ANAL CROHN'S DISEASE

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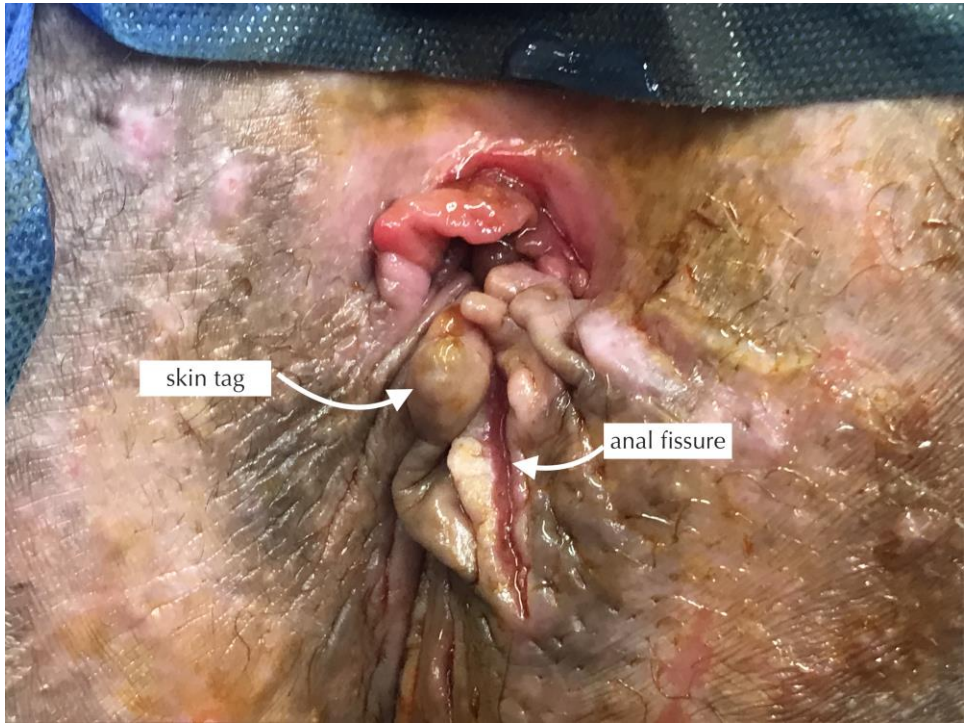
CROHN'S DISEASE (REGIONAL ENTRITIS, SKIPPED LESIONS, TERMINAL ILEITIS, TRANSMURAL, GRANULOMATOUS NON CASEATING)

- Chronic, unremitting, incurable inflammatory disorder.
- Affect any segment of the intestinal tract as well as extraintestinal sites.
- Disease behavior is classified as
  - Non stricturing, non penetrating.
  - Fibrostenotic.
  - Penetrating.



- Incidence of PCD 25-80%
- Fistulizing PCD 17-43%
- Symptomatic PCD is strongly associated with colonic and rectal involvement.
- Clinical course: skin tags, rectal stricture, anal fissures, fistulae
- Clinical presentation: part of the clinical coarse of the disease or denovo
- It isn't uncommon PCD can precede other CD manifestations

- Skin tags and anal fissure can be managed medically
- However, if persistent with pain and medical treatment failed minor surgical procedures can be carried on.

1980, Buchmann and Alexander-Williams classification: skin lesions, anal canal lesions, and fistulae.

- **The management of of PCD depends on**
  - **proper diagnosis.**
  - **Control of the disease**
  - **Management of the local condition**

Proper diagnosis

- **For Crohn's disease**
  - Inflammatory markers
  - Faecal calprotectin level
  - MRE
  - Endoscopy

- **For local condition**
  - EUA with biopsy
  - MRI
  - EUS

Control of the disease

- Abs
- Steroids
- Azathioprine/ 6-mercaptopurine
- Biologic therapy

Multidisciplinary team management is the best way to obtain a satisfactory outcome when managing this complex condition

Control of the local condition

Rules

- Drainage of any abscess is a must prior to any medical treatment protocols
- Dealing with the disease activity must precede the management of chronic PCD
- Patients with Crohn's disease are vulnerable to delayed healing or non healing
- Faecal incontinence can occur even with minor injury to anal sphincters (fistulotomy procedures).
- Crohn's perianal fisulae could be complex and internal openings could be any where even in the rectum

PERIANAL CROHN'S ACTIVITY INDEX

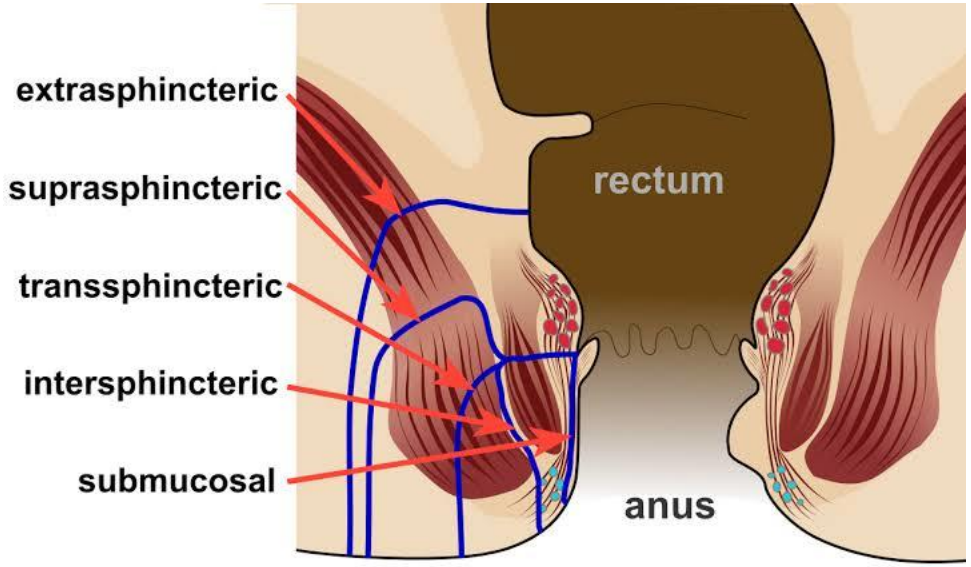
Feature	Score
Abscess	
None *or*	0
First occurrence, single abscess *or*	1
First occurrence, multiple abscesses *or*	3
First recurrence, single or multiple abscesses *or*	4
Multiple recurrence, single or multiple abscesses	5
Maximum abscess score	**8**
Fistula	
None	0
Short-term (<30 d) fistula *or*	1
Long-term (>30 d) fistula *or*	2
Persistent postsurgery fistula *or*	3
Recurrent fistula	3
Multiple fistulas	3
Rectovaginal/rectourethral fistula *or*	4
Recurrent rectovaginal/rectourethral fistula	6
Maximum fistula score	**14**
Ulcer and Fissure	
None	0
Short-term (<30 d) ulcer/fissure *or*	1
Long-term (>30 d) ulcer/fissure *or*	2
Single ulcer/fissure *or*	1
Multiple ulcers/fissures	2
Maximum ulcer/fissure score	**4**
Stenosis	
None	0
Short-term (<30 d) stenosis *or*	1
Long-term (>30 d) stenosis	2
Recurrent stenosis	4
Maximum stenosis score	**6**
Incontinence Score	
No incontinence *or*	0
Incontinence score of 1-6 *or*	1
Incontinence score of 7-14 *or*	3
Incontinence score >14	5
Maximum incontinence score	**5**
Concomitant Disease*	
None *or*	0, 0, 0
Moderate *or*	3, 2, 1
Severe	4, 3, 2
Active fistula	4, 3, 2
Maximum concomitant disease score	**18**

*Scores are for rectal, colonic, and small-bowel disease, respectively.

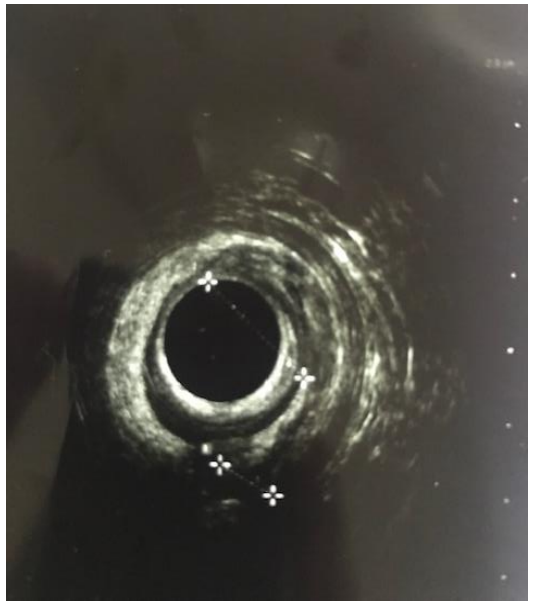
- To predict treatment protocol outcome (score of 20 or more means recurrence or persistence of symptoms after surgery)
- Follow-up after surgical treatment

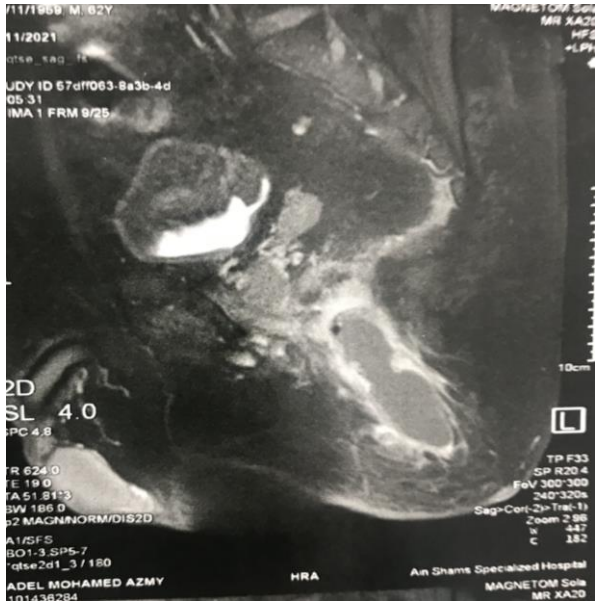
Perianal Crohn's fistula

- Cryptoglandular
- Transmural disease spread



MRI AND EUS

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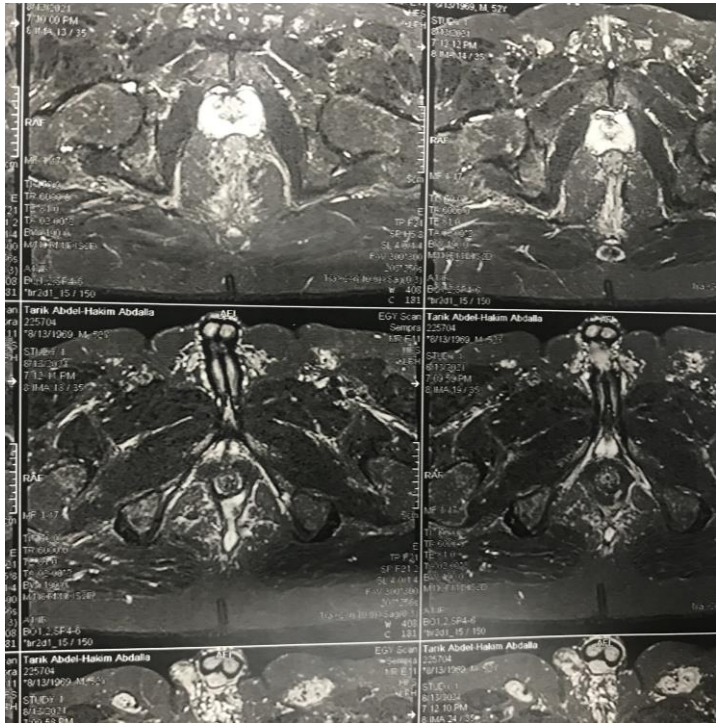
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Stem Cell Therapy For The Treatment Of Crohn's Disease; Current Obstacles And Future Hopes. (Mini-Review)

Sarah El-Nakeep. Curr Stem Cell Res Ther. 2021.

clinical trials. Moreover, mesenchymal stem cells and their related types (placental, adipose tissue, umbilical tissue, etc.) are the most safe and effective in clinical trials. Currently; the commercially available mesenchymal stem cells preparation (Darvadstrocel (Cx601)) is the only one approved by The United States Food and Drug Administration (FDA) for clinical use in refractory CD associated complex perianal fistula.

Conclusions: Stem cell therapy (SCT) shows promise in; inducing remission in refractory Crohn's colitis, and perianal fistula, but further research is required before SCT could be applied to clinical practice guidelines.

Keywords: Crohn's Disease; Hematopoietic; Inflammatory Bowel disease; Mesenchymal; Perianal fistula; Stem Cell Therapy.

SYSTEMATIC REVIEW

Reference	N	Study design	Rate of healing	Follow-up time	Other complications
Fistulotomy					
Hobbiss and Schofield[86]	22	Retrospective	80%	1–10 years	Minor anal stenosis
Halme and Sainio[48]	35	Retrospective	60%	Undocumented	Fecal incontinence
Scott and Northover[49]	27	Retrospective	81%	2 years	None reported
Fibrin glue					
Lindsey et al[53]	2	Randomized (fibrin vs seton, fistulotomy or flap)	100% (1 needed a second intervention)	12 weeks	None reported
Loungnarath et al[54]	13	Retrospective	31%	26 months	None reported
Grimaud et al[55]	36	Randomized (glue vs observation)	35%	16 weeks	Four abscess
Fibrin plugs					
Champagne et al[56]	46	Prospective	83%	6 months–2 years	None reported
Senejoux et al[57]	106	Randomized (plug vs seton removal)	31.5% (plug) vs 23.1% (seton)	12 weeks	None reported
LIFT					
Rojanasakul et al[58]	17	Prospective observational	94.4%	6 months	None reported
Zirak-Schmidt and Perdawood[59]	612	Systematic review	70.6%	4 weeks–26 months	None reported
Gingold et al[60]	15	Prospective observational	67%	12 months	None reported
Parthasarathi et al[61]	167	Prospective observational	94/1%	12.8 months	None reported
Endomucosal advancement flap					
Kobayashi and Sugihara[62]	2	Case report	100%	1 year	Fecal incontinence
van Koperen et al[63]	60	Randomized (plug vs flap)	29% (plug) vs 48% (flap)	11 months	None reported
Marchesa et al[64]	13	Retrospective	62%	1 year	None reported

Abbreviation: LIFT, intersphincteric fistula tract.

Combined therapy with infliximab and seton drainage for perianal fistulizing Crohn's disease with anal endosonographic monitoring: a single-centre experience

L Guidi et al. Tech Coloproctol. 2008 Jun.

adalimumab. Patients' anorectal function was well preserved and overall satisfaction with the treatment was high.

Conclusions

The results suggest that combining seton drainage with infliximab therapy improves the perianal fistula response rates in pediatric patients.

Article Navigation

JOURNAL ARTICLE

Treatment of complex perianal fistulas with seton and infliximab in adolescents with Crohn's disease FREE

Maria Hukkinen ✉, Mikko P. Pakarinen, Maija Piekkala, Antti Koivusalo, Risto Rintala, Kaija-Leena Kolho

Journal of Crohn's and Colitis, Volume 8, Issue 8, 1 August 2014, Pages 756–762,
https://doi.org/10.1016/j.crohns.2014.01.001
Published: 01 August 2014 **Article history** ▾

Anti-tumor necrosis factor (TNF)-α agent infliximab (IFX) is effective in closing and maintaining closure of perianal fistulas in adults, and current guidelines recommend its use as the initial medical treatment for complex fistulas.[1,7,8] Up to 40% of patients, however, lose response to IFX over time.[9,,11] Although fistulas usually improve rapidly after IFX induction, only about half of treated adults still show response after one year of maintenance therapy.[1,11] In addition, fistulas recur frequently following treatment discontinuation. Because persisting fistula tracks after premature skin closure predispose to abscess formation,[11,12] it is recommended to place non-cutting setons in fistula tracks to maintain drainage prior to IFX regimen.[1,5,13] Combining seton drainage with the medication

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Article Navigation

JOURNAL ARTICLE EDITOR'S CHOICE

Clinical Practice Guideline for the Medical Management of Perianal Fistulizing Crohn's Disease: The Toronto Consensus FREE

A Hillary Steinhart, MD ✉, Remo Panaccione, MD, Laura Targownik, MD, Brian Bressler, MD, Reena Khanna, MD, John K Marshall, MD, Waqqas Afif, MD, Charles N Bernstein, MD, Alain Bitton, MD, Mark Borgaonkar, MD ... Show more

Inflammatory Bowel Diseases, Volume 25, Issue 1, January 2019, Pages 1–13,
https://doi.org/10.1093/ibd/izy247
Published: 06 August 2018 **Article history** ▾

in clinical practice and includes anatomic variables that may not improve despite effective medical therapy (eg, a tract may still be visible radiologically after a fistula has "closed").

Table 3: Defining Remission and Response in Patients With Perianal, Fistulizing CD

Complete remission	**Symptomatic and radiographic remission (defined below)**
Symptomatic remission	Absence of both pain and drainage* from the fistula tract
Symptomatic response	Meaningful improvement in symptoms of pain and drainage as judged by both the patient and physician in the absence of remission. Response should not be considered a desirable final outcome, but is useful to assess early response to treatments
Radiographic remission	Absence of inflammation in any fistula tract and the absence of any abscess

*Absence of drainage is considered to be no drainage from the fistula tract with the application of gentle pressure

Table 4: Summary of Consensus Recommendations for the Management of Perianal Fistulizing Crohn's Disease*

1: In patients with Crohn's disease and signs and/or symptoms of active fistulizing disease, we recommend imaging (EUS or MRI, based on availability and local expertise) be obtained to delineate the anatomy of the fistula tract(s). **GRADE: Strong recommendation, very low-quality evidence.**
2: In patients with Crohn's disease and evidence of complicated fistulizing disease, we suggest surgical consultation. **GRADE: Conditional recommendation, very low-quality evidence.**
3: In patients with Crohn's disease and evidence of fistulizing disease, we suggest the use of antibiotic therapy for initial management to achieve symptomatic response. **GRADE: Conditional recommendation, very low-quality evidence**
4: In patients with Crohn's disease and evidence of fistulizing disease, we recommend the use of anti-TNF therapy, to induce symptomatic response. **GRADE: Strong recommendation, very low-quality evidence.**
5: In patients with Crohn's disease and evidence of fistulizing disease who have achieved symptomatic response on anti-TNF therapy, we suggest the use of continued therapy, to achieve and maintain complete remission. **GRADE: Conditional recommendation, low-quality evidence.**
6: In patients with Crohn's disease and evidence of

response on anti-TNF therapy, we suggest the use of continued therapy, to achieve and maintain complete remission. **GRADE: Conditional recommendation, low-quality evidence.**
6: In patients with Crohn's disease and evidence of fistulizing disease, when starting anti-TNF therapy, we suggest it be combined with a thiopurine or methotrexate over monotherapy to optimize pharmacokinetic parameters. **GRADE: Conditional recommendation, low-quality evidence for infliximab, very low-quality evidence for adalimumab.**
7: In patients with Crohn's disease and evidence of fistulizing disease, we suggest referral for surgical management when there has been an inadequate symptomatic response to medical management strategies. **GRADE: Conditional recommendation, very low-quality evidence.**

EUS, endoscopic ultrasound; MRI, magnetic resonance imaging; TNF, tumor necrosis factor; *The strength of each recommendation was assigned by the consensus group, per the GRADE system, as strong ("we recommend . . .") or conditional ("we suggest . . ."). A recommendation could be classified as strong despite low quality evidence to support it or conditional despite the existence of high quality evidence due to the 4 components considered in each recommendation (risk:benefit balance, patients' values and preferences, cost and resource allocation, and quality of evidence).


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