



SCHWEIZERISCHE ARBEITSGRUPPE FÜR KOLOPROKTOLOGIE
GROUPE SUISSE D'ETUDES COLOPROCTOLOGIQUES
GRUPPO SVIZZERO DI STUDIO PER LA COLOPROCTOLOGIA
SWISS STUDY GROUP FOR COLOPROCTOLOGY

Crohn's fistula: Surgeon's options

F. Ris



45. Schweizerische Koloproktologie-Tagung
42^{ème} Journée Suisse de Coloproctologie
27. Januar 2024, Kessel Ballen

THE UNUSUAL FISTULA
HOT TOPICS IN COLORECTAL CANCER



ECCO Guideline/Consensus Paper

ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment

Michel Adamina,^{a,b} Stefanos Bonovas,^{c,d} Tim Raine,^e Antonino Spinelli,^f Janindra Warusavitarne,^g Alessandro Armuzzi,^h Oliver Bachmann,ⁱ Palle Bager,^j Livia Biancone,^k Bernd Bokemeyer,^l Peter Bossuyt,^m Johan Burisch,ⁿ Paul Collins,^o Glen Doherty,^p Alaa El-Hussuna,^q Pierre Ellul,^r Gionata Fiorino,^{c,d} Comelia Frei-Lanter,^s Federica Furfaro,^g Christian Gingert,^t Paolo Gionchetti,^u Javier P. Gisbert,^v Fernando Gomollon,^w Marien González Lorenzo,^x Hannah Gordon,^x Tibor Hlavaty,^y Pascal Juillerat,^z Konstantinos Katsanos,^{aa} Uri Kopylov,^{ab} Eduards Krustins,^{ac} Torsten Kucharzik,^{ad} Theodore Lytras,^{ae} Christian Maaser,^{af} Fernando Magro,^{ag} John Kenneth Marshall,^{ah} Pär Myrelid,^{ai} Gianluca Pellino,^{aj} Isadora Rosa,^{ak} Joao Sabino,^{al} Edoardo Savarino,^{am} Laurents Stassen,^{an} Joana Torres,^{ao} Mathieu Uzzan,^{ap} Stephan Vavricka,^{aq} Bram Verstockt,^{ar} Oded Zmora^{as}; on behalf of the European Crohn's and Colitis Organisation [ECCO]

Special thanks to M. Adamina



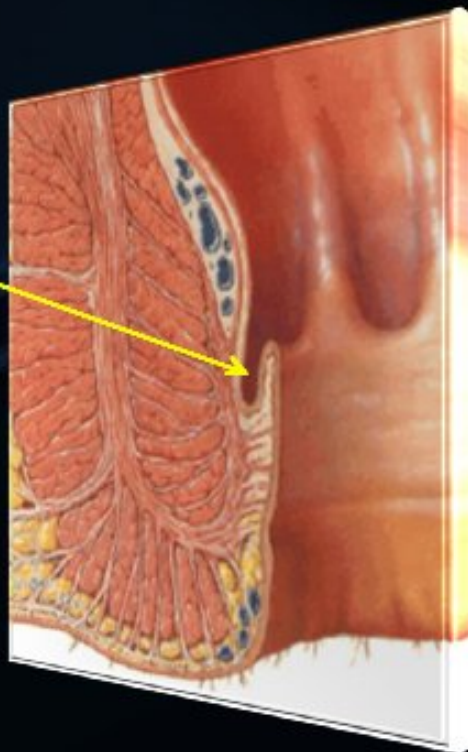
ETIOLOGY

90%

primary

crypto-glandular

Herman and Defosse glands



10% secondary

Hydroadenitis, sebaceous adenitis

Fissure

Pilonidal Cyst

Infectious disease: tbc, STD

Carcinoma: anal, rectum, leukemia

Post radiotherapy

Debilitating illnesses (leukemia, diabetes, AIDS)

Crohn's disease, HRC

Iatrogenic: injections, hemorrhoidectomy,
sclerotherapy, prostatectomy

Trauma: foreign body, penetrating wounds,
obstetrical tears

Perianal Crohn's disease

First Crohn manifestation in 10%



Fistula arises from penetrating abscess

Perianal Crohn's disease

Risk factors:

Disease severity

Duration (15% @5Y, 21%@10Y,26%@20Y)

Young age

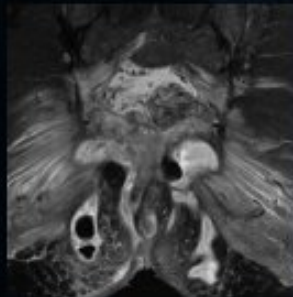
Smoking

Colonic extension (closer to the rectum worse)

Perianal fistulizing Crohn's

Classical **acute** abscess-fistula presentation **OR**
non-acute, chronic purulent discharge,
discomfort

Interdisciplinary management essential



Fistulizing disease predicts a more aggressive form of Crohn's disease with a poor long-term outcome

1/3

Proportion of patients
with Crohn's disease
affected
by perianal fistulas

50–80%

Proportion of
Crohn's perianal
fistulas
that are complex

42%

Recurrence rate of
Crohn's perianal
fistulas after 10-year
follow-up

Drain the sepsis – place a seton

Treat the disease

Close the fistula... if wanted



QOL oriented therapy



PISA II: combine perioperative anti-TNF with surgical closure (LIFT, Flap) for best clinical and radiological results

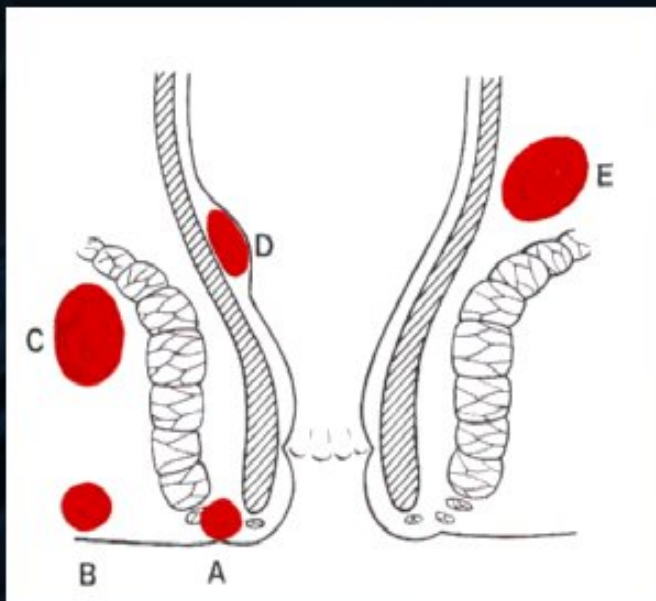
Gionchetti JCC 2017 Adamina JCC 2020 Meima-van Praag Lancet Gastr Hep 2022

Drain the sepsis

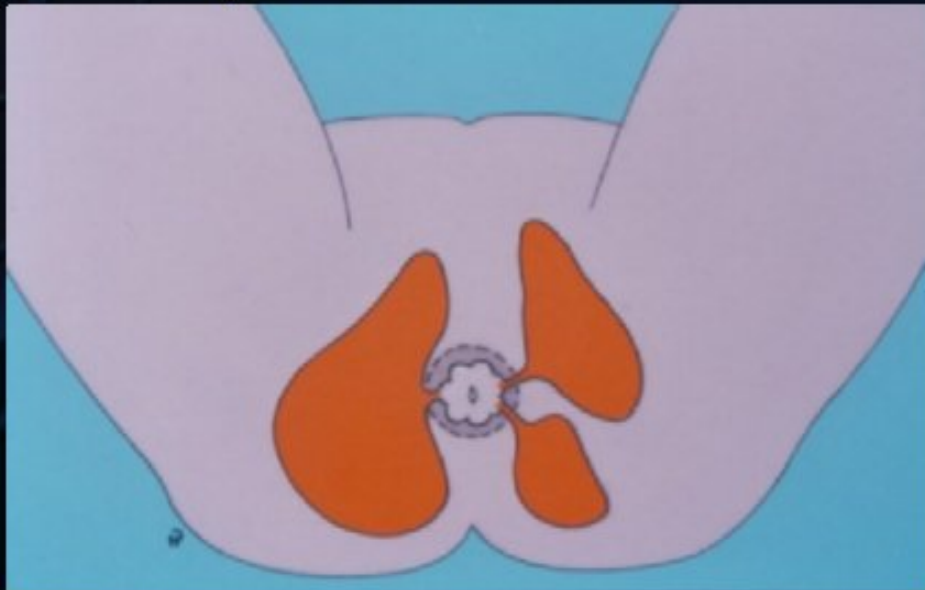
Primum movens of the fistula?



Different Abscess localisation



Abcess development possibilities



Simple drainage in anorectal abscess?



A surreal painting of a long, narrow hallway. The walls and floor are composed of numerous stacked wooden crates or boxes, creating a complex, geometric pattern. A small, dark figure is visible in the distance, walking away from the viewer down the center of the hallway. The lighting is dramatic, with a bright light source at the far end of the hallway, casting long shadows and highlighting the textures of the crates. The overall atmosphere is mysterious and surreal.

No need to find the fistula at first

Medical treatment (already discussed)



Medical treatment (already discussed)

Key component, yet taken **alone** consistently **fails**

Anti-TNF vs placebo: close to 50% initial success, later **35%**

Vedolizumab, ustekinumab: less than 25%

LIFT, advancement flap – established standards
enthusiastic initial success rate down to **65%** later



Imaging to understand the fistula



Imaging to understand the fistula

Prospective Comparison of Magnetic Resonance Imaging, Transrectal and Transperineal Sonography, and Surgical Findings in Complicated Perianal Crohn Disease

Renáta Bor, MD, Klaudia Farkas, MD, Anita Bálint, MD, Mónika Szűcs, PhD, Szabolcs Ábrahám, MD, Ágnes Milassin, MD, Mariann Rutka, MD, Ferenc Nagy, MD, Péter Milassin, MD, Zoltán Szepes, MD, Tamás Molnár, MD



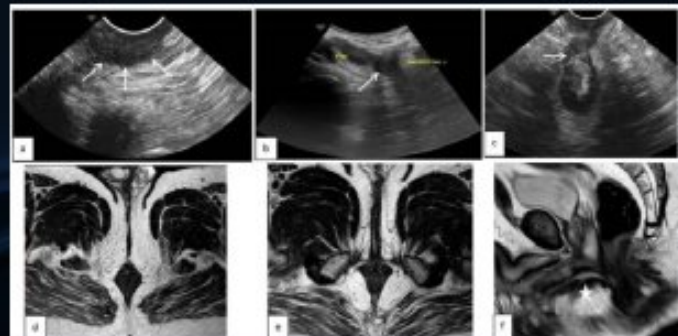
Bor R, et al.. Prospective Comparison of Magnetic Resonance Imaging, Transrectal and Transperineal Sonography, and Surgical Findings in Complicated Perianal Crohn Disease. J Ultrasound Med. 2016 Nov;35(11):2367-2372. doi: 10.7863/ultra.15.09043.

Imaging to understand the fistula

Table 3. Accuracy of Transrectal Sonography, Transperineal Sonography, and MRI in Perianal Crohn Disease

Modality	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Fistula				
Transrectal sonography	84.6	81.80	20.0	20.0
Transperineal sonography	100	100	100	100
MRI	84.6	100	100	20.0
Abscess				
Transrectal sonography	92.8	76.4	71.4	100
Transperineal sonography	100	86.6	83.3	100
MRI	58.8	92.8	90.9	65.0
Rectal involvement				
Transrectal sonography	86.3	0	100	25.0
Transperineal sonography	95.4	100	95.4	0
MRI	95.4	0	100	50.0

NPV indicates negative predictive value; and PPV, positive predictive value.



Roman Boles et al. Egypt J Radiol Nucl Med (2022) 53:141

High degree of accuracy in detection of distal collections
MRI can be kept for cases of supralelevator extension or side branches

Imaging to understand the fistula

Transperineal sonography is very accurate and easy-to-perform for evaluation of complicated perianal Crohn disease



RESEARCH ARTICLE

WILEY

Role of ultrasonography in evaluation of perianal fistula—A study of 200 cases

Manohar Kachare  | Alamgir Khan 

Powerful screening modality,
which can obviate the need of
MRI in a majority of cases.



FIGURE 12 Extra sphincteric fistula: The above mention image of transperineal ultrasonography using transrectal probe the patient was examine in lithotomy and left lateral position shows hypoechoic fistulous tract with collection within in the Extra sphincteric draining into the anal canal (AC) at internal opening (IO) at 8–9 o'clock position from above the levator sling (L). ES, external sphincter; IS, internal sphincter.

MRI best modality for CD anal fistula
EAUS is a good alternative
any modality **combined with examination under anesthesia** improves accuracy



Schwartz et al, Gastroenterology 2001, Spinelli et al, Curr Drug Targ 2012



What are the options?

Long-term seton

Attempt to heal surgically

OPTIONS

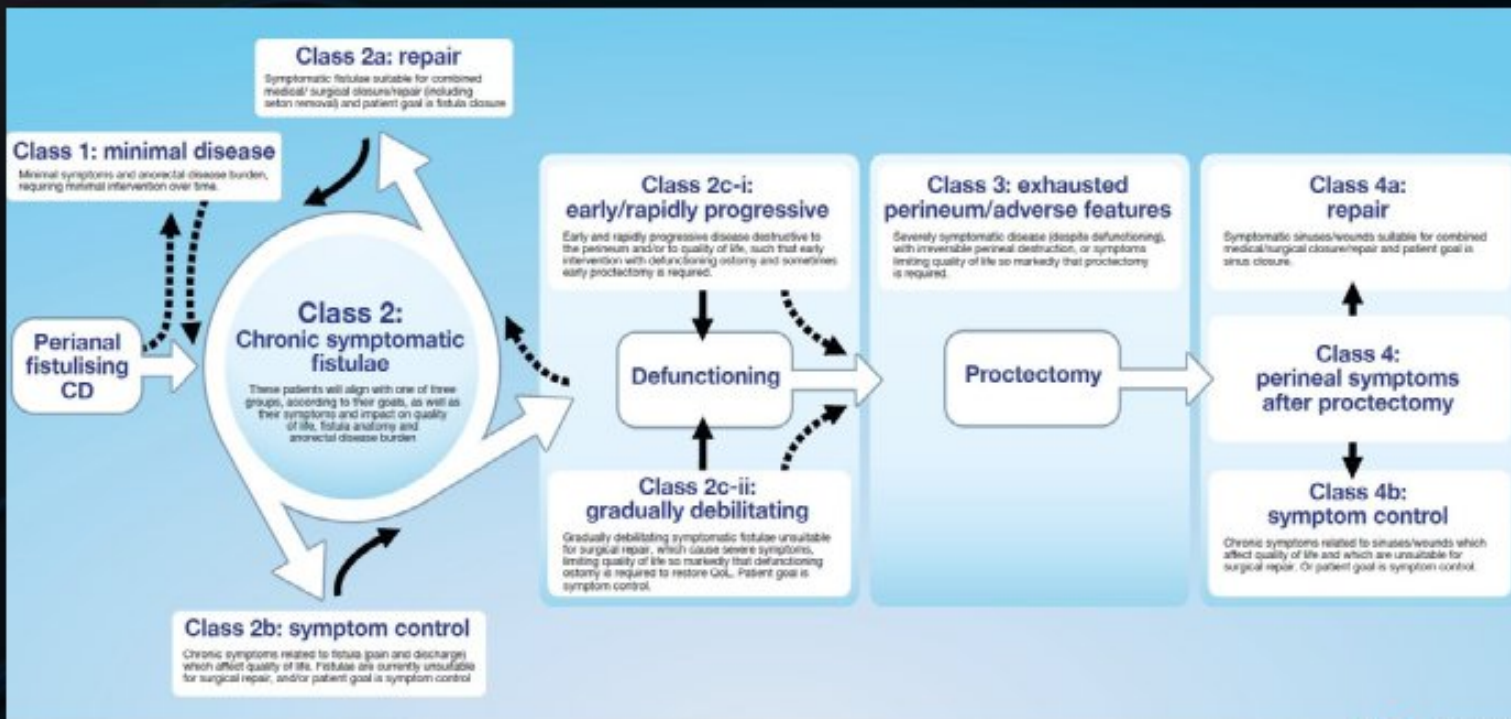
Remove seton only

Remove seton and
attempt to heal medically

Do only in *controlled situations*:

- ✓ No sepsis
- ✓ Seton in situ
- ✓ Established on immunomodulators

Goal-directed therapy



Goal-directed therapy symptoms control

Class 2a: repair

Symptomatic fistulae suitable for combined medical/surgical closure/repair (including seton removal) and patient goal is fistula closure

Class 1: minimal disease

Minimal symptoms and anorectal requiring minimal intervention only

Perianal
fistulising
CD

Class 2b: symptom control

Chronic symptoms related to fistula (pain and discharge) which affect quality of life. Fistulae are currently unsuitable for surgical repair, and/or patient goal is symptom control

Class 2c-ii: gradually debilitating

Gradually debilitating symptomatic fistulae unsuitable for surgical repair, which cause severe symptoms, limiting quality of life so markedly that defunctioning ostomy is required to restore QoL. Patient goal is symptom control

Class 2b: symptom control

Chronic symptoms related to fistula (pain and discharge) which affect quality of life. Fistulae are currently unsuitable for surgical repair, and/or patient goal is symptom control

Initial Surgical management

Seton drainage, for up to 3-6 months

After healing of the abscess cavity, in case of residual fistula

Prevent recurrence of the abscess

Initial Surgical management

Seton drainage, used from Greek

Hippocrates used horse hair



Test with air...



**Blind probing
should be avoided !**



Initial Surgical management



Vessel loops



Prolène 4-0 is good, 2 stiches



Initial Surgical management

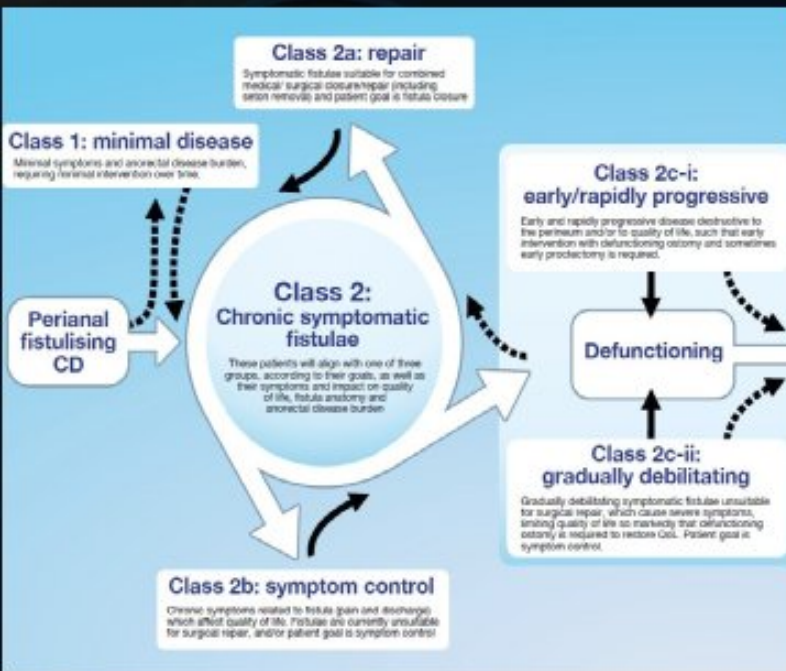


When should we pull them out ?

If the initial response is good with decrease leakage, an attempt can be performed after 6 weeks of treatment

It can be left in place forever if necessary
Usually well tolerated

Goal-directed therapy, 2a, repair



Class 2a perianal fistula
Goal is fistula control and ultimately closure

Can be difficult: ~70%

Geldof Lancet Gastro Hep 2022
Eglington TW DCR 2012 Schwartz DA
Gastroenterology 2002

Class 2a: repair

Symptomatic fistulae suitable for combined medical and surgical closure or repair (including seton removal) and patient goal is fistula closure

Try to avoid sphincter damaging surgical management

Cutting setton (40-60% risk of incontinence)

Van Tests. BLS 1995;82:895-7

Hämäläinen KP. Dis Col Rect 1997;40:1443-7

Garcia-Aguilar J. BJS 1998;85:243-5

Transsphincteric fistulectomy and sphincter reconstruction (>30% incontinence

Herold invited lecture ECC St Gallen 2012)

Both avoided because of fecal incontinence

Sphincter damaging surgical management

COLORECTAL



ANZJSurg.com

Long-term results of the cutting seton for high anal fistula

Vicki Patton,*† Chung Ming Chen*‡ and David Lubowski*†

*Department of Colorectal Surgery, St George Hospital, Sydney, New South Wales, Australia

†University of New South Wales, Sydney, New South Wales, Australia and

‡Mount Elizabeth Novena Specialist Centre, Affinity Surgery Centre, Singapore

78% had normal continence or minor incontinence (score 0–6),
13.5% moderate incontinence (score 7–12) and 8.5% severe
incontinence (score >12)

Sphincter preserving surgical management

Statement 1.2. ECCO CD Treatment GL [2019]

Advancement flaps are a therapeutic option for patients with Crohn's disease and complex perianal fistulae [EL4].

Preoperative care

Mucosal flap technique:

Antibiotic prophylaxis

No Enema

No Epilation

No Stoma



Flap surgery principles

1) Preemptive anesthesia

Perineal bloc

(Long lasting LA)

Infiltration

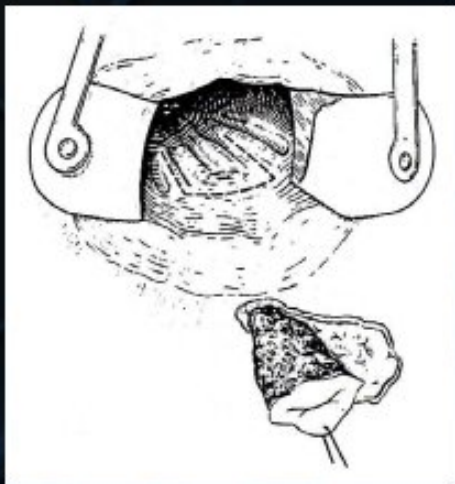
(Epinephrine + LA)

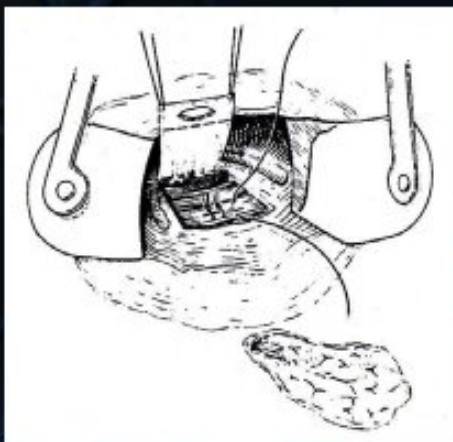


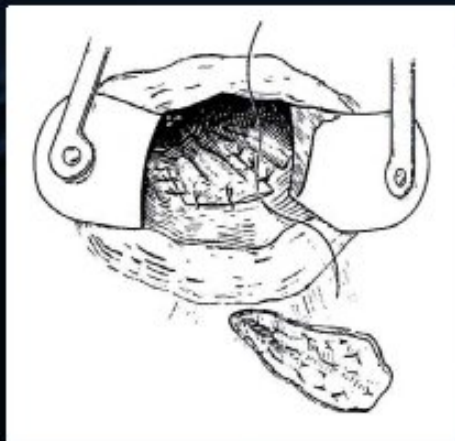
**2) Go from known to unknown
follow closely the fistula tract**

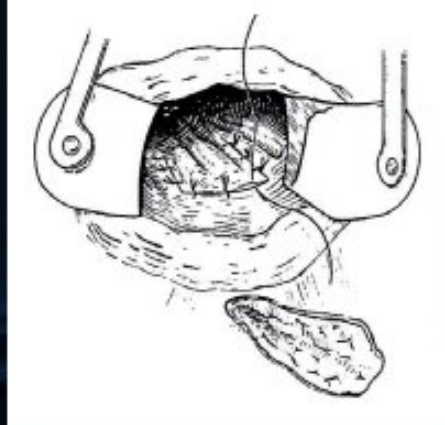
**Don't use electrocoagulation in
dangerous zone (sphincter)**











**5) Prepare a mucosal sub mucosal
flap**

don't traumatize the flap

Flap without tension

Wash wash wash...



Mucosal flaps

61/66% success rate in patients with CD perianal fistula,

However, incontinence rates were significantly higher after flaps [7.8% versus 1.6%].

Stellingwerf ME, van Praag EM, Tozer PJ, Bemelman WA, Buskens CJ. Systematic review and meta-analysis of endorectal advancement flap and ligation of the intersphincteric fistula tract for cryptoglandular and Crohn's high perianal fistulas. BJS Open 2019;3:231-41.

Other Therapies

Statement 1.4. ECCO CD Treatment GL [2019]

Ligation of the intersphincteric fistula tract is an option for treatment of patients with Crohn's disease and complex perianal fistulae [EL4].

LIFT procedure

LIFT procedure

LIFT

Ligation of Inter-sphincteric Fistula Tract

Described by Rojanasankul in 2007

Success rates of > 94%

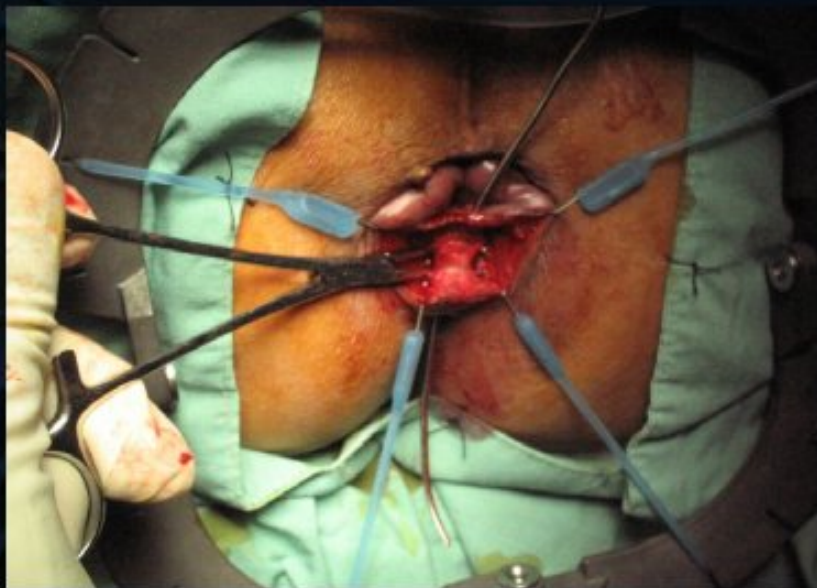
No deterioration in continence

LIFT procedure



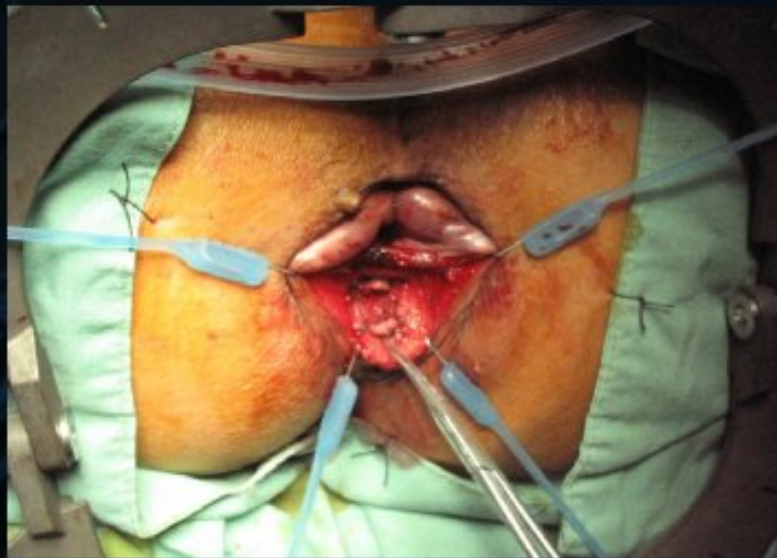
Tract probed and circumanal incision

LIFT procedure



Complete dissection of tract

LIFT procedure



Tract suture ligated and divided

LIFT procedure



LIFT wound closed

Tech Coloproctol (2014) 18:685–691

DOI 10.1007/s10151-014-1183-3

REVIEW

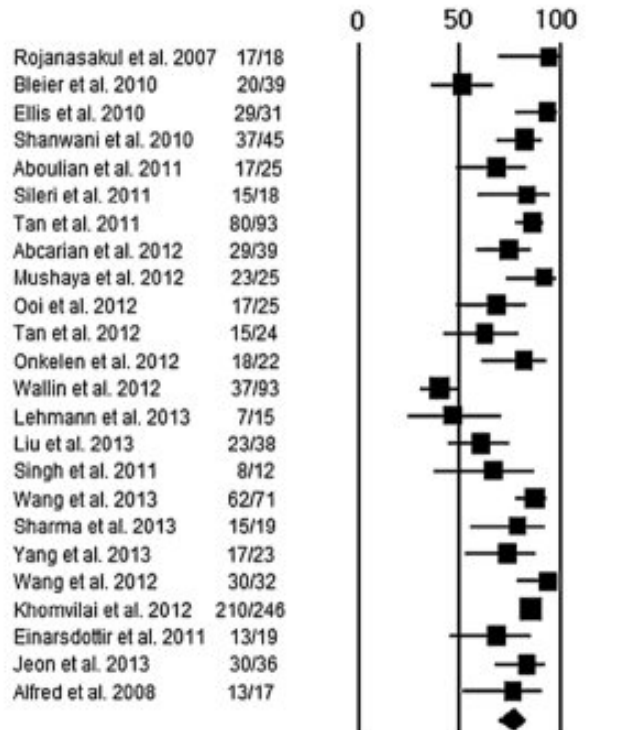
Ligation of intersphincteric fistula tract (LIFT) to treat anal fistula: systematic review and meta-analysis

**K. D. Hong · S. Kang · S. Kalaskar ·
S. D. Wexner**

Source	Study design	Surgical method	Patient no.	Success rate (%)	Follow-up duration* (month)	Quality score
Rojanasakul et al. [8]	Prospective case series	LIFT	18	94.4	3	2
Bleier et al. [7]	Retro case series	LIFT	39	51.3	4.7	3
Ellis et al. [15]	Retro case series	bio-LIFT	31	93.5	15	3
Shanwani et al. [11]	Prospective case series	LIFT + coring out	45	82.2	9	3
Aboulain et al. [18]	Retro case series	LIFT	25	68	6.3	3
Sileri et al. [26]	Prospective case series	LIFT	18	83.3	6	3
Tan et al. [27]	Retro case series	LIFT	93	86	5.4	2
Abcarian et al. [28]	Retro case series	LIFT	41	74.4	4.2	3
Mushaya et al. [24]	RCT (LIFT vs. ARAF)	LIFT	25 versus 14	92 versus 92.9	16.4 versus 30	5
Ooi et al. [29]	Prospective case series	LIFT	25	68	5.1	4
Tan et al. [25]	Case control (LIFT vs. ARAF)	LIFT	24 versus 31	62.5 versus 93.5	13 versus 6	3
Onkelen et al. [14]	Retro case series	LIFT + coring out	22	81.9	19.5	3
Wallin et al. [9]	Retro case series	LIFT	93	39.8	19	3
Lehmann et al. [10]	Prospective case series	LIFT	17	47	3.7	3
Liu et al. [30]	Retro case series	LIFT	38	60.5	26	3
Singh et al. [31] [†]	Retro case series	LIFT	12	66.7	4	
Wang et al. [19] [†]	Case-control (LIFT vs. LIFT + previous seton)	LIFT	53 versus 18	87.3	4.4	
Sharma et al. [32] [†]	Retro case series	LIFT	19	78.9	2.8	
Yang et al. [16] [†]	Case-control (LIFT vs. bio-LIFT vs. AFP)	LIFT or bio-LIFT	14 versus 9 versus 32	78.6 versus 66.7 versus 9.3	6.5 versus 2.1 versus 8.2	
Wang et al. [17] [†]	Prospective case series	LIFT + fistula plug	32	93.8	8	
Khomvilai et al. [33] [†]	Retro case series	LIFT	250	85.2	2.8	
Einarsdottir et al. [34] [†]	Retro case series	LIFT	19	68.4	3	
Jhon et al. [12] [†]	Prospective case series	LIFT + coring out	36	83.3	17.2	
Alfred et al. [13] [†]	Prospective case series	LIFT + coring out	17	76.5	n.a.	

Study name

Success rate and 95%CI (%)



Pooled 76.4% (68.9-82.5)

LIFT procedure

The LIFT procedure is simple, safe and effective

The LIFT procedure has no reported adverse effects on continence

“Failures” at LIFT can be transformed to “secondary closures” (transphincteric fistula into low inter-sphincteric fistulae amendable to fistulotomy)

LIFT procedure

The LIFT procedure is simple, safe and effective

The LIFT procedure has no reported adverse effects on continence

“Failures” at LIFT can be transformed to “secondary closures” (transphincteric fistula into low inter-sphincteric fistulae amendable to fistulotomy)

LIFT procedure in Crohn's disease

- ◆ 15 CD patients (9 women; mean age = 34.8 years)
- ◆ LIFT site healing was seen in 8 of the 12 patients (67%) with complete 12-month follow-up

Annals of Surgery • Volume 260, Number 6, December 2014



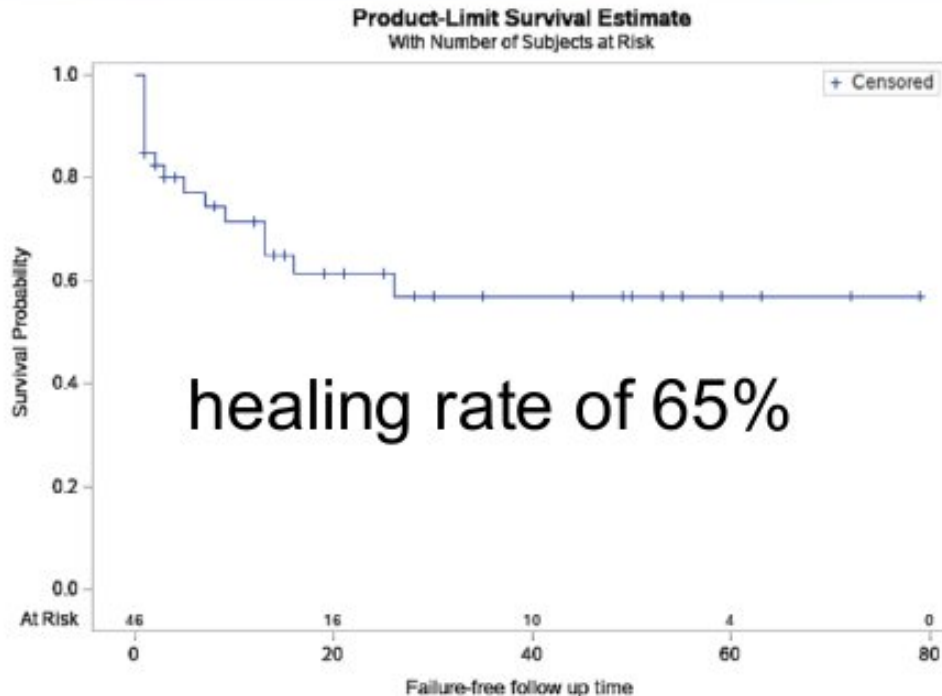
Increasing experience with the LIFT procedure in Crohn's disease patients with complex anal fistula

T. Wood¹ · A. Truong¹ · A. Mujukian¹ · K. Zaghiyan¹ · P. Fleshner¹

Received: 8 August 2021 / Accepted: 21 January 2022 / Published online: 1 February 2022
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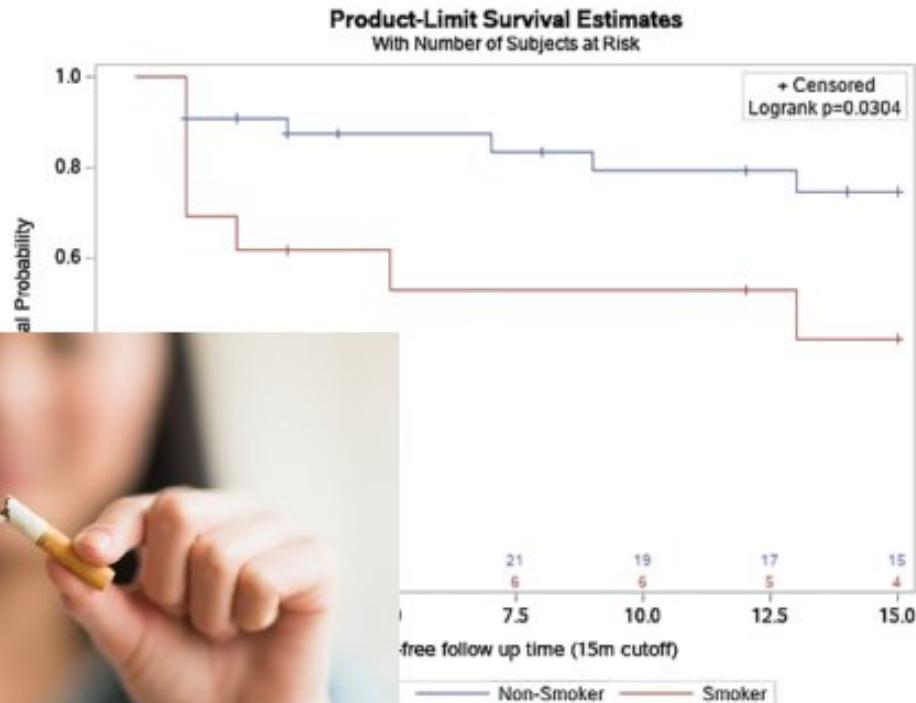
Wood T, Truong A, Mujukian A, Zaghiyan K, Fleshner P. Increasing experience with the LIFT procedure in Crohn's disease patients with complex anal fistula. *Tech Coloproctol.* 2022 Mar;26(3):205–212. doi: 10.1007/s10151-022-02582-4. Epub 2022 Feb 1. PMID: 35103901.

Fig. 1 LIFT failure over time.
Number at risk displayed on
horizontal axis. Failure-free
follow-up time displayed in
months



Wood T, Truong A, Mujukian A, Zaghiyan K, Fleshner P. Increasing experience with the LIFT procedure in Crohn's disease patients with complex anal fistula. *Tech Coloproctol.* 2022 Mar;26(3):205-212. doi: 10.1007/s10151-022-02582-4. Epub 2022 Feb 1. PMID: 35103901.

Fig. 2 LIFT failure over time comparing smokers and non-smokers. Log-rank p value 0.03. Number at risk displayed on horizontal axis. Failure-free follow-up time displayed in months. Data censored at 15 months



Wood T, Truong A, Mujukian A, Zaghiyan K, Fleshner P. Increasing experience with the LIFT procedure in Crohn's disease patients with complex anal fistula. *Tech Coloproctol.* 2022 Mar;26(3):205-212. doi: 10.1007/s10151-022-02582-4. Epub 2022 Feb 1. PMID: 35103901.

LIFT procedure

the role of LIFT for the treatment of perianal CD fistulae remains unclear, although the complication rate seems to be reasonably low. RCTs are needed to clarify the role of LIFT in CD fistulae, perhaps by comparing LIFT with advancement flap as a control arm.



Other Sphincter preserving fistula treatment

Other Sphincter preserving treatment



Plugs

VAAFT

FiLaC

Fibrin Glue

OVESCO

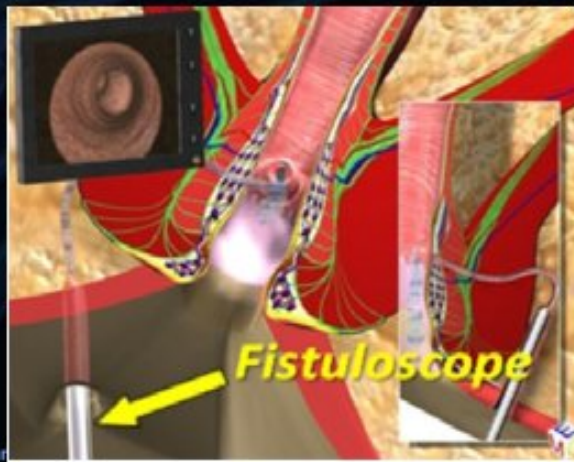
Statement 1.5. ECCO CD Treatment GL [2019]

Anal fistula plugs [AFP] should not be routinely considered for ano-perineal fistula closure in Crohn's disease, as seton removal alone is equally effective [EL3].

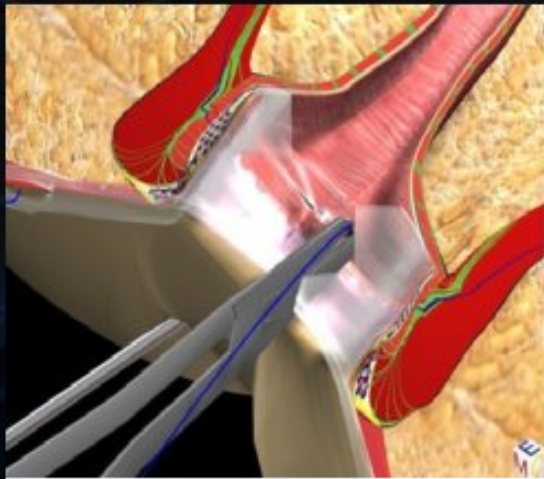


Video-assisted anal fistula treatment (VAAFT)

- ♦ a novel sphincter-saving procedure to repair complex anal fistulas, rigid fistuloscopy

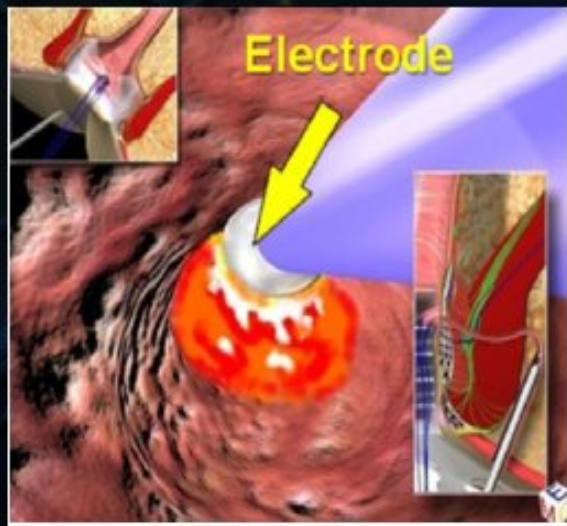


Video-assisted anal fistula treatment (VAAFT)



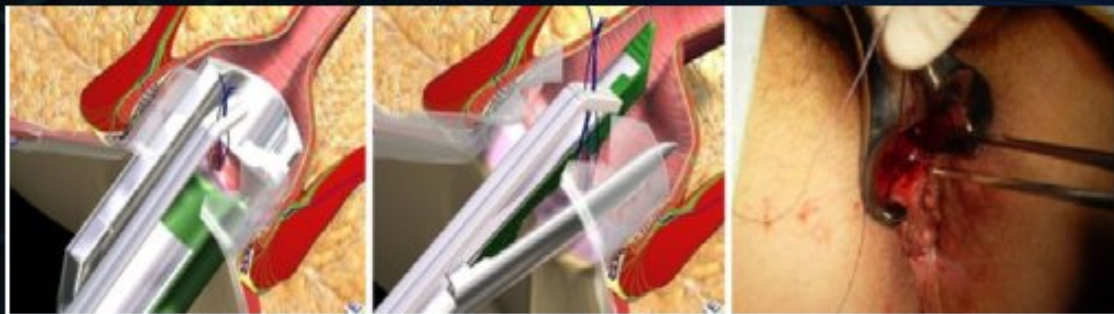
Identification and lifting
of the internal opening

Video-assisted anal fistula treatment (VAAFT)



Cleaning of the tract by
fulguration, brushing
and washing

Video-assisted anal fistula treatment (VAAFT)



Closure of the internal opening with a stapler or a flap

+ injection of cyanoacrylate glue below the staple line!

Video-assisted anal fistula treatment (VAAFT)

136 patients using VAAFT.

98 patients were followed up for a minimum of 6 months.

No major complications

Primary healing in 72 patients (73.5%) at 2–3 months.

followed up **>1 year for 62 patients**, among them **87.1%** healed

Video-assisted anal fistula treatment (VAAFT)

82 patient treated VAAFT.

85% success in non Crohn's patients

15% recurrence

2013

SCIENTIFIC PAPER

JSLS

Video-Assisted Anal Fistula Treatment

Gaurav Kochhar, MS, Sudipta Saha, MS, Manoj Andley, MS, Ashok Kumar, MS,
Gyan Saurabh, MS, Rahul Pusuluri, MS, Vikas Bhise, MBBS, Ajay Kumar, MCh

Original Article

Symptom Amelioration in Crohn's Perianal Fistulas Using Video-Assisted Anal Fistula Treatment (VAAFT)

Samuel O. Adegbola^{a,b}, Kapil Sahnan^{a,b}, Philip J. Tozer^{a,b},
Raimund Strouhal^a, Ailsa L. Hart^{a,b}, Phillip F. C. Lung^{a,b},
Robin K. S. Phillips^{a,b}, Omar Faiz^{a,b}, Janindra Warusavitarne^{a,b}

^aRobin Phillips Fistula Research Unit, St Mark's Hospital and Academic Institute, Harrow, UK; ^bDepartment of Surgery and Cancer, Imperial College, London, UK

Corresponding author: Samuel Adegbola, Clinical Research Fellow, St Mark's Hospital, Watford Road, Harrow, Middlesex HA13UJ, UK. E-mail: sama@doctors.net.uk

VAAFT reduces the main symptoms, pain and discharge in patients with complex refractory anal fistulas

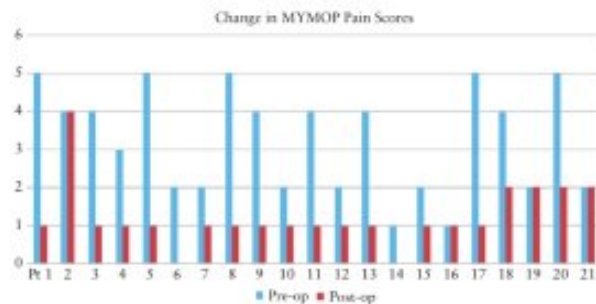


Figure 1. Pre- and postoperative MYMOP pain scores.

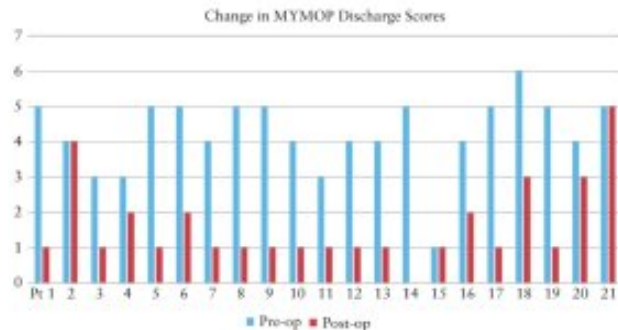


Figure 2. Pre- and postoperative MYMOP discharge scores.

Video-assisted anal fistula treatment (VAAFT)

Sound principle

Cost? (equipment and staplers)

Target healing vs QOL

FiLaC® – (Fistula-tract Laser Closure)

Minimally invasive treatment for fistulas by using radial laser radiation for the elimination and collapsing of the fistula tract



FiLaC® – (Fistula-tract Laser Closure)

Few centers

50%-60% success rate (ICF 2013)

No adverse events so far

What if they do the brush without the laser



REVIEW



Efficacy and safety of FiLaC™ for perianal fistulizing Crohn's disease: a systematic review and meta-analysis

D. Cao¹ · W. Li² · Y. Ji² · X. Wang³ · Z. Cui^{1,3}

Table 2 Characteristics of the included studies

Study	Country	Year	Study design	Time period	Median follow-up	No. of pfCD participants	Healed	Primary healing rate	Recurrence
Giamundo [9]	Italy	2015	Retrospective	Jul 2010–May 2014	30 (6–46) months	2	2	100%	N.A
Wilhelm [5]	Germany	2017	Retrospective	Oct 2009–Jul 2014	25.4 (6–60) months	13	9	69%	N.A
De Hous [10]	Belgium	2019	Retrospective	Nov 2016–Dec 2018	9 (4–26) months	2	2	100%	0
Alam [13]	France	2020	Retrospective	Mar 2016–Nov 2018	7.1 (2–22.5) months	20	11	55%	N.A
Wolicki [11]	Germany	2020	Retrospective	Jan 2011–Dec 2017	41.99 (4–87) months	2	1	50%	N.A
Nordholm-Carstensen [12]	Denmark	2021	Retrospective	Mar 2017–Jul 2019	19 (12–26) months	11	6	55%	0

pfCD perianal fistulizing Crohn's disease, N.A. not available

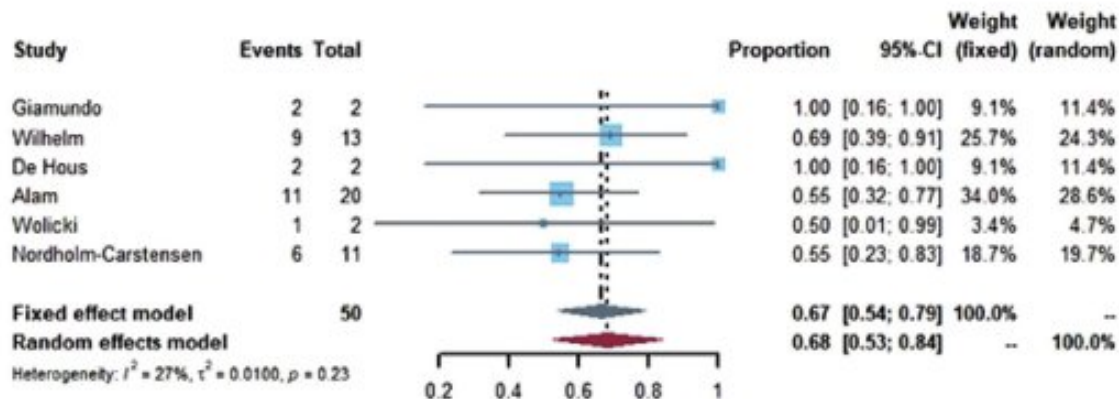


Fig. 2 The proportion meta-analysis plot (random effects) of all 6 studies showed a pooled primary healing rate of 68% (95% CI 53.0–84.0%, $I^2 = 27\%$, $p = 0.23$)

FiLaC™ for pfCD patients has a high primary healing rate and is associated with only minimal fecal incontinence or other surgical complications

Fibrin Glue

Statement 1.3. ECCO CD Treatment GL [2019]

Fibrin glue may be a potential treatment, with limited efficacy, for patients with complex perianal Crohn's disease [EL4].



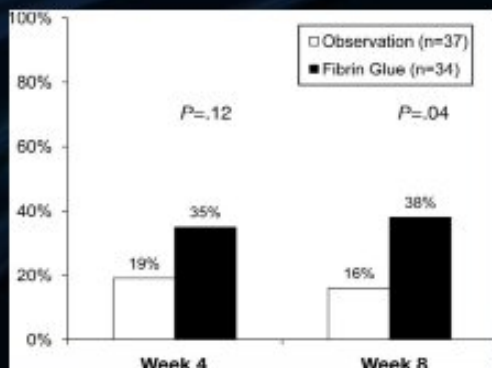
Fibrin Glue

RCT (12 centers)

clin remission in **38%** vs 16% ($P=0.04$) @8 wks

LIMITATIONS

- healing with MRI or EUS not assessed. (may even be lower than reported clinical remission of 38%?)
- short f-up @8 weeks
- Heterogeneity in surgical manag before glue



Grimaud, Gastroenterology, 2010

A Lightner, Gastroenterol Clin N Am (2017)

Ovesco clip



Prosst et al, Minimally Invasive Therapy. 2012;21:307-312

Ovesco clip

Int J Colorectal Dis (2015) 30:621–624

DOI 10.1007/s00384-015-2146-5

ORIGINAL ARTICLE

Easy clip to treat anal fistula tracts: a word of caution

M. Gautier · P. Godeberge · R. Ganansia · G. Bozio ·
B. Godart · M.A. Bigard · M. Barthet · L. Siproudhis · For
the Groupe de Recherche en Proctologie SNFCP France

Accepted: 23 January 2015 / Published online: 13 February 2015

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Treatment of anal fistula by placing a clip on the internal opening is disappointing and deleterious for some patients. A better assessment before dissemination is recommended.

Stem cell therapy

Statement 1.7. ECCO CD Treatment GL [2019]

Allogeneic adipose-derived stem cell therapy could be an effective and safe treatment for complex perianal fistulae in patients with Crohn's disease [EL2].

Statement 1.8. ECCO CD Treatment GL [2019]

Autologous adipose-derived stem cells may have positive effect for patients with Crohn's disease and complex perianal fistulae with good tolerability and safety [EL4].

Regenerative therapies

Process of renewing, engineering or replacing human cells, tissues or organs to **restore or establish normal function by stimulating the body's own repair mechanism** to functionally heal previously irreparable tissue or organ

Cell-based approaches

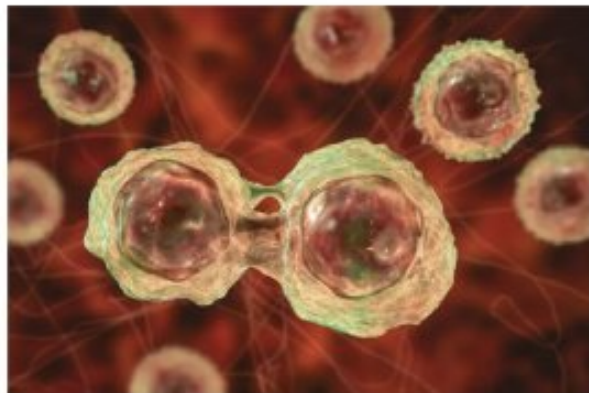
Autologous stem cell

Heterologous stem cell

By Susan Buckles

Early Mayo Clinic research finds hope in stem cell therapy for perianal fistulas in patients with Crohn's disease

March 2, 2023



<https://newsnetwork.mayoclinic.org/discussion/early-mayo-clinic-research-finds-hope-in-stem-cell-therapy-for-perianal-fistulas-in-patients-with-crohns-disease/>

REVIEW

Open Access



Mesenchymal stem cells transplantation for perianal fistulas: a systematic review and meta-analysis of clinical trials

H. Wang¹, H. Y. Jiang², Y. X. Zhang³, H. Y. Jin⁴, B. Y. Fei^{4*} and J. L. Jiang^{1*}

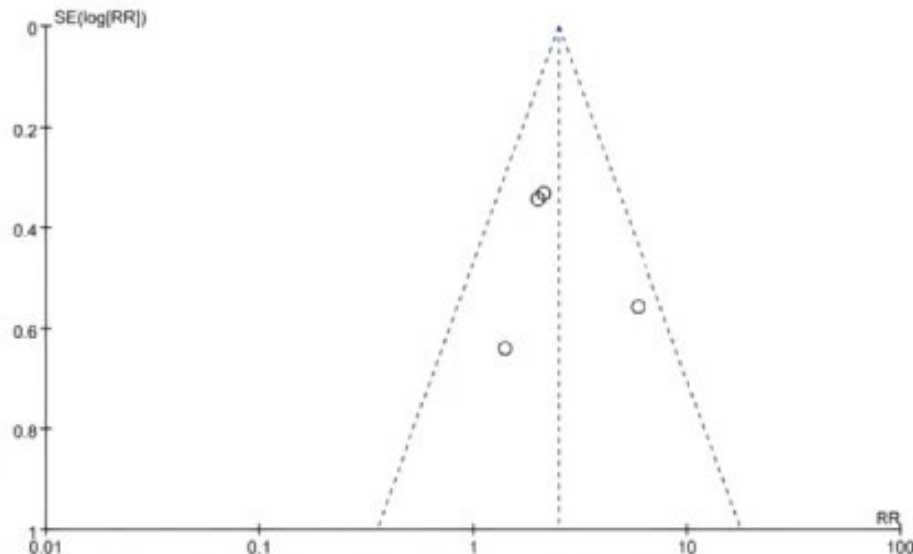
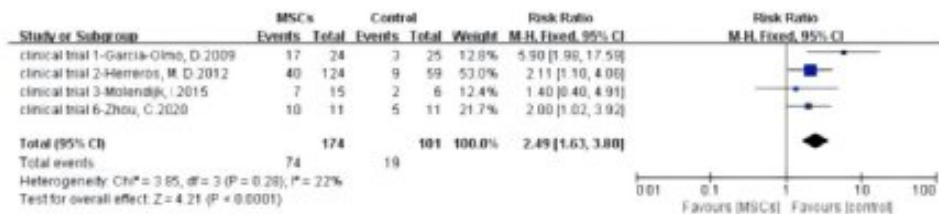
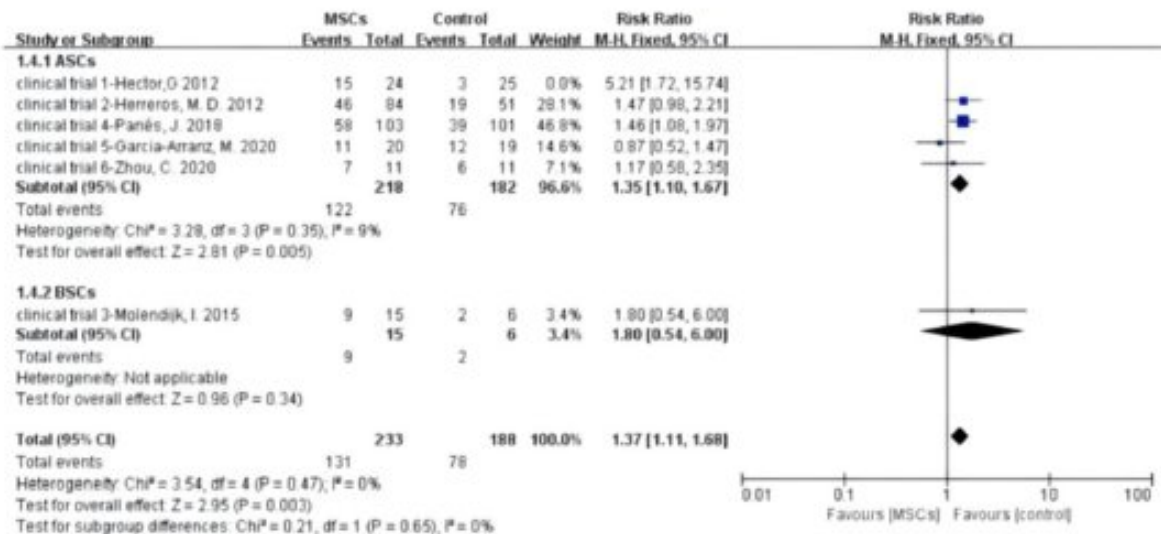


Fig. 4 Efficacy of MSCs group versus the control group in short-term follow-up phase (forest plot and funnel plot)



Autologous stem cell

Expanded adult stem cells (eASCs) (liposuccion)

Randomised study , n=49 , 35 vs 14 Crohn's



Autologous stem cell

Expanded adult stem cells (eASCs) (liposuccion)

Randomised study , n=49 , 35 vs 14 Crohn's

	Healing at 8 weeks	Healing rate at 1 year
Fibrin glue	3/25 (12%)	3/25 (12%)
Fibrin glue + eASCs	17/24 (71%)	15/24 (63%)

Autologous stem cell

Expanded adult stem cells (eASCs) (liposuccion)

Randomised study , n=49 , 35 vs 14 Crohn's

	Healing at 8 weeks	Healing rate at 1 year	End of FU 38 months
Fibrin glue	3/25 (12%)	3/25 (12%)	2/25(8%)
Fibrin glue + eASCs	17/24 (71%)	15/24 (63%)	7/21(33%)

Autologous stem cell

Open-label, phase 2 study
N= 43 patients.

Treatment included curettage, irrigation, and suturing of the internal opening. The fistula tract was filled with a mixture of ASCs and fibrin glue. ASCs were injected into the lesion site (A second injection of ASCs was performed for patients who did not show complete closure of the fistula at 8 weeks).

After 12 months, 88.5% of the patients showed sustained fistula healing.

Lee WY, Park KJ, Cho YB, et al. Autologous adipose tissue-derived stem cells treatment demonstrated favorable and sustainable therapeutic effect for Crohn's fistula. Stem Cells 2013;31:2575-81.

Durable Response in Patients With Refractory Fistulizing Perianal Crohn's Disease Using Autologous Mesenchymal Stem Cells on a Dissolvable Matrix: Results from the Phase I Stem Cell on Matrix Plug Trial

Eric J. Dozois, M.D.¹ • Amy L. Lightner, M.D.¹ • Allan B. Dietz, Ph.D.²
Joel G. Fletcher, M.D.³ • Yong S. Lee, Ph.D.³ • Jessica J. Friton, M.A.⁴
William A. Faubion, M.D.⁴

1 Department of Colon and Rectal Surgery, Mayo Clinic, Rochester, Minnesota

2 Department of Laboratory Medicine, Mayo Clinic, Rochester, Minnesota

3 Department of Radiology, Mayo Clinic, Rochester, Minnesota

4 Department of Gastroenterology, Mayo Clinic, Rochester Minnesota

N=20

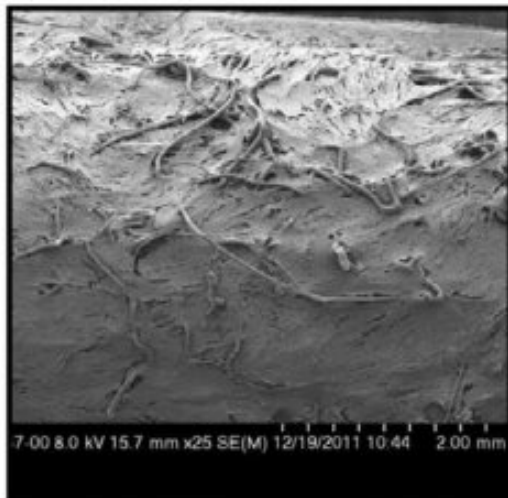
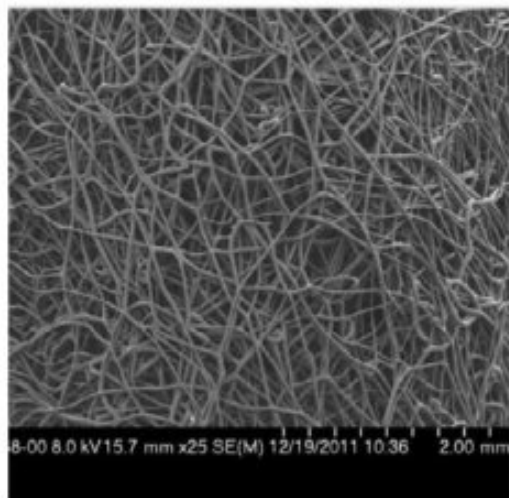


FIGURE 1. MSC adhering to matrix, without cells (left) and after cell adherence (right). MSC = mesenchymal stem cells.

Twenty patients (12 females; mean age 36 y) were treated with the stem cell-loaded plug.

3 study withdrawal.

Complete clinical healing occurred in 14 of 18 patients (77%) at 6 months and 13 of 17 patients at 12 months (76%).

Heterologous stem cell

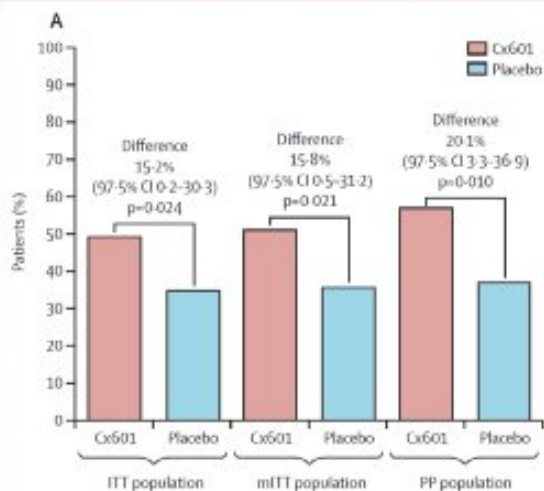
Darvadstrocel , CX 601

Bone marrow derived
stem cells

Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial



Julián Panés, Damián García-Olmo, Gert Van Assche, Jean Frederic Colombel, Walter Reinisch, Daniel C Baumgart, Axel Dignass, Maria Nachury, Marc Ferrante, Lili Kazemi-Shirazi, Jean C Grimaud, Fernando de la Portilla, Eran Goldin, Marie Paule Richard, Anne Leselbaum, Silvio Danese, for the ADMIRE CD Study Group Collaborators*



Lancet 2016

212 pts randomly assigned:
→ 107 to Cx601
→ 105 to placebo

High success rate, high placebo success rate...

Follow-up Study to Evaluate the Long-term Safety and Efficacy of Darvadstrocel (Mesenchymal Stem Cell Treatment) in Patients With Perianal Fistulizing Crohn's Disease: ADMIRE-CD Phase 3 Randomized Controlled Trial

Damián García-Olmo, M.D., Ph.D.¹ • Inmaculada Gilaberte, M.D., Ph.D.²
Matthias Binek, M.D., Ph.D.³ • André J.L. D'Hoore, M.D., Ph.D.⁴ • Dirk Lindner, M.Sc.³
Francesco Selvaggi, M.D.⁵ • Antonino Spinelli, M.D., Ph.D.^{6,7} • Julian Panés, M.D.⁸

1 Universidad Autónoma de Madrid, Fundación Jiménez Díaz, University Hospital, Madrid, Spain

2 Takeda Pharmaceuticals S.L., Madrid, Spain

3 Takeda Pharmaceuticals International AG, Zurich, Switzerland

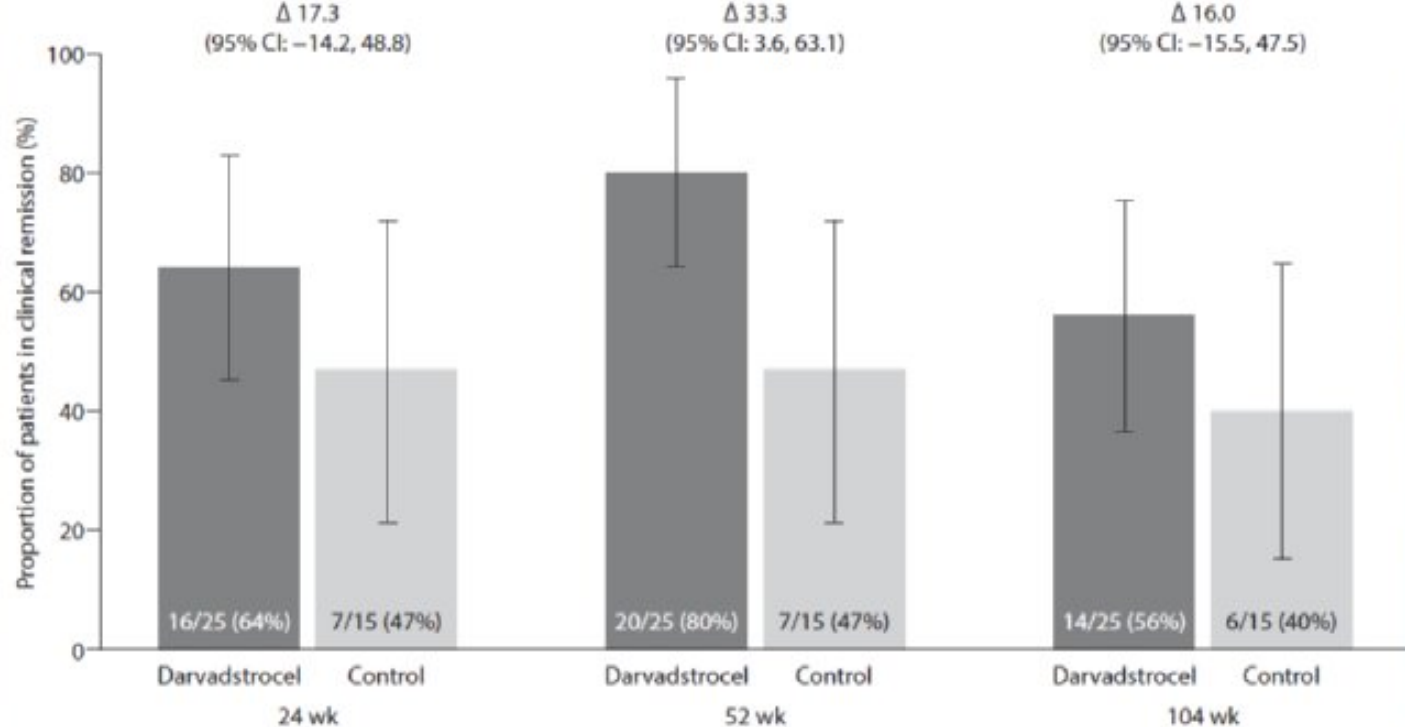
4 Universitair Ziekenhuis Leuven, Leuven, Belgium

5 Colon and Rectal Surgery Unit, Department of Advanced Medical and Surgery Sciences, Luigi Vanvitelli University, Naples, Italy

6 Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy

7 IRCCS Humanitas Research Hospital, Division of Colon and Rectal Surgery, Rozzano Milan, Italy

8 Inflammatory Bowel Disease Unit, Hospital Clinic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain



Darvadstrocel

Garcia-Olmo Dis Colon Rectum 2022; 65: 713–720

37/40 completed the long term follow-up.

At week 104, clinical remission was reported in 14/25 (56%) patients in the darvadstrocel group and 6/15 (40%) patients in the control group



Efficacy of cx601 (darvadstrocel) for the treatment of perianal fistulizing Crohn's disease – A prospective nationwide multicenter cohort study

Christopher Dawoud  · Kerstin Melanie Widmann · Sascha Czipin · Michael Pramhas · Martina Scharitzer · Anton Stift · Felix Harpain · Stefan Riss

Received: 25 May 2023 / Accepted: 9 September 2023

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14 Crohn's disease patients
Median follow-up of 92 weeks, successful fistula closure
in 57.1% (n=8)

Direct Injection of Ex Vivo Expanded Allogeneic Bone Marrow–Derived Mesenchymal Stem Cells for the Treatment of Pediatric Crohn's Perianal Fistulizing Disease

Amy L. Lightner, M.D.¹ • Jacob Kurowski, M.D.²
Ana M. Otero-Pinerio, M.D., Ph.D.³

¹ Department of Colorectal Surgery, Scripps Clinic, San Diego, California

² Department of Pediatric Gastroenterology, Pediatric Institute, Cleveland Clinic, Cleveland Ohio

³ Department of Gastrointestinal Surgery, Hospital Clinic, Barcelona, Spain

Completely healed

A Phase IB/IIA Study of Ex Vivo Expanded Allogeneic Bone Marrow–Derived Mesenchymal Stem Cells for the Treatment of Perianal Fistulizing Crohn's Disease

Amy L. Lightner, M.D.¹ • Jane Reese, M.B.A.²
Justin Ream, M.D.³ • Douglas Nachand, M.D.³ • Xue Jia, M.A.⁴
Neda Dadgar, Ph.D.⁵ • Scott R. Steele, M.D., M.B.A.¹ • Tracy Hull, M.D.¹

1 Department of Colorectal Surgery, Digestive Disease Surgical Institute, Cleveland Clinic, Cleveland, Ohio

2 National Center for Regenerative Medicine, Cleveland, Ohio

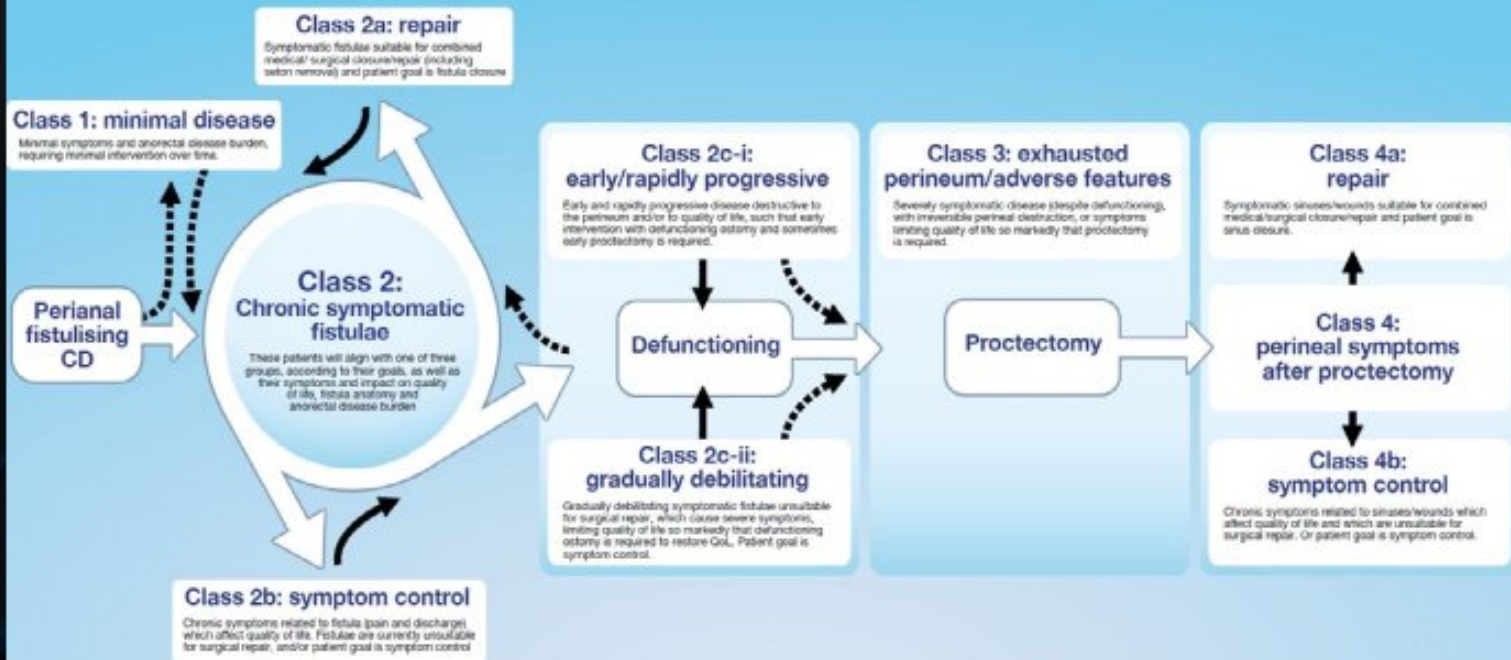
3 Department of Abdominal Radiology, Digestive Disease Surgical Institute, Cleveland Clinic, Cleveland, Ohio

4 Department of General Surgery, Statistics, Digestive Disease Surgical Institute, Cleveland Clinic, Cleveland, Ohio

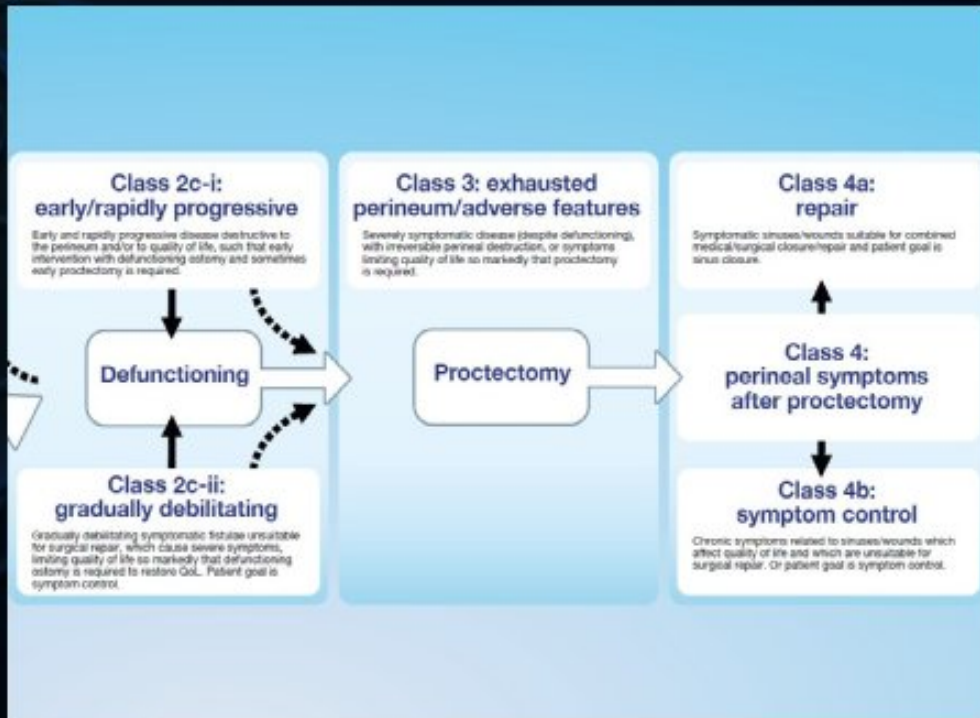
5 Department of Inflammation and Immunity, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio

N= 23 patients were enrolled, 18 test and 5 were control.
At 6 months, 83% of the treatment group and 40% of the control group had complete clinical and radiographic healing.

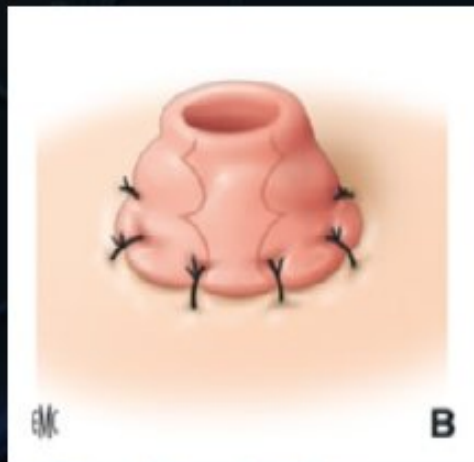
Goal-directed therapy



Goal-directed therapy



Defunctioning



Defunctioning



Goal-directed therapy

Class 3: exhausted perineum/adverse features

Severely symptomatic disease (despite defunctioning), with irreversible perineal destruction, or symptoms limiting quality of life so markedly that proctectomy is required.

Proctectomy

When there is no other choices...

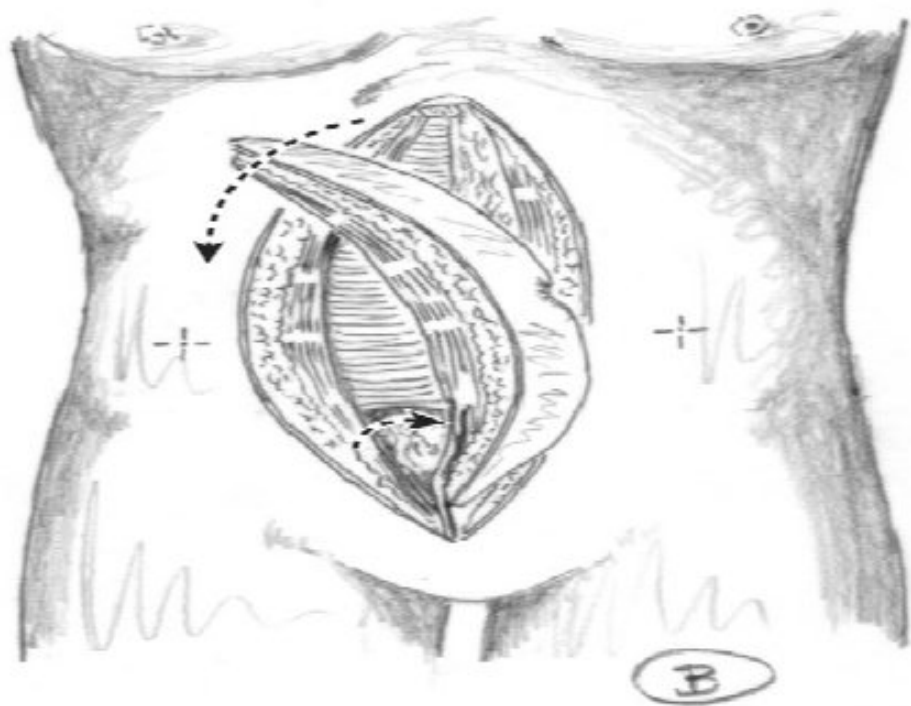


VRAM









Pelvic reconstruction



Long term results



Conclusion...

Complex perineal CD disease remains a clinical challenge

Combining surgical & luminal treatment key to success

The best surgical option is to work together with the gastroenterologist



Conclusion...



Many techniques with limited experience
Stem cell therapy is promising

Conclusion...

Drain the sepsis – place a seton

Treat the disease

Close the fistula... if wanted



E. Liot



F. Ris



G. Meurette



J. Meyer

Consultants



C.R. Scarpa
Yverdon



A. Sgroi
Nyon



V. Delaune
CDC scientifique



A. Balaphas



J. Robert-Yap



B. Roche
Grangettes



N. Buchs
La Tour



B. Schiltz
Bienne

Collaborations: R. Chautems (Neuchâtel), G. Zufferey (Nyon), JM Michel (Fribourg), F. Cherbanyk (Fribourg)



Geneva University Hospitals
Proctology unit
Service of visceral Surgery



Service of visceral Surgery

27th Advanced course in coloproctology and pelvic floor disorder

PROCTOLOGY

5-8th of February 2024

Course director
Prof F. Rüs

