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REVIEW ARTICLE

Management of anoperineal lesions in Crohn's disease: a French National Society of Coloproctology national consensus

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Abstract

The French National Society of Coloproctology established national recommendations for the treatment of anoperineal lesions associated with Crohn's disease. Treatment strategies for acute abscesses, active fistulas (active denovo and still active under treatment), fistulas in remission, and rectovaginal fistulas are suggested. Recommendations have been graded following the international recommendations, and when absent, professional agreement has been established. For each situation, practical algorithms have been drawn.

Keywords Crohn's disease · Anal fistula · Treatment

Abbreviations

APL	Anoperineal lesion
CD	Crohn's disease
PA	Professional agreement
EA	Expert agreement
MRI	Nuclear magnetic resonance imaging
IS	Immunosuppressant

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Methodology

The management of anoperineal lesions (APL) in patients with Crohn's disease (CD) is often complex and the existing recommendations date back to 2014 and does not cover all types of lesions [1]. A working group of 14 national experts in the management of APLs associated with CD was formed in January 2017. Work on the development of recommendations took place between February and November 2017, and used the DELPHI methodology. For each clinical situation, the group developed a management decision algorithm based on the international recommendations, French clinical practice recommendations, available publications, and clinical/surgical experience, with graded recommendations (Table 1). The first draft was initially submitted to all group members. A summary of the corrections was made by a panel of 4 members of the group. In November 2017, all nine decision algorithms were circulated to all members of the French National Society of Coloproctology. At the society's national conference on November 26, 2017, the issues that were not the subject of consensus were put to the vote of the 300 delegates present. These responses were then integrated into the algorithms as "professional agreements" (PA).

Definitions

Anal lesions of Crohn's disease (CD), ulcerations, fistulas, and stenosis, have been described by the Cardiff classification [2]. Parks' classification, established for the description of non-specific anal fistulas, can be used to describe the passage through the sphincter, the site of the internal orifice, and the existence of secondary extensions [3]. In practice, nowadays, the Cardiff and Parks classifications are little used and the American Gastroenterological Association [4] distinguishes, in a pragmatic way, simple fistulas (low fistulas with a single external orifice, not opening into the vagina, without abscess or stenosis, and without rectal inflammation), from complex fistulas (all the others). However, this description does not take into account any associated lesions and the active nature of the suppuration [4]. A fistula is clinically inactive if the orifices are not producing discharge spontaneously or when gentle compression is applied, if there is no localized sensitivity, no infiltration, and no abscess (EA). In magnetic resonance imaging (MRI), the inflammatory activity of a fistula is defined by hyperintensity in the T2 mode (it can be quantified or evaluated as absent, moderate, or significant) (EA). In MRI terms, an abscess or liquid collection considered as small when less than 2 cm (EA). In the absence of validated patient-reported outcomes, the impact of an APL in CD can be assessed using the Allan [5] or Irvine [6] indexes. The latter evaluates the symptoms (pain, discharge, and local infiltration) and the functional and sexual repercussions (Grade B).

Suppuration (Figs. 1, 2, 3, and 4)

A—assessment

> Imaging is recommended for the management of suppurative complications of CD, especially when they are complex, recurrent, and/or multi-operated (Grade B).
> MRI is the gold standard imaging technique due to its sensitivity and specificity in the detection of lesions, (Grade A), and also for the assessment of their inflammatory nature (Grade B). Moreover, it can evaluate any associated rectal involvement (Grade A).

MRI is complementary to exploration under general anesthesia. In particular, it allows the quality of drainage to be improved in 10–20% of cases and to significantly reduce the rate of recurrence [7] by highlighting collections, fistula tracts, and their internal orifices as well as their secondary branches that may be overlooked by clinical examination alone [8]. It also reduces by 75% the rate of recurrence after surgical treatment and can predict its site in 52% of cases [8]. Endorectal ultrasonography (possibly under general anesthesia) also complements the clinical examination in a similar way [9, 10]. Nevertheless, it is MRI that is recommended for the first-line examination in Crohn's disease patients because of its ability to visualize deep lesions remote from the anal canal, to differentiate active inflammatory lesions from healing lesions, and, furthermore, because the results are less operator-dependent.

B—treatment

> Antibiotic therapy alone (without surgical management or additional medical treatment) has no place in treating suppurations associated with CD (EA).

Antibiotic treatment, although very widely used, is of limited value. Its prescription can even be dangerous when it delays surgical management. Historical studies have only shown an improvement in subjective symptoms.

The two most studied molecules are metronidazole (750–1500 mg/day) and ciprofloxacin (500–1000 mg/day).

Table 1 Grades of recommendations

A	Directly based on level I evidence
B	Directly based on level II evidence or extrapolated recommendations from level I evidence
C	Directly based on level III evidence or extrapolated recommendations from level I or II evidence
D	Directly based on level IV evidence or extrapolated recommendations from level I, II, or III evidence

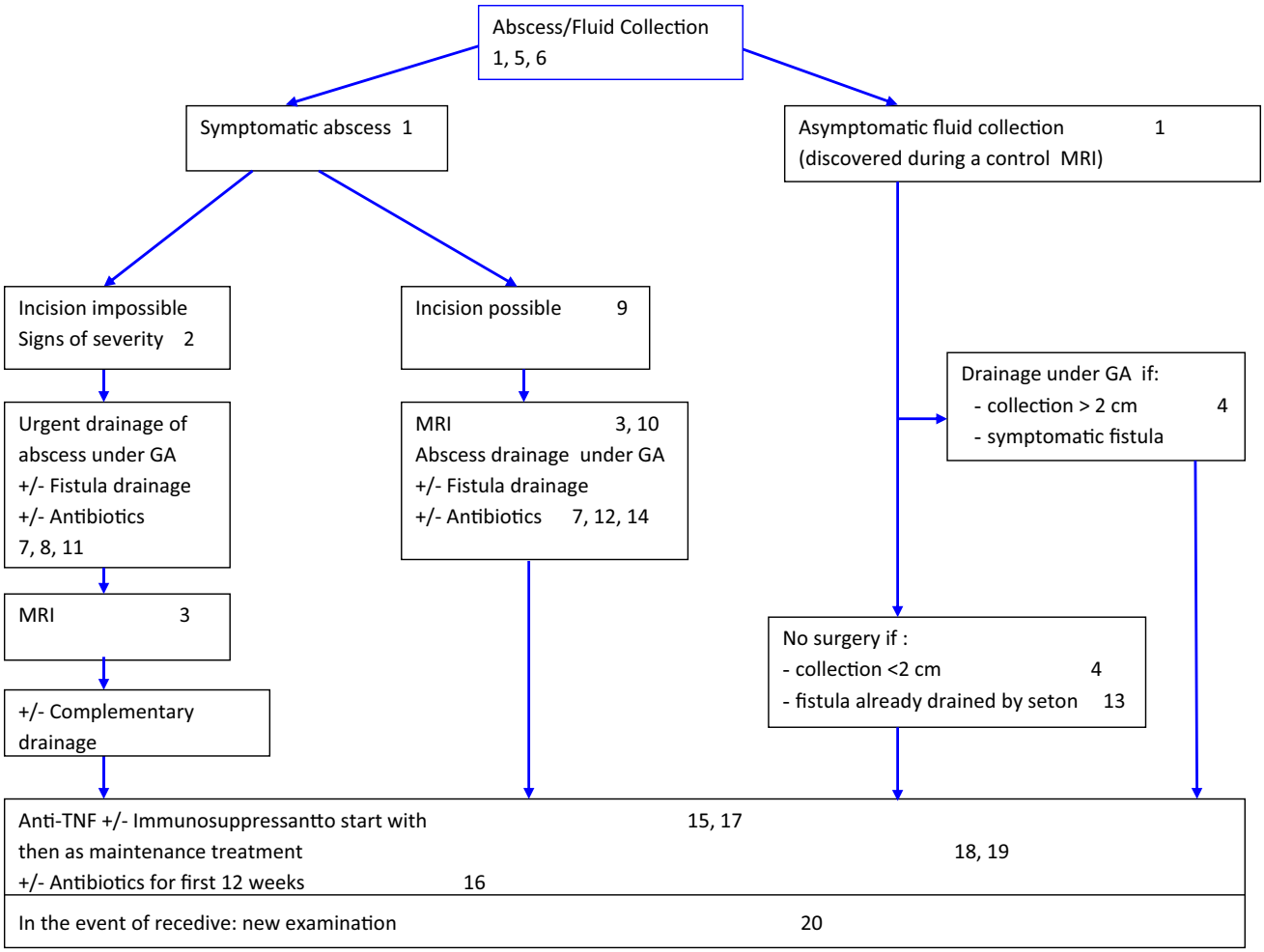

Fig. 1 Management of an anal abscess, or fluid collection, associated with Crohn's disease

The available studies on the isolated administration of antibiotics are of low power with heterogeneous inclusion and evaluation criteria. In addition, the "cure" rates of suppuration, even with prolonged treatment for several weeks, were modest, ranging from 0 to 56%, and recurrences almost always inevitable at the end of treatment [11]. A placebo-controlled randomized trial showed no significant effect on healing of fistula tracts after 10 weeks of treatment, while side effects were frequent [12]. Topical metronidazole was evaluated in a single open trial, and while it showed a positive effect on pain and discharge, there was no reduction in the Perianal Disease Activity Index (PDAI) score [13].

Short-term antibiotic treatment, before surgery and without delaying it, may be proposed depending on the site, to limit the spread of sepsis (EA).

Antibiotic treatment prescribed for 12 weeks together with anti-TNF induction might accelerate the improvement of symptoms associated with suppuration in CD (Grade C).

A double-blind, multicenter randomized-controlled trial showed a significantly higher fistula closure rate with a combination of ciprofloxacin (12 weeks) and adalimumab over adalimumab alone at week 12, that disappeared at week 24 [14]. However, a second randomized-controlled trial did not show any benefit on healing and symptoms of a combination of ciprofloxacin with infliximab over infliximab alone [15].

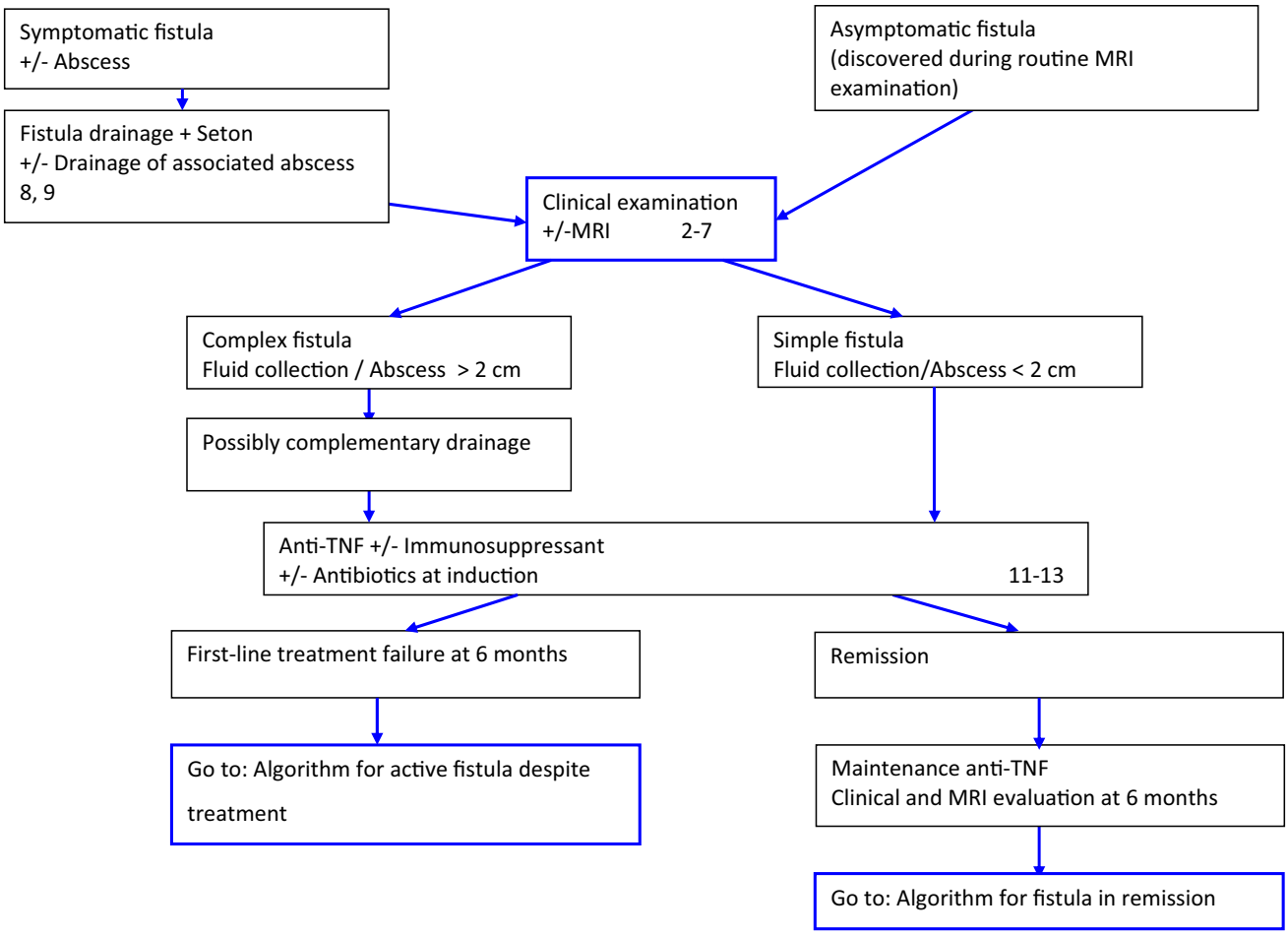

Fig. 2 Management of an untreated active anal fistula in Crohn's disease, detected clinically and/or by MRI

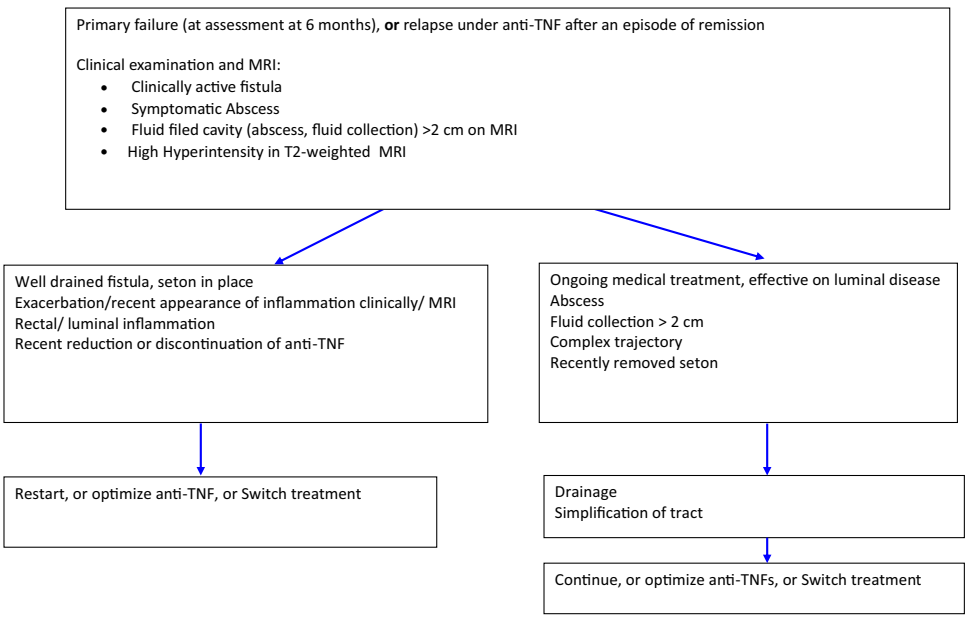

Fig. 3 Management of clinically active and/or MRI visible fistula in Crohn's disease despite ongoing anti-TNF treatment

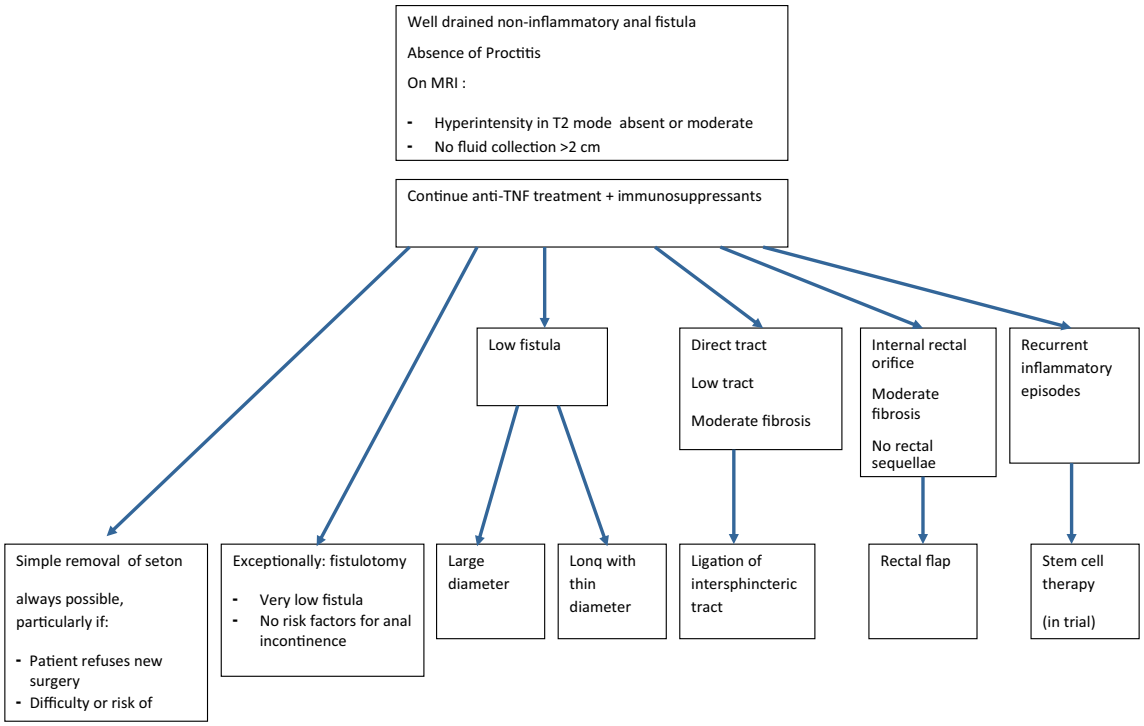

Fig. 4 Management of an anal fistula that is in remission (with or without seton) in Crohn's disease

In children, antibiotics may be proposed to improve the symptoms of CD associated suppuration (Grade C).
They should not be a substitute for surgical drainage.

In children, in cases of severe suppuration, antibiotic treatment may be proposed as an adjuvant to the main treatment (Grade B).

This indication may be used for severe suppuration [16].

In the absence of signs of severity, a palpable symptomatic abscess at the anal margin can be urgently incised under local anesthesia during an outpatient consultation (EA).

If signs of severity are present, emergency drainage under general anesthesia is indicated (EA).

There is no specific study on the emergency management of a symptomatic anoperineal abscess in a patient with Crohn's disease seen in outpatient consultation. Our recommendations are, therefore, based on the usual emergency management of a non-specific abscess. Thus, when the abscess is palpable and accessible, the first thing to do is to drain it by incising it under local anesthesia, performed during the consultation [17].

This simple gesture relieves the patient's pain and limits the extent of the suppuration. In addition, it allows additional time for possible preoperative imaging before exploration under general anesthesia and drainage.

After incision of an anal abscess, if the patient is relieved, but there is suspicion of a complex suppuration, it is better to operate without urgency after an MRI, which will guide the surgical procedure (Grade B).

In case of a symptomatic abscess inaccessible to incision, it is urgent to drain the abscess without waiting for imaging, if this will delay the drainage (EA).

For anal suppuration associated with CD, rapid surgical treatment is indicated, together with the initiation of medical treatment (anti-TNF ± an immunosuppressant) (Grade B).

The treatment should aim to quickly control sepsis, and to limit tissue and sphincter damage caused by the suppuration. The preservation of the anatomical and functional capacities of the patient depends on rapid, effective, and lasting control of the activity of the suppuration. A combination of appropriate surgical drainage and optimal medical treatment based on anti-TNF + immunosuppressant (IS) was shown, in a retrospective open study, to be more effective in obtaining healing of anoperineal lesions in CD than either of these two treatments alone [18]. Evaluation of suppurations, followed by drainage combined with infliximab therapy at weeks 0, 2 and 6, was shown to rapidly improve symptoms, but the medium-term healing rate was low [19]. Surgical treatment associated with anti-TNF, followed by maintenance anti-TNF therapy, improved the closure rate of fistulas and significantly reduced the rate of recurrence of abscesses [20, 21].

In children, rapid surgical drainage of suppurations combined with the initiation of medical treatment including anti-TNF is indicated (Grade C).

In children with CD and anal lesions treated with infliximab (112 patients), more than half showed a complete response 6 weeks after the start of treatment and two-thirds had a complete response at 1 year [22]. The GETAID pediatric group retrospectively collected data on the management of suppurative anal lesions in 101 children (27 centers): after induction treatment, 88% of patients had a favorable response and half of them achieved complete response [23]. In children with suppurative anal lesions, the European Crohn's and Colitis Organisation (ECCO) recommends the drainage of the fluid collections and the introduction of anti-TNF both in the treatment of the acute episode and then as maintenance treatment, because these lesions are indicative of a poor prognosis [16].

The surgical aspect of the treatment of an anal suppuration associated with CD is to drain the abscess and its possible secondary extensions towards the skin or the rectal cavity, and to drain the fistula, if it can be located, using a loosely knotted flexible drain (seton) (Grade C).

The inflammatory nature of acute lesions makes visualization of tracts and abscesses difficult, and, hence, the value of imaging prior to surgery [15]. The experience of the proctologist is also important when faced with this type of patient, because the detection rate of fistulae is superior and the classification of trajectories is better [21] (Grade C).

Setons should be "loose", because, in CD positioning, a "tight" seton for subsequent traction is not recommended due to the high risk of anal incontinence [24, 25] (Grade C).

Other than the positioning of the seton, no guidance can be given about the procedure on the fistula itself; should it be reduced or shortened to increase the chances of remission? In analogy with non-specific fistulas, drainage of the intersphincteric portion of the fistula tract may decrease the risk of recurrence of suppuration [26]. In all cases, it is necessary to drain the associated diverticulae as much as possible (EA).

In the specific case of the existing anoperineal disease already operated on several times, the quality of the previous drainage must be evaluated by imaging to ensure the absence of residual suppurations that could be a source of recurrence despite optimal medical treatment [27, 28].

Fistulotomy is not recommended except for an isolated superficial fistula in the absence of proctitis in a patient with no risk factors for anal incontinence (PA).

This option is rarely compatible with CD because of the immediate risk of continence disorders, the frequency of diarrhea in these patients, and the recurrent nature of CD APLs that may require iterative procedures.

A delay between draining the suppuration and starting anti-TNF + immunosuppressant therapy is not justified (EA).

The medical component of the treatment of suppurations associated with CD is based on anti-TNFs + immunosuppressants (Grade A).

This treatment must be started immediately after surgical drainage and control of any septic syndrome. For this indication, the three anti-TNF molecules available are infliximab, adalimumab (Grade A for both), and certolizumab pegol, even if the first studies that validated these molecules did not systematically associate surgical treatment. For infliximab, two randomized-controlled trials on fistulizing CD have been published. The first pilot study by Present et al. demonstrated the efficacy of this treatment at a dose of 5 mg/kg at induction [29], then the ACCENT II study demonstrated the persistence of remission at the 54th week in 46% of responders versus 23% in the placebo group [30]. For adalimumab (40 mg every week or every 2 weeks), there is no specific controlled trial for fistulizing disease, but, in the CHARM trial, a subgroup analysis of patients with a drained fistula at baseline showed a statistically significant rate of healing of 33%, versus 13% in the placebo group [31]. Another study showed that 90% of patients responding to adalimumab were still in remission after 2 years of continuing treatment [32]. A meta-analysis evaluating the efficacy of the different anti-TNFs in fistulizing CD concluded that the infliximab literature was more abundant and robust, but with no evidence of superior efficacy versus adalimumab [33]. For certolizumab pegol, there is no specific trial, but the post hoc analysis of the PRECISE 1 and 2 studies showed a rate of closure that was statistically superior to placebo [34]. Finally, Sandborn et al. reported the beneficial effects, also in post hoc analysis, of 300 mg vedolizumab every 8 weeks, at induction and in maintenance, on the closure rate of fistulas (41% versus 11.1%, $p=0.03$) [35].

Ustekinumab has not been evaluated in the treatment of CD fistulas.

Thiopurines administered alone possibly have some moderate efficacy on CD APLs (in adults and in children) (Grade C).

Consequently, they are exceptionally indicated alone, but then only in cases of simple fistula, that have been well drained surgically, without residual diverticulae > 2 cm, without anal or rectal mucosal inflammatory involvement in patients without anatomical or functional risk factors, and under close supervision.

The two available meta-analyses on the induction of remission by thiopurines alone are contradictory, since the first found a positive effect [36], while the second was negative [37]. The two most frequently cited controlled trials evaluating the early introduction of azathioprine during CD, with comparable enrolment and follow-up, showed that, for one, there is a decrease in the need for perineal surgery at 3 years [38], and for the other, an absence of difference in the incidence of perineal suppurations [39]. In maintenance therapy, the benefit of only thiopurines is modest and has a low level of evidence [40]. The very modest and poorly documented that the efficacy of thiopurines alone discourages their use except for patients with mild lesions who have intact anatomical and functional capacity (including no previous history of perineal surgery, digestive resection, and diarrhea) in whom aggravation of suppuration would not be a major annoyance, especially regarding anal continence.

Data on the efficacy of methotrexate and cyclosporine are limited [41]. Finally, tacrolimus may have a positive effect but requires therapeutic monitoring because of the frequency of adverse effects [42] (Grade C).

It is advisable to associate an immunosuppressant with infliximab and with adalimumab (EA).

When initiating or restarting anti-TNFs in adults; it is recommended to add an immunosuppressant for 6–12 months. Combined therapy may increase the effectiveness of infliximab and adalimumab. Above all, it reduces the immunogenicity of anti-TNF treatment. It is advisable to adopt the optimal conditions of use of anti-TNFs as these are the only molecules that have, at present, proven effectiveness on APL in CD (EA).

Recent data on combined treatment with infliximab and thiopurines suggest a greater effect compared with monotherapy, especially in patients with proctitis [43, 44]. Although the combination of an immunosuppressant with infliximab treatment has not been demonstrated to be superior to infliximab alone for the treatment of anoperineal fistulas, by analogy with the recommendations for luminal CD, it is recommended to associate infliximab with an immunosuppressant. Combined therapy could also be proposed when adalimumabis used. Since these two molecules are the only ones that have been shown to be effective in the treatment of anal fistulas, the combination with an immunosuppressant could reduce the risk of immunization and subsequent loss of efficacy.

Given the need for efficacy in the treatment of anoperineal suppurations in CD, the other approaches have been explored: dosage of biotherapeutics above those recommended for the luminal disease, monitoring of blood levels of the drugs, or local adjuvant treatment using stem cells [45, 46].

The presence of rectal involvement at the beginning of the management of a suppuration associated with CD and its persistence during follow-up is poor prognostic factors and demands maximal medical treatment from the outset and/or its optimization as soon as possible (Grade C).

The detection of inflammatory activity in the rectum on MRI is prognostic of failure of medical treatment [47, 48]. New prognostic factors including NOD2/CARD15, duration of fistulating disease, distribution of CD, and fistulae anatomy have yet to be assessed before being used to inform research and clinical practice [49].

In children, the medical aspect of the treatment of complex suppurations is based on anti TNF ± immunosuppressant (Grade B).

The anatomo-clinical target to achieve at 6 months in the treatment of suppurations in CD is as follows:

- a dry, non-inflammatory fistula;
- the absence of a fluid collections > 2 cm on MRI;
- absent or significantly decreased hyperintensity in T2 MRI (PA).

Clinically, the most commonly used criteria used for evaluating response to treatment were those of Present et al. Improvement under treatment was defined as the closure and the absence of discharge (under gentle compression) in at least 50% of the fistulous orifices over a period of 4 weeks (two consecutive consultations) with a decrease in the pain and induration felt by the patient; in completely asymptomatic patients healing, defined as the total absence of discharge [29]. Improvement in MRI is defined, according to van Assche's criteria, by the absence of any fluid cavity of more than 3 mm, a sharp decrease in the enhancement of the walls of the fistulous tract(s) on the T2 sequences, and a clear improvement in any rectal inflammation. This evolution may be observed with varying frequencies and over various timespans. In general, complete radiological remission (disappearance of the fistula and of any inflammation) is rarely observed, but radiological improvement (anatomical and inflammation) is seen in at least 50% of patients, and it occurs later than clinical improvement, after a period of several months [34, 47, 48]. A cohort study in a specialized center that included 59 patients treated by surgical drainage and long-term infliximab showed an improvement in MRI (van Assche's global score and tract inflammation) from a median of 11 weeks of follow-up, then at 44 weeks, with stability at 94 weeks. Although at the last time point, there was an improvement in the van Ascche score and more specifically in inflammation, in, respectively, 14% and 55% of patients, 92% of patients still had a visible fistulous tract, with 75% showing inflammation in the tract wall [50]. MRI improvement (disappearance of fluid-filled cavities, simplification of tracts, and reduction of inflammation) is a good prognostic factor for clinical improvement, and also for the persistence of remission under maintenance treatment [34, 50, 51], making it a relevant therapeutic target. Improvement in the MRI, under treatment, would, therefore, be a minimal target to achieve. However, the quantification of such improvement and the extent at which it can be considered as significant remain to be defined. In fact, two recent studies have included MRI evaluation in the clinical response [45, 46]. In these 2 studies, healing was defined by the absence of discharge and of fluid-filled cavities > 2 cm on MRI.

Patient-reported outcomes, when they become available, could also be included in the definition of clinical remission. Some studies suggest that clinical response to treatment is early and should not be waited for a long time. In the study by Present et al., the median time to the first follow-up visit showing clinical closure of tracts was 14 days [30]. However, other authors suggest that more patience is needed. In a trial evaluating adalimumab, the maximum clinical healing rate was achieved at 16 weeks (3.6 months) and remained the same at 56 weeks [52]. In addition, in the large retrospective cohort of Gaertner et al., the average time to clinical healing of fistulas in the infliximab plus surgery group was 6.5 months [53]. In a comparable study involving 156 patients, the median time to fistula closure was 1 year after the start of infliximab [21]. Overall, it appears that a rapid clinical response (and/or the possibility of early removal of the seton) under an anti-TNF would be a favorable prognostic factor [44, 54]. Simple clinical improvement would be an insufficient objective and the remission, in MRI terms, of suppurations associated with CD should be an objective to attain, especially in young patients seeking optimal quality of life, because of its possible association with a reduced risk of relapse.

A small asymptomatic fluid collection (< 2 cm) can initially be medically treated with anti-TNF + immunosuppressant, on condition of subsequent evaluation by clinical examination and imaging (PA).

Thanks to the high performance of MRI, we can, nowadays, visualize small fluid collections in asymptomatic patients, and sometimes in those under treatment. This situation, which is far from being exceptional in current practice, has not yet been addressed in the literature.In practice, we should consider abstaining from surgery. Surveillance should be instigated; association with antibiotic therapy is far from being consensual and, therefore, left to the discretion of the practitioner. Optimization of the medical treatment of the

underlying CD should be discussed especially if complete luminal remission has not been obtained.

When an anal fistula in the context of CD has been put in remission by an anti-TNF, this treatment must be continued as maintenance therapy (Grade B).

Maintaining potentially destructive lesions in remission is essential to preserving the anatomic and functional capital of the patient. Maintenance therapy with infliximab or adalimumab increases the rate of healing even after the induction phase, and keeps the level of acquired healing stable, significantly higher than placebo [30, 52]. A relapse of the suppuration during maintenance treatment indicates a new morphological evaluation (ideally with MRI), to discuss the optimization of medical treatment and/or surgical drainage. Maintenance treatment with infliximab or adalimumab significantly decreases the global need for perineal surgery, over a year, compared to placebo. However, the specific frequency of interventions for new anal abscesses was not decreased [55, 56] and the incidence of appearance of a perineal abscess was similar to that associated with placebo (19 vs. 17%) [57]. These data suggest that there is still room for improvement of maintenance treatment concerning anoperineal suppurations in CD. To date, treatment regimen and monitoring required to ensure prolonged perineal remission have not been defined. Likewise, the duration of maintenance treatment and the criteria for its reduction have not yet been determined.

The exacerbation of a fistula during maintenance treatment for CD is a significant event indicating morphological evaluation, and secondary discussion of a new surgical drainage procedure and/or optimization of medical treatment (Grade B).

In cases of a relapse of suppuration in patients under maintenance treatment, and after clinical and anatomical evaluation, and possibly endoscopy and MRI, the options are:
1. Surgical treatment (possibly without optimization of the medical treatment) in cases of: abscess > 2 cm, fistula with complex tract, recently removed seton
2. Optimization of medical treatment (possibly without new surgical drainage) in cases of: a well-drained fistula and seton in place, aggravation, or recent appearance of an inflammatory aspect to the fistula tracts, rectal, anal, or luminal inflammation.

The occurrence of an anal abscess in the context of maintenance treatment for luminal CD indicates the need to evaluate the treatment so as to optimize it.

It is recommended to stop biotherapies in a patient with a symptomatic abscess, unless an urgent drainage procedure is performed, because of the safety rules regarding the use of these therapies (EA).

The recommendation to discontinue biotherapy treatment in a patient with an undrained symptomatic anal abscess is based on common sense and the general recommendations concerning this type of treatment. However, there are no specific studies concerning the effect of the continuation of biotherapy in the presence of an undrained abscess. Therefore, this recommendation can probably be nuanced in an asymptomatic patient presenting a small collection that would not normally be subject to surgery.

Under effective medical treatment, a surgical procedure to close a well-drained, non-inflammatory fistula tract with no abscess on MRI could be proposed to decrease residual symptoms such as soiling and gas leakage (EA).
Its benefit in the prevention of relapse has not been demonstrated.

At least one case series has shown a good medium-term result for the combination: closure + induction and maintenance medical treatment on fistulas associated with CD [58]. The choice between simple seton removal and closure is not based on any scientific data. However, a trial by the French Proctology Research Group is currently being analyzed and may provide some answers (Abramowitz for the GREP, FACC study). Similarly, we have no evidence to support the superiority of one closure technique over another, because there are too few available studies, the methodologies are too heterogeneous, and most include patients who have not received optimal medical treatment. The two randomized studies available (using fibrin glue or plugs) are too isolated to attribute a recommendation grade [59, 60]. Data on ligation of the intersphincteric fistula tract (LIFT) in CD are insufficient to support its indication for CD patients. Nevertheless, it could be an alternative in some cases [61]. The conditions for performing transanal advancement flap repair are rarely met during the course of CD [62–65]. The efficacy of stem cell injection has been shown in two randomized, phase 3 trials for complex anal fistulas (excluding rectovaginal fistulas) [45, 46].

The optimal timing of closure techniques has not been determined; however, such techniques should only be proposed after remission under medical treatment and never during an inflammatory episode.

Removal of a seton, if present, and/or a closure technique is possible when:
1. the fistula is well drained and non-inflammatory;
2. absence of rectal inflammation is demonstrated endoscopically and/or by MRI;
3. the MRI shows the absence of diverticula or any significant fluid collection (> 2 cm) and a clear decrease in inflammation on the T2 sequences (EA).

It is recommended to remove a seton when the tract is no longer clinically inflammatory and healing is well advanced. However, the ideal time for removal has not been determined. The only available data are the finding that inability to withdraw a seton or keeping a seton in place beyond 34 weeks are pejorative factors for fistula healing [44, 54]. However, this delay may reflect the lack of medical control of the underlying CD.

Ano- and rectovaginal fistulas (Fig. 5)

In cases of ano- or rectovaginal fistula, the achievement of remission of any anal or rectal involvement is essential (Grade B).

For an ano- or rectovaginal fistula, in the event of failure to control associated rectal involvement, or the failure of the first-line local surgical treatment (EA), a derivation stoma can be proposed before subsequent fistula surgery (Grade C).

In the event of failure of healing and disabling symptoms, a derivation stoma can be realized, in association with a new conservative fistula strategy. Although its importance has long been debated, it has recently been shown, in a series of 286 procedures, that the presence of a derivation stoma is an independent predictor of success of the surgical procedure [66]. In contrast, an isolated derivation stoma, without any subsequent procedure, has been shown as not being of importance in healing.

Indication for surgical treatment of a non-inflammatory ano- or rectovaginal fistula depends on functional symptoms (EA).
An asymptomatic or pauci-symptomatic ano- or rectovaginal fistula may not require treatment (EA).

For ano- or rectovaginal fistulas, several local conservative treatments are possible.

In the context of ano- or rectovaginal fistula, there is no place for fistulotomy or a section-reconstruction technique (Musset technique) in the context of CD because of the risk of sphincter lesions and thus of anal incontinence. Biological glues and plugs have not been proven to be significantly more effective than the simple removal of the seton. Reports of two small series described modest results with button fistula plugs in fistulas between the ileal pouch and the vagina after ileoanal anastomosis [67, 68]. A rectal advancement flap is a simple, minimally invasive procedure that can be repeated. In a meta-analysis, it was associated with a success rate of about 50% and comparable to that of a vaginal flap [66]. The realization of a rectal flap could be impeded in the presence of associated anorectal stenosis or inflammation, which is a factor for almost systematic failure of any localized procedure [69, 70]. If a rectovaginal fistula persists despite conservative strategies with a protective stoma, muscle interposition procedures could be attempted, the most common being Martius flap [66] and graciloplasty [70]. Repeat muscle interposition procedures could be performed if a previous procedure fails. Also proposed, the interposition of prosthetic material has not shown effectiveness [68].

In the event of significant persistent symptoms following the failure of both medical treatment and that of conservative surgery, a proctectomy may be proposed (EA).

If after all the different strategies, the rectovaginal fistula still persists, the last resort is abdominoperineal amputation with a definitive stoma. However, despite improving the quality of life of patients, it is sometimes associated with a risk, of about 20% persistent perineal sinus for which the management is difficult. The interest of other techniques such as direct or delayed coloanal anastomosis or ileoanal anastomosis has not been clearly reported in the context of a rectovaginal fistula associated with CD.

Conclusions

Literature about treatment of anoperineal lesions associated with CD is scarce. These recommendations add expert and professional agreement to available demonstrated data, and, therefore, can help specialists to discuss optimal treatment for these difficult patients.

The critical point is control of associated luminal disease when present, especially proctitis.

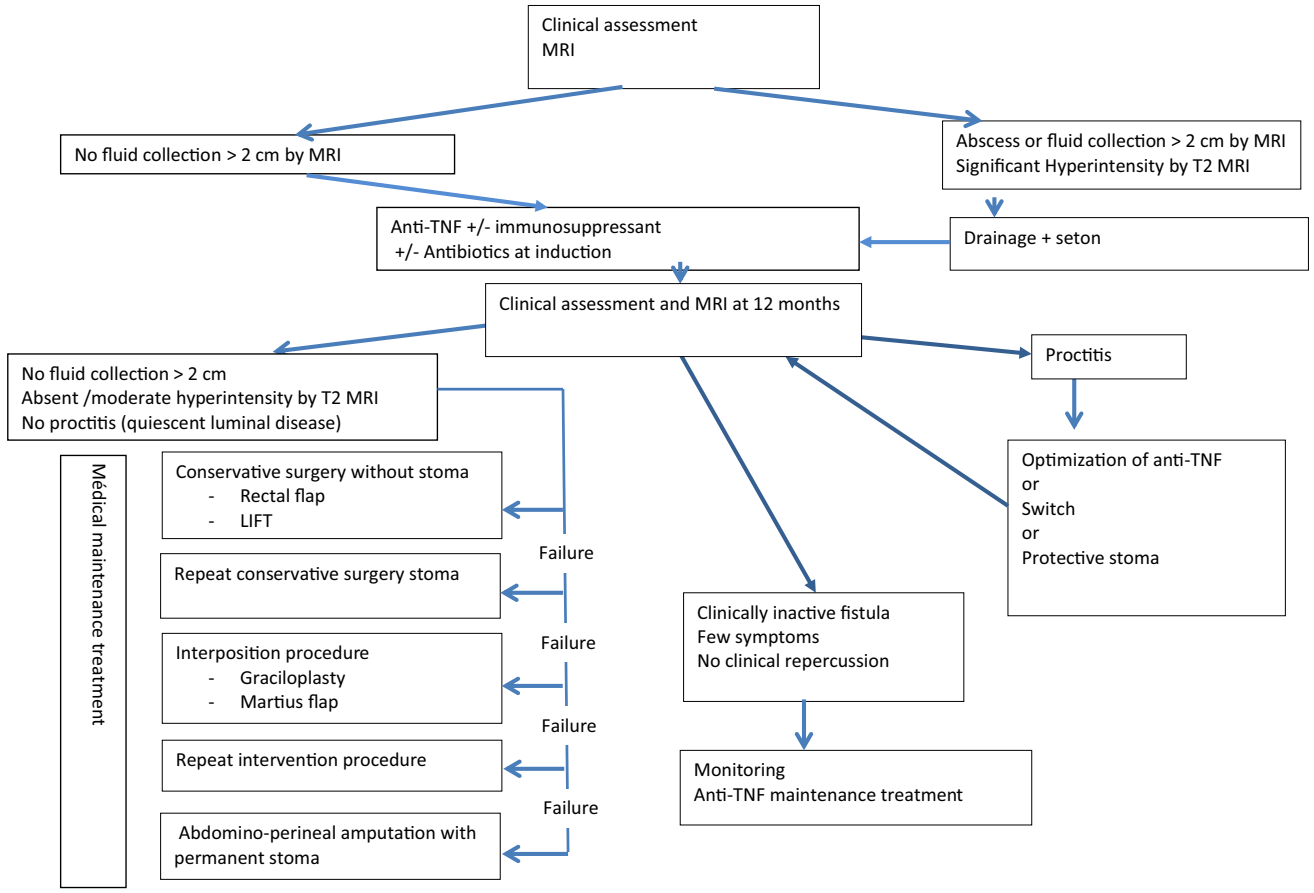

Fig. 5 Management of ano- or rectovaginal fistulas in the context of Crohn's disease

The initial treatment of suppurations/fistulas should always associate surgical drainage (plus seton insertion when fistula is demonstrated) and medical treatment without delay. Today, only anti-TNFs have demonstrated an efficacy on fistulas; to ensure a maximal effect, they should be associated with an immunosuppressive drug during the first months. When fistulas are simple and luminal disease quiescent, simple watch and wait follow-up may be proposed, sole immunosuppressive treatment efficacy possibly not being superior.

When remission is obtained, it is proposed to continue anti-TNF treatment. Surgical obturation of a fistula tract might not be superior to simple seton ablation, but could be considered when fistula is associated with persistent symptoms, especially in case of ano/rectovaginal tracts.

Further studies should evaluate (and then include) more stringent therapeutic targets such as the absence of a > 2 cm collection, and also hyperintensity decrease on MRI.

In case of treatment failure, MRI evaluation might help to choose between optimisation of medical treatment and a new surgery.

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Compliance with ethical standards

Conflict of interest Dominique Bouchard is the recipient of fees for education and consulting from Abbvie, François Pigot is the recipient of fees for lectures from Abbvie, Laurent Siproudhis is the recipient of fees for consulting, teaching and research from Abbvie, Ferring, MSD and Takeda, Laurent Abramowitz is the recipient of fees for research from Abbvie and Takeda, Jean-Luc Faucheron is the recipient of fees for consulting and research from AMI and Medtronic, David Laharie is the recipient of fees for consulting and research from Abbvie, Janssen, MSD and Takeda, Ghislain Staumont, Paul Benfredj, Charlène Brochard, Nadia Fathallah, Thierry Higuero, Yves Panis, Vincent de Parades, and Béatrice Vinson-Bonnet have no conflict of interest or financial ties to disclose.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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