1</td>
<td>36</td>
<td>Ileocolic</td>
<td>Ileocolic and ileal fistula</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
<td>F</td>
<td>2</td>
<td>60/121</td>
<td>Ileocolonectomy/anastomotic resection</td>
<td>Ileocolic fistula</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>M</td>
<td>2</td>
<td>0/36</td>
<td>Right hepatico/duodenal and jejunal resection</td>
<td>Appendicitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>12</td>
<td>33</td>
<td>M</td>
<td>1</td>
<td>72</td>
<td>Right ileocolonectomy</td>
<td>Abscess</td>
<td>Ileocolic and ileal fistula</td>
</tr>
<tr>
<td>13</td>
<td>35</td>
<td>M</td>
<td>1</td>
<td>0</td>
<td>Right ileocolonectomy</td>
<td>Abscess</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>14</td>
<td>51</td>
<td>M</td>
<td>1</td>
<td>36</td>
<td>Ileocolonectomy</td>
<td>Carcinoind fistula</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>F</td>
<td>1</td>
<td>0</td>
<td>Right ileocolonectomy</td>
<td>Appendicitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>16</td>
<td>50</td>
<td>F</td>
<td>1</td>
<td>60</td>
<td>Ileocolonectomy</td>
<td>Ileocolic fistula</td>
<td>Ileocolic</td>
</tr>
</tbody>
</table>
Efficacy of hydrostatic balloon dilatation of anastomotic Crohn’s disease strictures

Table II. Characteristics of patients treated by hydrostatic dilatation.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Length of stricture (cm)</th>
<th>Ulcerations of stricture</th>
<th>Time from surgery to first HD (months)</th>
<th>Medical treatment</th>
<th>Number of HD</th>
<th>Follow-up after HD (months)</th>
<th>Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>-</td>
<td>62</td>
<td>Aza (2)</td>
<td>4</td>
<td>30</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>+</td>
<td>120</td>
<td>Aza (2)</td>
<td>3</td>
<td>36</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>+</td>
<td>113</td>
<td>Aza then MMF (2)</td>
<td>3</td>
<td>27</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>-</td>
<td>8</td>
<td>MTX (1)</td>
<td>1</td>
<td>21 (surgery)</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>-</td>
<td>98</td>
<td>Aza (2)</td>
<td>8</td>
<td>53</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>-</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>+</td>
<td>174</td>
<td>0</td>
<td>Pred</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>-</td>
<td>5</td>
<td>Aza (1)</td>
<td>0</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>+</td>
<td>145</td>
<td>Aza (1)</td>
<td>0</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>+</td>
<td>2</td>
<td>0</td>
<td>Pred</td>
<td>4</td>
<td>54</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>+</td>
<td>73</td>
<td>0</td>
<td>Pred</td>
<td>1</td>
<td>47</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>+</td>
<td>48</td>
<td>Aza (1)</td>
<td>Bud</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>13</td>
<td>6</td>
<td>+</td>
<td>12</td>
<td>0</td>
<td>Bud</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

Note: data not available
Aza: azathioprine; MMF: myofetil mycofenolate; MTX: methotrexate; Pred: prednisone; Bud: budenoside
(1) or (2): treatment given during first or second hydrostatic dilatation (HD)

active in all of our patients at the time of HD and that the anastomotic strictures signaled disease recurrence [6]. The goal was a high rate of technical success of HD, in terms of preventing surgical recurrence, which reached 100% at one year and 88% at two years in our patients. Success rates reported by others are difficult to compare with ours due to technical differences: reports of HD for anastomotic and spontaneous stricture without distinguishing the results, imprecision of failure criteria (particularly surgery for anastomotic and spontaneous stricture without distinguishing between anastomotic and spontaneous recurrence), reporting of the results, imprecision of failure criteria (particularly surgery after one or two HDs), variable associated medical treatment (systemic or local corticosteroids, immunosuppressors), expression of results. Three studies have reported actuarial survival curves taking surgical recurrence as the end point. For Sabat et al. [20] the rate of successful HD in terms of prevention of surgical recurrence was 71% and 63% at one and two years respectively. Couckuyt et al. [14] reported corresponding figures of 75% and 43%. In their controlled study, Rassler et al. [16] found a 20% rate of surgical recurrence at one year when HD was associated with azathioprine and budesonide and 33% when associated with placebo (P = 0.02). The patients in these three studies, like ours, required repeated HD to delay surgery. The rate of clinical recurrence after a single HD was 39% and 73% at one and two years respectively. The mean duration of clinical remission after one HD was about one year. This relatively short remission, particularly in comparison with that obtained after surgical treatment, is the main limitation of the method. It would however be rational to propose repeated HD when the treatment is effective in patients with a high risk of short bowel and for patients who develop early postoperative recurrence. For other patients requiring several repeated HDs in a short period of time, surgical treatment should probably be proposed since remission is usually longer. The number of HD procedures has varied from 1 to 18 in published series [21]. In the two largest series, only 26% [19] and 33% [14] of patients had more than one HD. In our series, 54% of patients had one HD, a possible expression of better results in terms of preventing surgical recurrence.

We did not find that associating medical treatment with HD significantly affected the duration of clinical remission. Unlike the results reported by Rassler et al. [16], our data did not show longer clinical remission after HD in patients given immunosuppressor treatment, but our methodology limits any conclusions concerning the possible benefit of immunosuppressor treatment. Furthermore, because of the small number of patients, and considering the rank effect of the HD, we could not compare remission times after a first and second HD as a function of associated treatment. We decided to introduce immunosuppressors only in patients who experienced recurrence rapidly, which introduces another bias against a favorable effect of immunosuppressor treatment. Most of our patients who did not receive immunosuppressors after the first HD did not experience recurrence during the follow-up period. Sabat et al. [20] were also unable to demonstrate any benefit of immunosuppressor treatment in 32 patients given immunosuppressors in association with HD. Nevertheless, they reported retrospective results which may have included patients with more severe Crohn’s disease and possibly higher risk of early recurrence. It would be of interest to assess the usefulness
of giving azathioprine, which has a demonstrated beneficial effect in Crohn’s disease, in association with HD in a prospective study. The report by Raedler et al. [16] is still not available in full article five years after publication of the abstract. Azathioprine and its derivatives are generally considered as effective treatment for the prevention of postoperative recurrence. In a controlled therapeu tic trial enrolling 131 operated patients followed for two years, the efficacy of azathioprine (50 mg/d) was significa ntly superior to that of placebo for the prevention of endoscopic and clinical recurrence [22]. In a recent retrospective study [23], 38 patients with Crohn’s disease were treated with azathioprine for the prevention of postoperative recurrence. The probability of clinical relapse was 9%, 16% and 28% at 1, 2 and 3 years respectively. These relapse rates are lower than usually reported [7-10]. Our study does not provide any evidence in favor of a beneficial effect of systemic corticosteroids in this indication. We have been unable to find any data concerning a possible benefi cial effect of systemic corticosteroids after HD. The only data avail able concern local injections [15, 17-19]. These studies reported results for 6 to 13 patients followed for 3 to 73 months and found a long-term success rate of 100%. Nevertheless, the superiority of this technique over simple HD is not established because none of these studies included a control group.

The technical aspects of HD have not been standardized, particularly the duration of the dilatation and the minimal diamet er necessary for successful HD. Passing a colonoscope through the stricture after HD is probably a good way to determine the effi cacy of the HD. Couckuyt et al. [14] observed that for other reports, the rates have varied from 45% to 73% [14, 20, 21]. The rate of technical failure has ranged from 0 to 29% and, as in our series, has generally been due to inability to catheterize a very tight stenosis or to an angle preventing introduction of the balloon. The length of the stricture was not a cause of failure but most of our anasto motic strictures were relatively short (4.7 cm on average). Longer strictures to the order of 20 cm have been dilated successfully by others [14, 17]. All of our failures were observed in our first HD procedures (19% of patients). We did not note any particular technical problem for repeated HD. In our patients, the presence of ulc erations at the level of the stricture did not appear to be a cause of failure. Similarly, there is no evidence of relationship between disease activity and long-term success of HD [14].

The risk of complications appears to be limited. In series reporting more than 10 patients [13, 14, 20, 21], the complication rate has varied from 0% to 16%. The most common complica tions are perforation (about 3%) [13, 14, 20], which requires surgery in about one out of two cases. Digestive bleeding is usually benign and has been observed in 0 to 7.5% of patients [14, 20].

In conclusion, hydrostatic dilatation of anastomotic strictures in patients with Crohn’s disease is a safe and effective method. It can retard the need for surgery which can be avoided in the mid term. The procedure must be repeated in most patients to obtain sustained results. The supplementary benefit of associating immunosuppressor treatment remains a question of debate. HD can be recommended for the first-intention treatment of anastomotic strictures in Crohn’s disease, particularly in patients who do not respond to corticosteroid treatment and who have a risk of short bowel syndrome.

REFERENCES