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 of 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, obstruction: acute abdominal pain, Koenig syndrome, obstructive syndrome). 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, obstruction: acute abdominal pain, Koenig syndrome, obstructive syndrome). Endoscopic stenosis was defined as a narrow portion of the intestinal lumen which could not be crossed with the endoscope (stenosis on barium study). Hydrostatic dilatation (HD) of anastomotic strictures of Crohn’s disease and the impact of medical treatment on the duration of HD effects were evaluated. Endoscopic stenosis was defined as a narrow portion of the intestinal lumen which could not be crossed with the endoscope (stenosis on barium study). HD was considered effective 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 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.

SUMMARY

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

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 fulminating 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 initiated at the first HD in the event of early postoperative recurrence or steroid dependence 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 beclomethasone 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...
Results

HD could not be performed in three patients (19%) (patients n° 14, 15, 16) because the stenosis could not be catheterized or the balloon could not be introduced. The anastomosis was ulcerated 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 two or more. One patient (n° 12) underwent two HD of supplementary strictures situated above the anastomosis. After HD, the endoscope passed through correctly in 30 of 32 attempts (93.7%). There were no complications (perforation, hemorrhage). One patient developed a painful abdomen with no signs of peritoneal involvement which resolved 24 hours after the HD. Median follow-up after the first HD was 24 months (8-54). None of the patients were lost to follow-up.

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 (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 methotrexate (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 second HD was not statistically different (P = 0.24) between patients undergoing HD with or without immunosuppressor treatment (11.3 ± 8.8 months, range 5-30 versus 8.0 ± 6.9 months, range 2-17).

Discussion

With the exception of two studies [14], 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 anastomotic strictures diagnosed in patients with symptoms suggestive of intestinal obstruction which did not respond to short-term corticosteroid therapy: this type of patient would appear to be the best candidate for HD [14]. We considered that Crohn’s disease was

Table I – 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>Ileectomy</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>Ileectomy</td>
<td>Peritonitis</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>3</td>
<td>58</td>
<td>F</td>
<td>1</td>
<td>96</td>
<td>Subtotal ileectomy</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>Ileectomy</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 ileectomy</td>
<td>Resistance 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>Sigmoïd-bladder fistula</td>
<td>Colorectal</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>F</td>
<td>1</td>
<td>0</td>
<td>Right ileocectomy</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>Resistance 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>Ileectomy</td>
<td>Ileocolic and ileal (5 and 10 cm)</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
<td>F</td>
<td>2</td>
<td>60/121</td>
<td>Ileectomy/anastomosis resection</td>
<td>Fistral stenosis/anastomotic stricture</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>M</td>
<td>2</td>
<td>0/36</td>
<td>Right ileocolonic/transverse and jejunal resection</td>
<td>Appendicitis/pyocolecolic fistula</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>12</td>
<td>33</td>
<td>M</td>
<td>1</td>
<td>72</td>
<td>Right ileocectomy</td>
<td>Abscess</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>13</td>
<td>35</td>
<td>M</td>
<td>1</td>
<td>0</td>
<td>Right ileocectomy</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>Ileectomy</td>
<td>Caecosigmoid fistula</td>
<td>Ileocolic</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>F</td>
<td>1</td>
<td>0</td>
<td>Right ileocectomy</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>Ileectomy</td>
<td>Ileal stenosis</td>
<td>Ileocolic</td>
</tr>
</tbody>
</table>

was proposed for a second HD procedure if the patient presented anastomotic stricture. We noted 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 medical treatment (azathioprine, N = 17). Time between the first and second HD was not statistically different (P = 0.24) between patients undergoing HD with or without immunosuppressor treatment (11.3 ± 8.8 months, range 5-30 versus 8.0 ± 6.9 months, range 2-17).

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 medical treatment (azathioprine, N = 17). Time between the first and second HD was not statistically different (P = 0.24) between patients undergoing HD with or without immunosuppressor treatment (11.3 ± 8.8 months, range 5-30 versus 8.0 ± 6.9 months, range 2-17).

Discussion

With the exception of two studies [14], 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 anastomotic strictures diagnosed in patients with symptoms suggestive of intestinal obstruction which did not respond to short-term corticosteroid therapy: this type of patient would appear to be the best candidate for HD [14]. We considered that Crohn’s disease was
Table II – Characteristics of patients treated by hydrostatic dilatation.

Table:<br>
<table>
<thead>
<tr>
<th>Patients</th>
<th>Length of stricture (cm)</th>
<th>Ulcersations 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></td>
<td></td>
<td></td>
<td></td>
<td>Immunosuppressors</td>
<td>Steroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>na</td>
<td>+</td>
<td>62</td>
<td>Aza (2)</td>
<td>Bus</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>+</td>
<td>120</td>
<td>Aza (2)</td>
<td>Pred</td>
<td>3</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>+</td>
<td>113</td>
<td>Aza from MMF (2)</td>
<td>Bus</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>na</td>
<td>+</td>
<td>8</td>
<td>MTX (1)</td>
<td>Pred</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>-</td>
<td>98</td>
<td>Aza (2)</td>
<td>Pred</td>
<td>8</td>
<td>53</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>na</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>
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<tr>
<td>11</td>
<td>5</td>
<td>+</td>
<td>73</td>
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</tr>
<tr>
<td>12</td>
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<td>+</td>
<td>48</td>
<td>Aza (1)</td>
<td>Bus</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>13</td>
<td>6</td>
<td>+</td>
<td>12</td>
<td>0</td>
<td>Bus</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

use: data not available
Aza: azathioprine; MMF: mofetil mycofenolate, MTX: methotrexate; Pred: prednisone; Bus: 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 after one or two HD), variable associated medical treatment (systemic or local corticosteroids, immunosuppressors), expression of the results. Three studies have reported actuarial survival curves taking surgical recurrence as the end point. Sabat et al. [20] reported figures of 75% and 43%. In their controlled study, Raedler et al. [16] found a 20% rate of surgical recurrence at one year when HD was associated with azathioprine and budenoside 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 Raedler et al. [16], our data did not show a 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 HD in such patients.
of giving azathioprine, which has a demonstrated beneficial effect in Crohn’s disease, in association with HD in a prospective study. The report by Raeder et al. [14] is still not available in full article form 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 thera-
peutic trial enrolling 131 operated patients followed for two years, the efficacy of azathioprine (50 mg/d) was signifi-
cantly 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 diame-
ter 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 when the stric-
ture could be crossed after HD, clinical remission was significantly longer (P = 0.007). We were able to pass through the stricture in 93.7% of our patients. For other reasons, 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 gen-
erally 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 ulcerations 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 complica-
tion rate has varied from 0% to 16%. The most common complica-
tions are perforation (about 5%) [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 associated immunosuppressant treatment remains a question of debate. HD can be recommended for the first-intention treatment of anasto-
motic strictures in Crohn’s disease, particularly in patients who do not respond to corticosteroid treatment and who have a risk of short bowel syndrome.

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