Perianal Crohn's Disease

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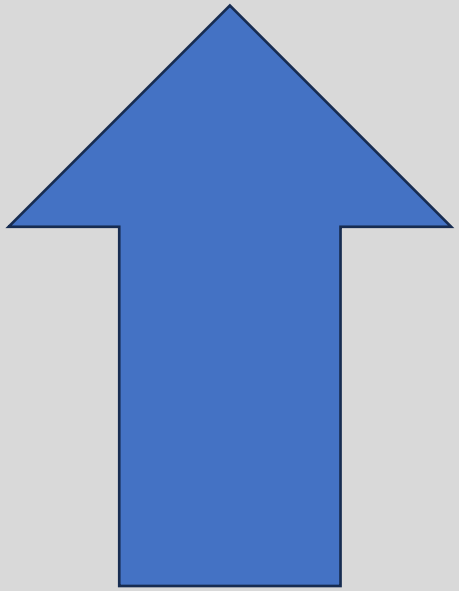
Outline of presentation

1. Epidemiology
2. Perianal anatomy
3. Pathogenesis
4. Classification
5. Clinical assessment
6. Diagnostic evaluation
7. Medical and surgical management

Epidemiology of Perianal CD

- Perianal Disease is common
- Incidence is 18-43% of all patients CD
  - ➢Fistulizing Chron's disease = 25%
  - ➢10 % = other perianal manifestations
- Perianal CD **precedes** luminal disease in 45% of patients
  - ➢Median time = 4.5 years
- **5% of patients = Isolated perianal disease** with no luminal involvement
- associated with **significant morbidity** and decreased Quality of life
  - Refractory non-healing perianal disease is common, debilitating and difficult to treat

Epidemiology of Perianal CD



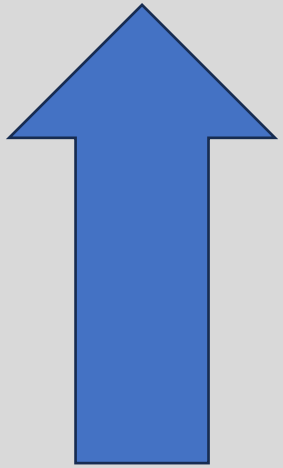
- Developing EIM
- Luminal fistula (5X)
- Surgery (2X)

Risk factors for Perianal CD

- Distal colonic disease (92%) > ileal disease (12%)
- Male
- Longer duration
- Extra-intestinal manifestations of CD
- Use of steroids
  - ➢Lower risk with early usage of steroid-sparing agents

Perianal fistula (CD-PAF)

- Severe phenotype of CD
- May present before or after luminal disease
- 10-30% precede luminal disease
- Associated with:



Hospitalization
Financial cost
Immunosuppressives
Surgery (2/3 require)
Complications

Pathogenesis

- Poorly understood

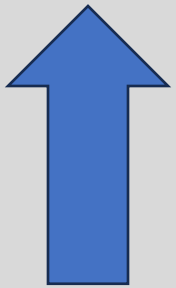
Genetic predisposition → Aberrant immune response to GUT microbiobes

↓

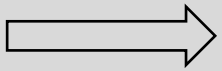
Intestinal inflammation

Pathogenesis

- **CD-PAF:**



TNF-ά
Transforming growth factor – B
IL-13



Mesenchymal cell transition and cell invasion

Pathogenesis

Perianal abscess

⇓

spontaneous drainage/penetration into adjacent organ/skin

perianal skin + groin, vagina, bladder

⇓

Residual fistulous tract

Non-CD PAF – originates from infected anal cyptoglandular complex

Incidence of CD fistula

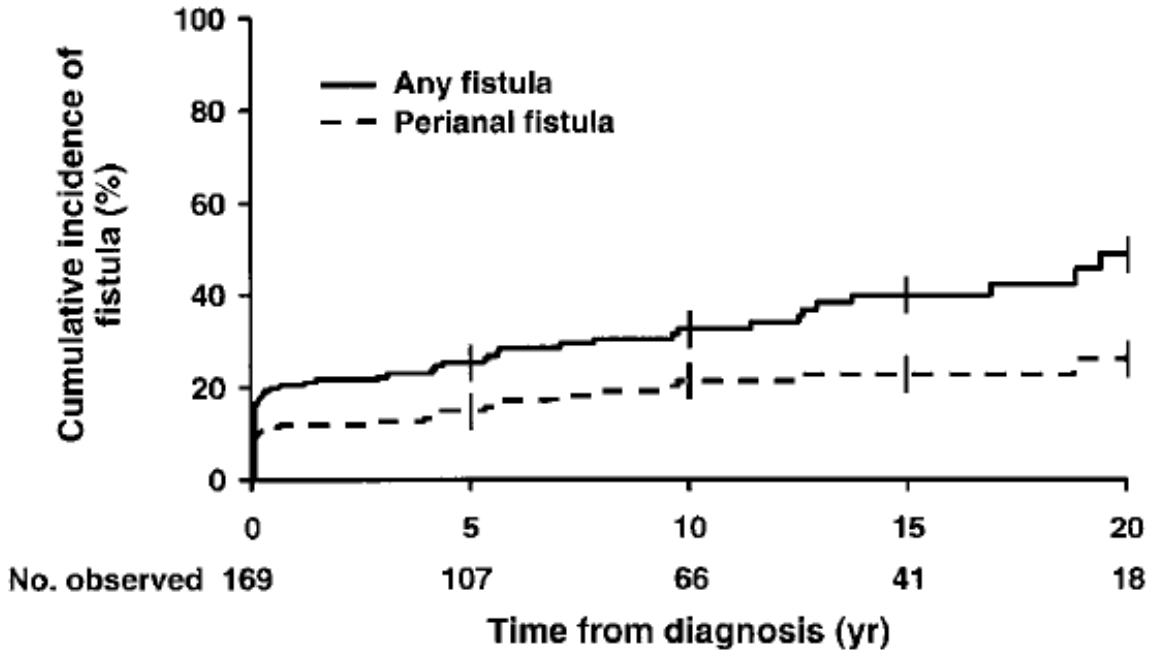
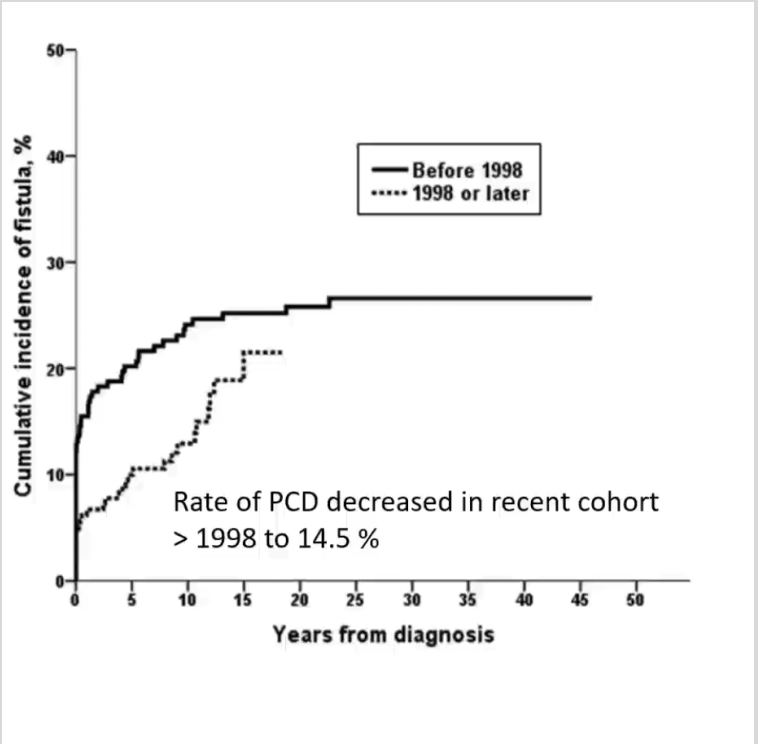


Figure 1. Cumulative incidence of overall fistulas (*solid line*) and perianal fistulas (*dashed line*) among 176 Olmsted County, Minnesota residents diagnosed with Crohn's disease from 1970 to 1993.

Decreasing incidence since 1998 due to early usage of biologics



Common fistulas in CD

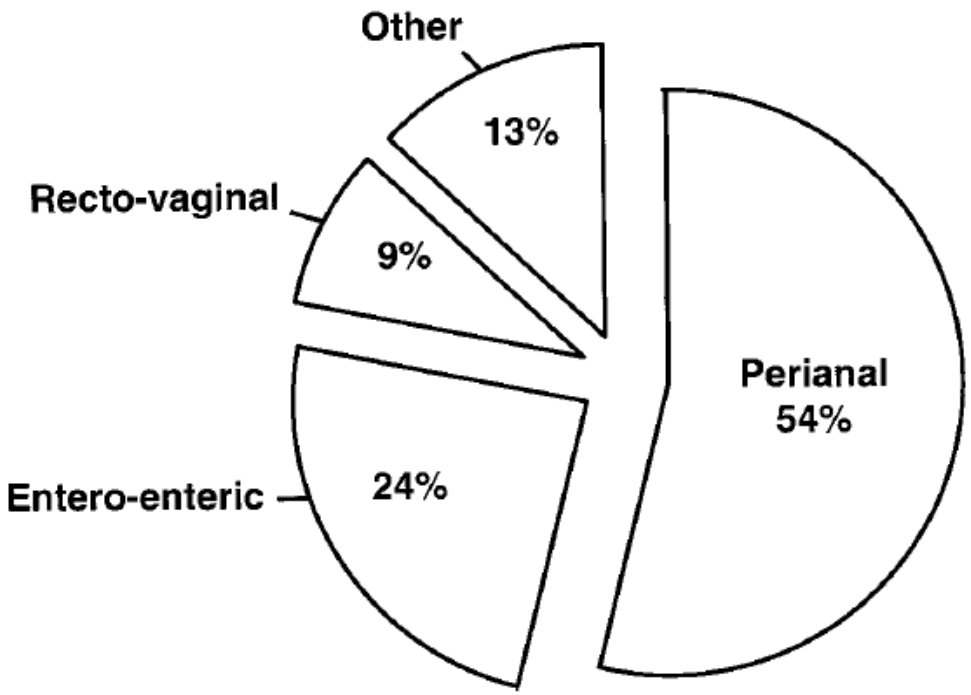


Figure 3. Percentage of fistulas by type (perianal, enteroenteric, rectovaginal, and other).

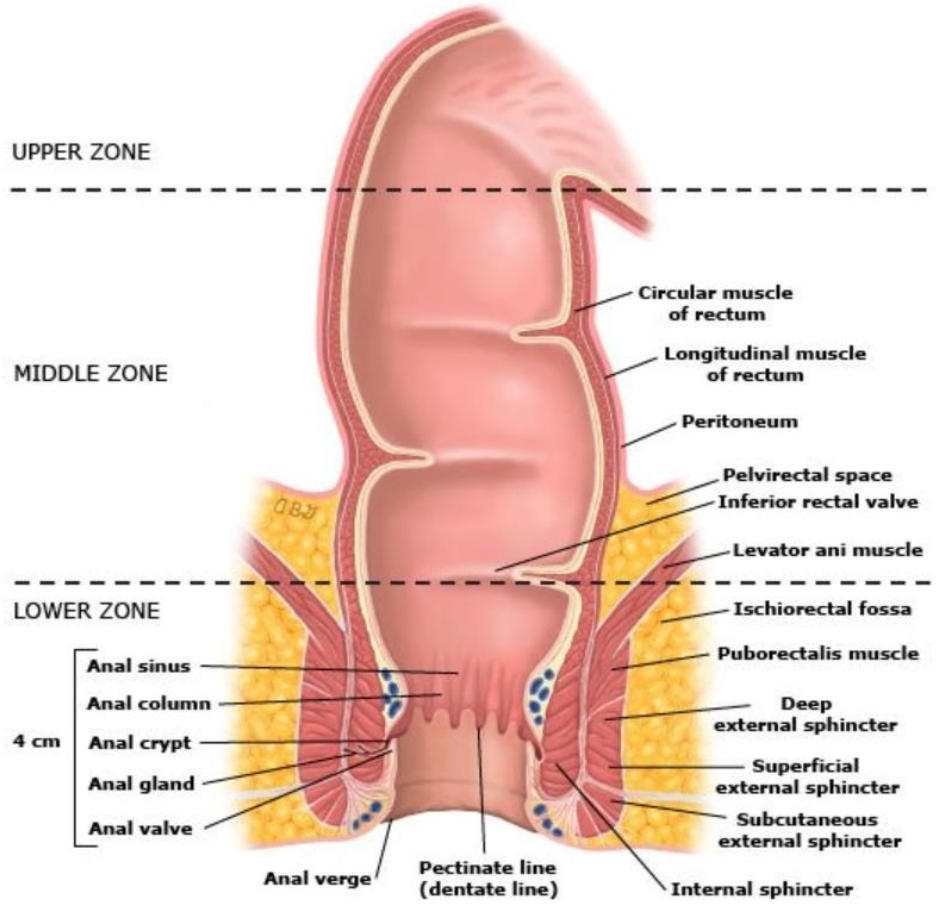
Long term fistula outcomes

- Retrospective study from Leiden
- 232 pts CD PAF – 10-year follow-up
- **78% = complex fistulas**
  - ➢ long term healing only in 37%
  - ➢53% pts required surgery

➢Proctectomy rate in recent Mayo cohort unchanged at **19%**

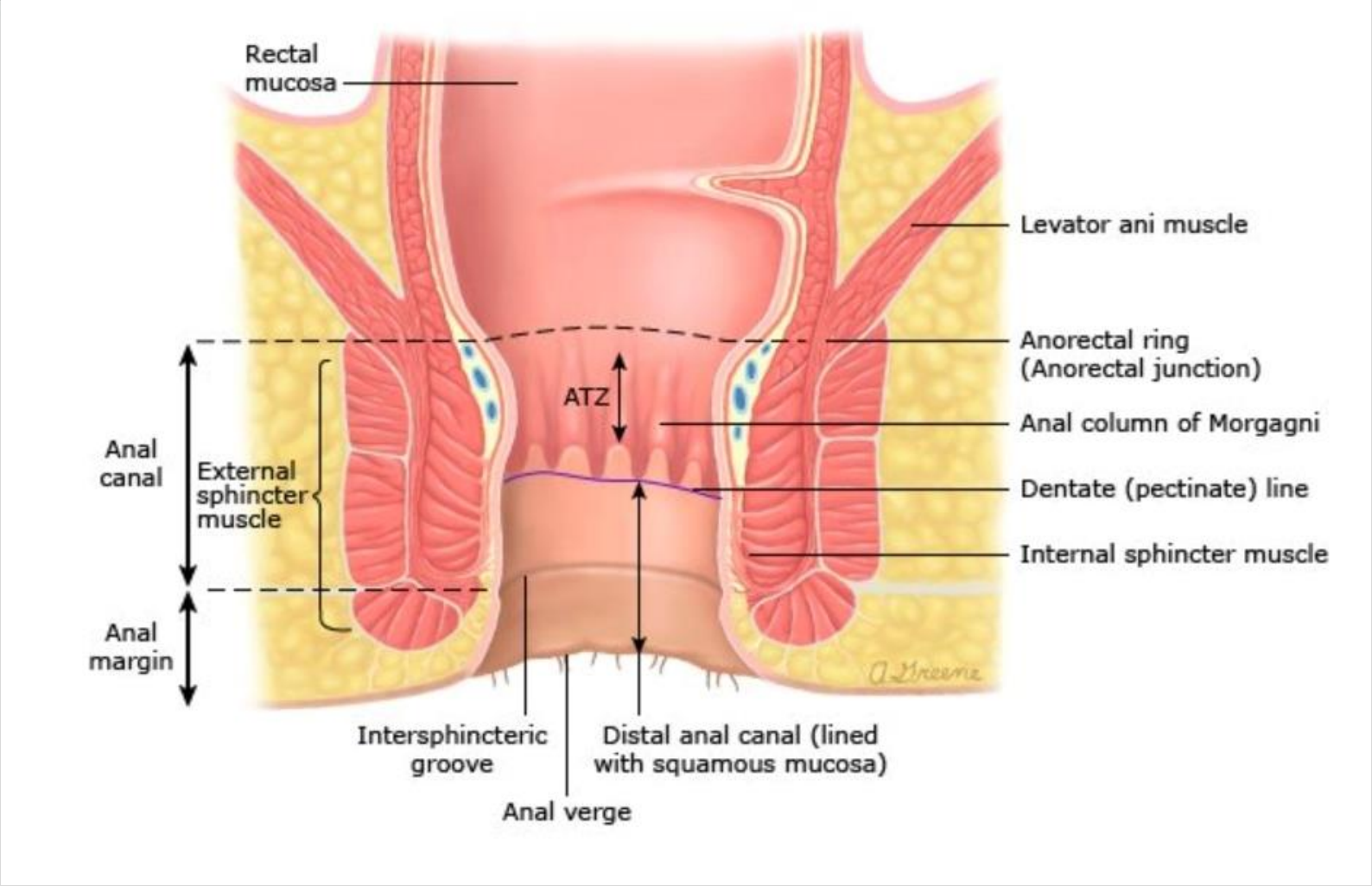
Molendijk etal IBD 2014

Anatomy of the anal canal and rectum

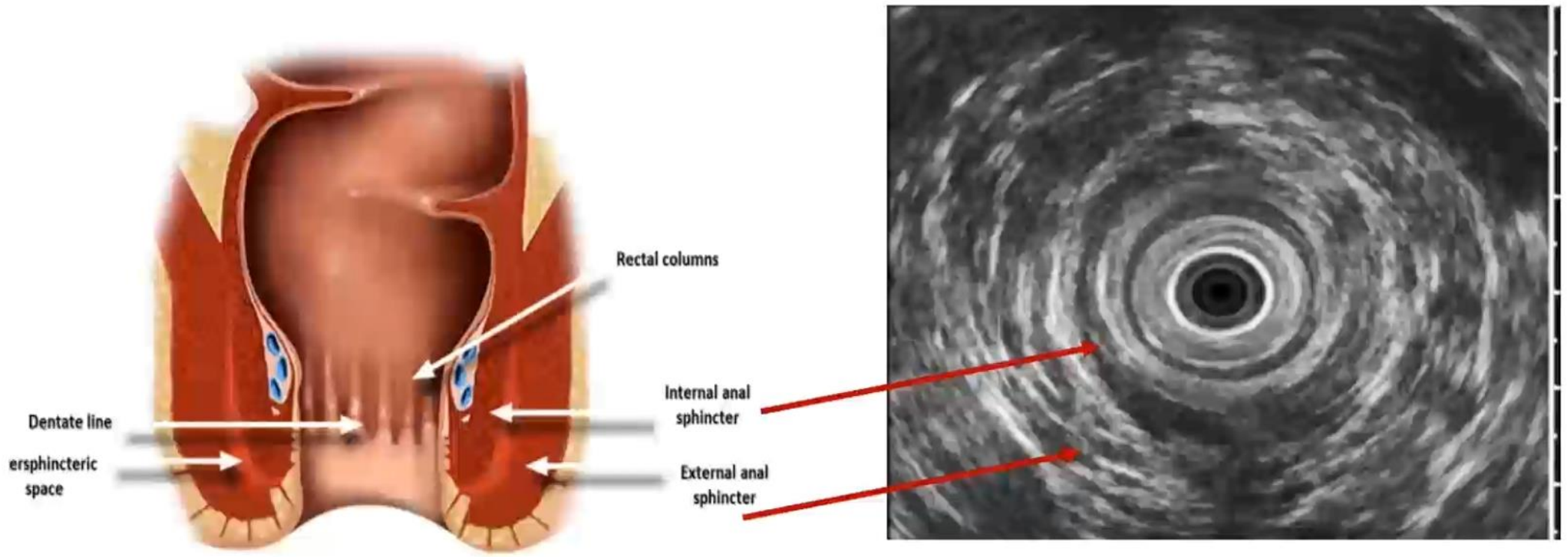


This figure illustrates the anatomy of the rectum and anal canal. Note the anal crypts and glands; 90% of anorectal fistulas originate in a cryptoglandular abscess. Also note the relationship of the crypts and glands to the internal and external sphincters.

Perianal anatomy



Normal Radial EUS Anatomy



Typical history

Perianal pain: Rest, movement, dyschezia

Perianal discharge

Passing stool or gas with urination

Fecal Incontinence

Previous perianal fistula

Signs of systemic infection with perianal abscess

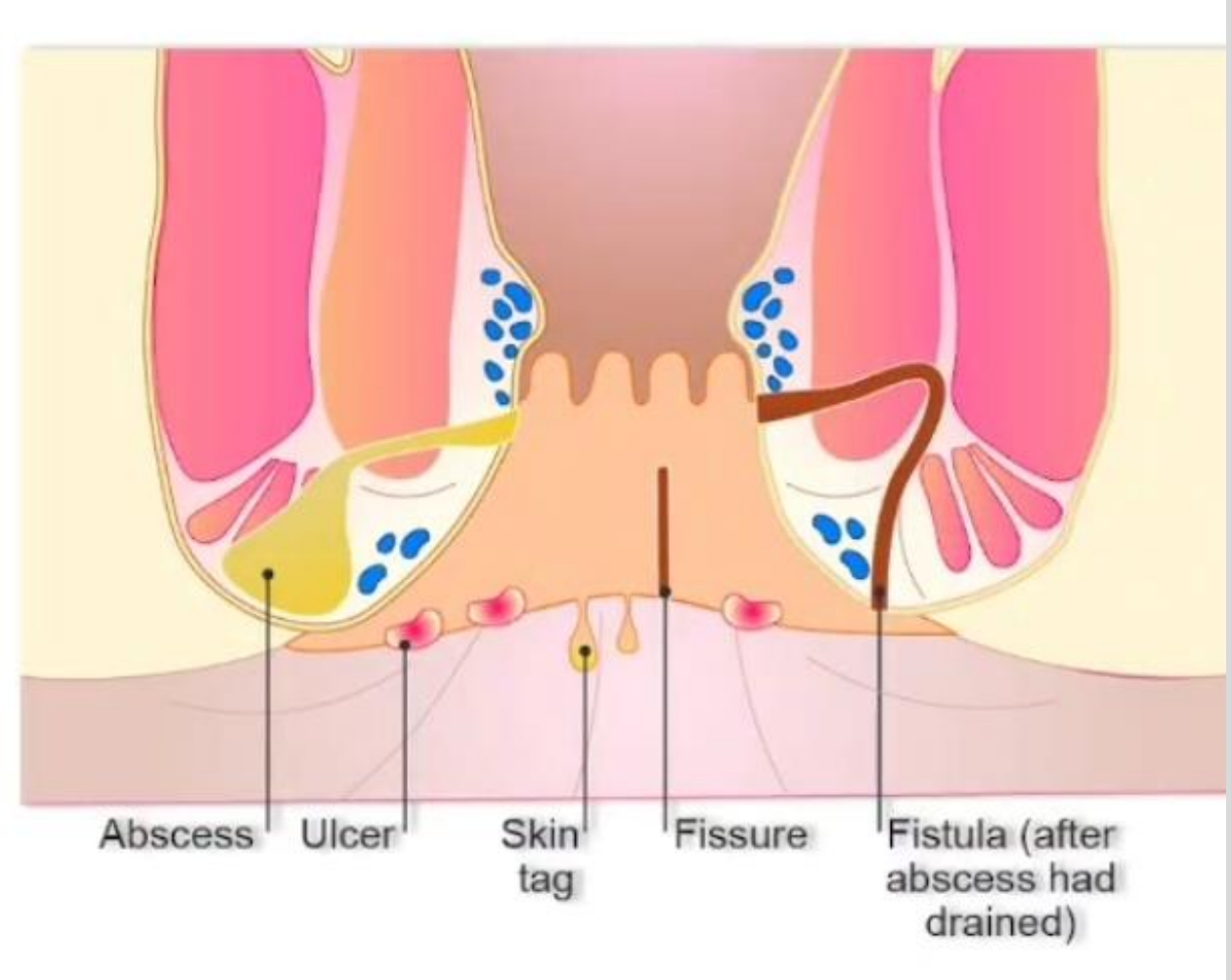
Symptoms of luminal IBD/CD – diarrhoea, urgency, PR bleeding

Past history associated with CD (if known)

Family history of IBD

EIM manifestations of IBD

Manifestions of Perianal CD



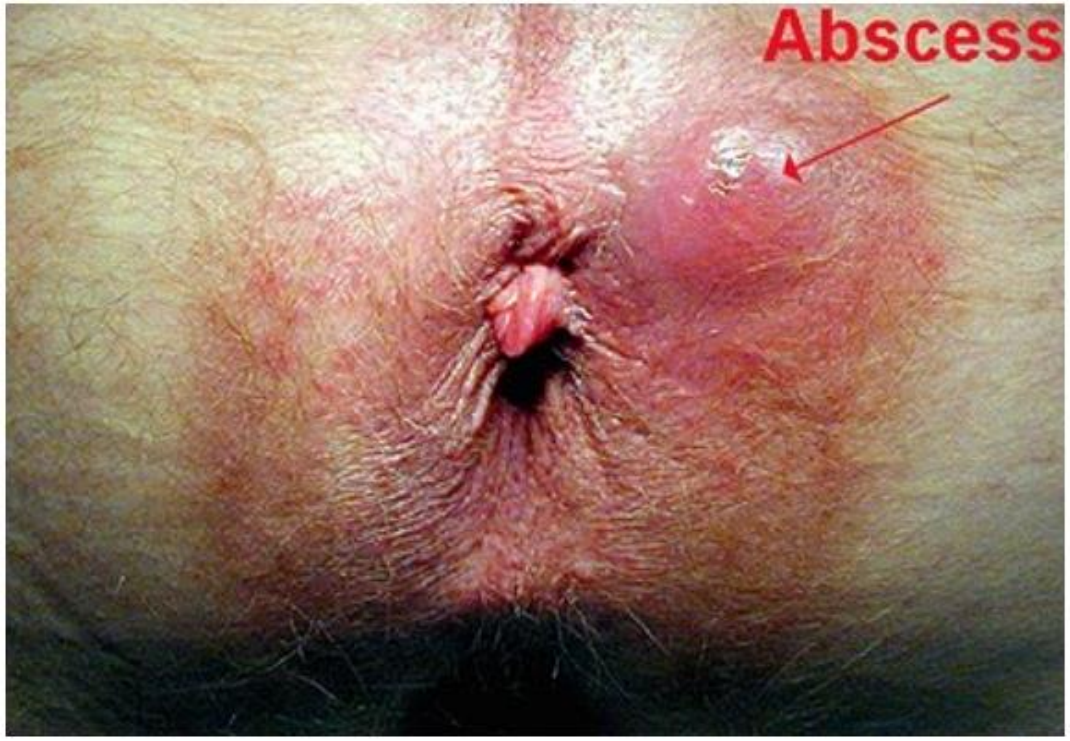
Other:

Haemorrhoids

Anal stricture

Anal cancer

Perianal abscess



A perianal abscess is apparent as an erythematous, fluctuant bulge with surrounding edema.

Skin tags

Fig. 5 (**A**) Edematous skin tags with surrounding erythema are typical findings in perianal Crohn's disease. (**B**) *Elephant skin* tags are also highly suggestive (Photos—M. Valente).

Skin tags

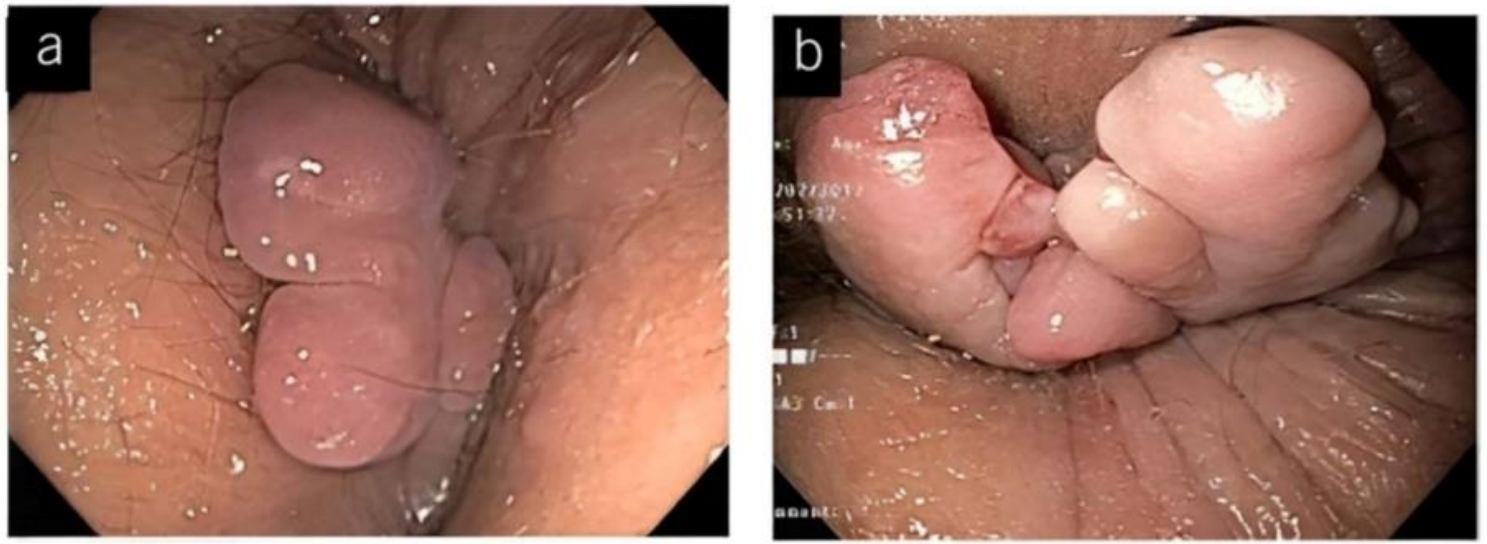


Figure 4. Examples of "elephant ear" skin tags characteristic of perianal Crohn's disease. Reprinted from atlas of endoscopy imaging in inflammatory bowel disease. Shen B, ed. Shen B. Chapter 7—Endoscopic evaluation of perianal Crohn's disease, 2020, with permission from Elsevier (117).

Anal fissure

Chronic anal fissure

In **posterior midline** – most common site for fissure formation

Raised edges and **fibrotic appearance** distinguishes it from an acute anal fissure (“paper cut”/fresh laceration)

Perianal ulcer

Fig. 8 The arrow points to a painless perianal ulcer associated with Crohn's disease (Photo—M. Valente).

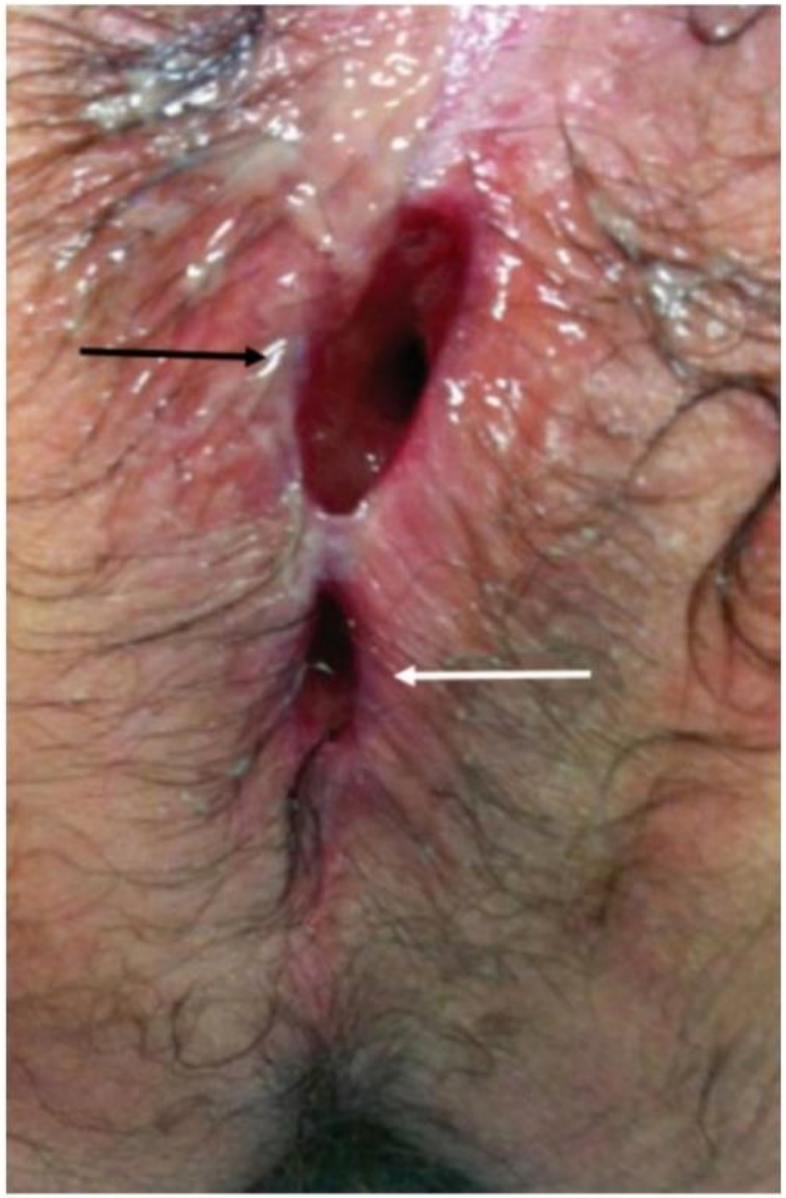


Fig. 1 A nonhealing wound (black arrow) above the anus (white arrow) is evident months following incision and drainage of a perirectal abscess. This observation should raise concerns for perianal Crohn's disease (Photo—M. Valente).

Haemorrhoids

Image courtesy of Dr. Amy Lightner

Perianal fistula

Fig. 2 Multiple external openings of multiple fistulas are present (white arrow) surrounded by erythema and induration (black arrow). Investigation for enteric Crohn's disease is warranted (Photo—A. Ortega).

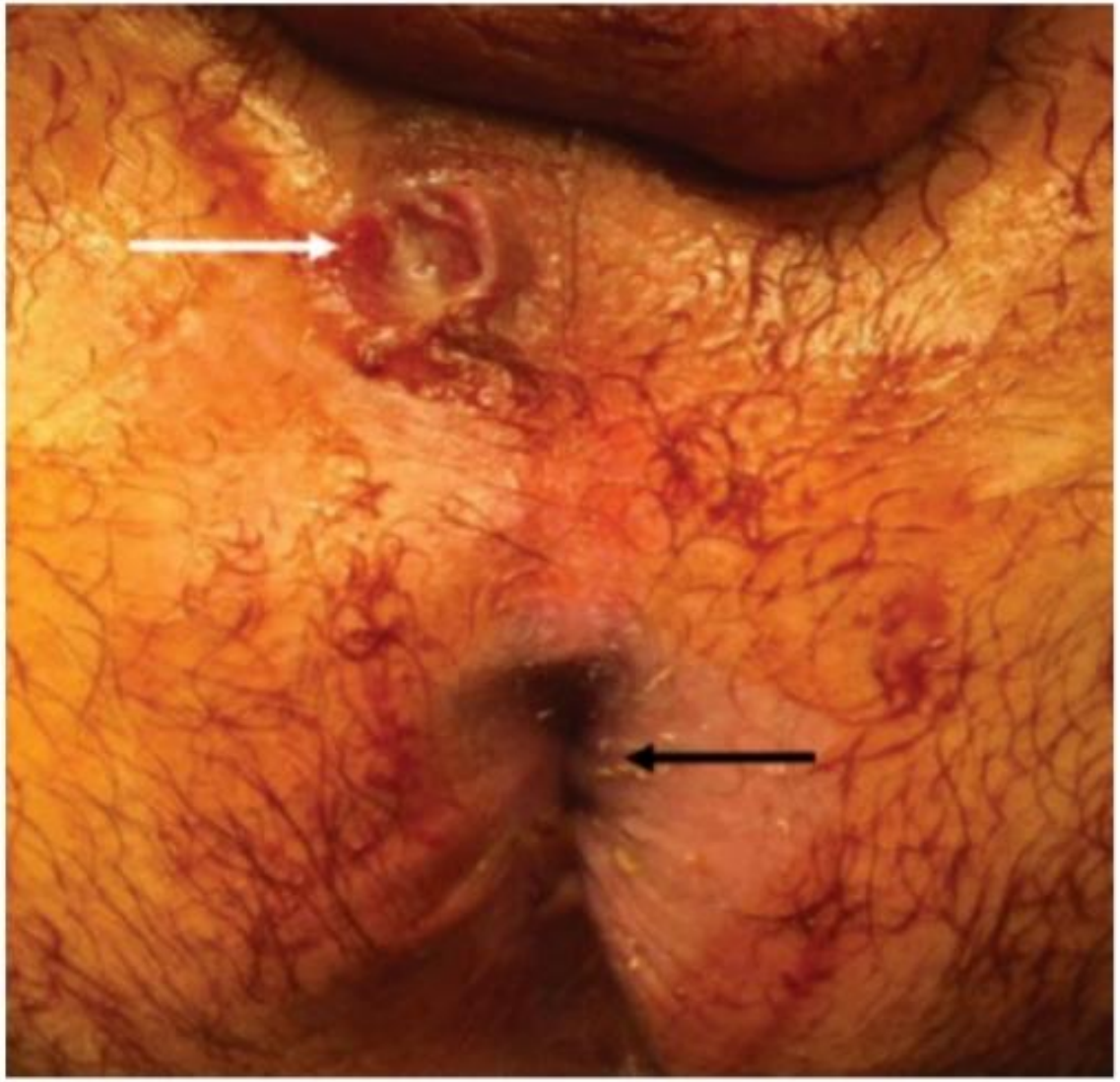


Fig. 3 A *wide-mouthed* anal fistula (white arrow) is evident anterior to the anus (black arrow)—a characteristic finding in perianal Crohn's disease (Photo—J. Salgado, G. Salgado).

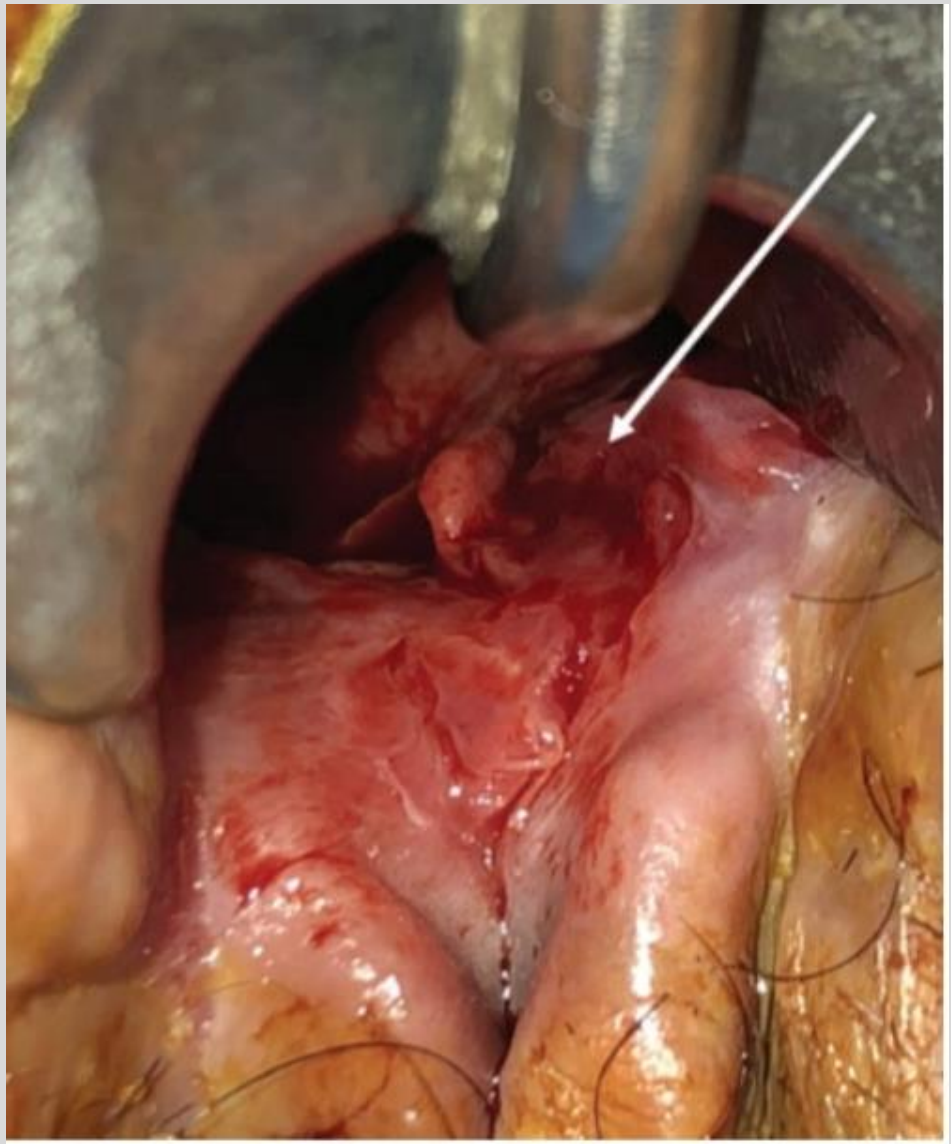
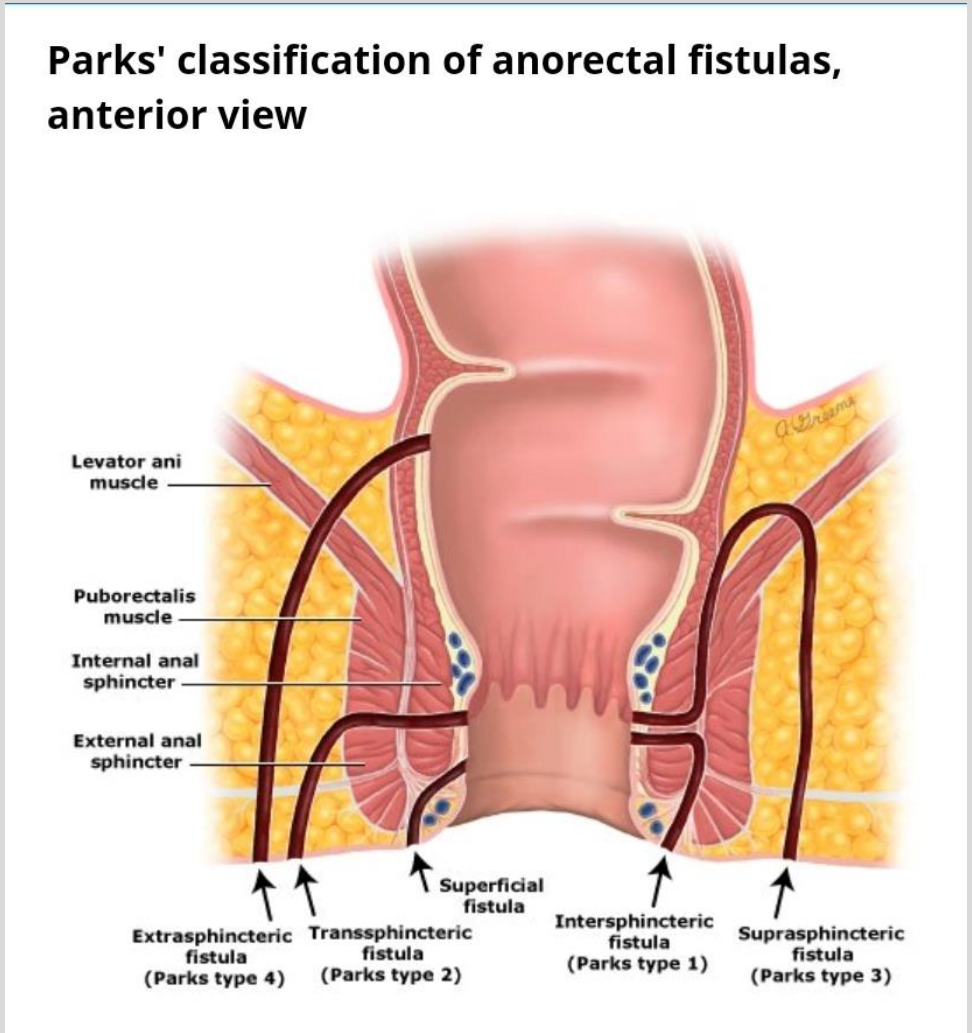


Fig. 4 Proctitis (arrow) in the setting of an anal fistula is almost pathognomonic of perianal Crohn's disease (Photo—J. Salgado, G. Salgado).

Fistual + Proctitis = CD

Classification of CD-PAF
PARK'S CLASSIFICATION

- Based on the anatomical position of main fistula tract relative to the **external anal sphincter**
- **4 types** of fistulas that can originate from cryptoglandular infections



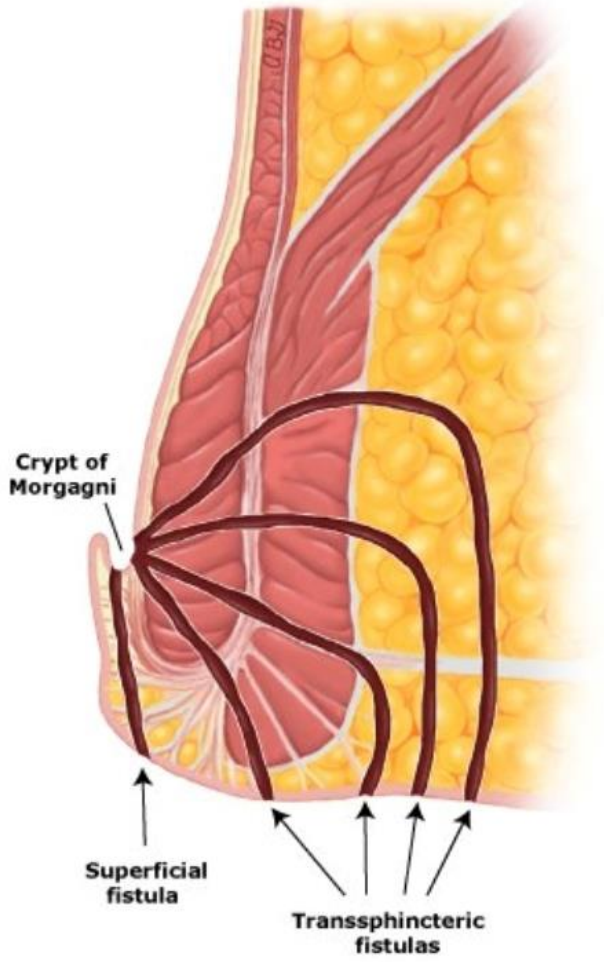
Type 1 is an intersphincteric fistula that travels along the intersphincteric plane.

Type 2 is a transsphincteric fistula that encompasses a portion of the internal and external sphincter.

Type 3 is a suprasphincteric fistula that encompasses the entire sphincter apparatus.

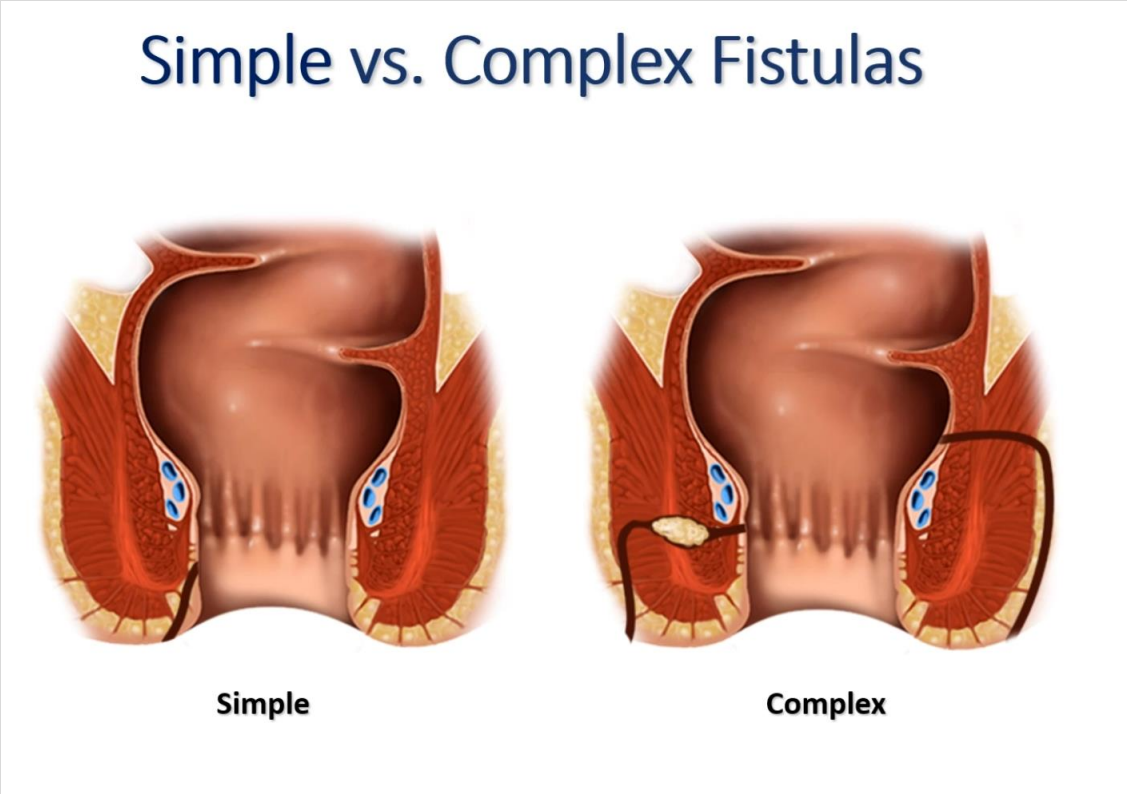
Type 4 is an extrasphincteric fistula that extends from a primary opening in the rectum, encompasses the entire sphincter apparatus, and opens onto the skin overlying the buttock.

Anorectal fistulas, lateral view



In this lateral view of anorectal fistulas, a superficial fistula has been included. It is not a component of the original Parks' classification. This figure also illustrates the potential pathways of transsphincteric fistulas.

Simple vs Complex fistulas



- Released by AGA in 2003
- Simple vs complex depending on
  - Fistula tract anatomy
  - Number of external openings
  - Presence of perianal abscesses
  - Presence of proctitis

- **Sphincter involvement is key**

Simple vs complex

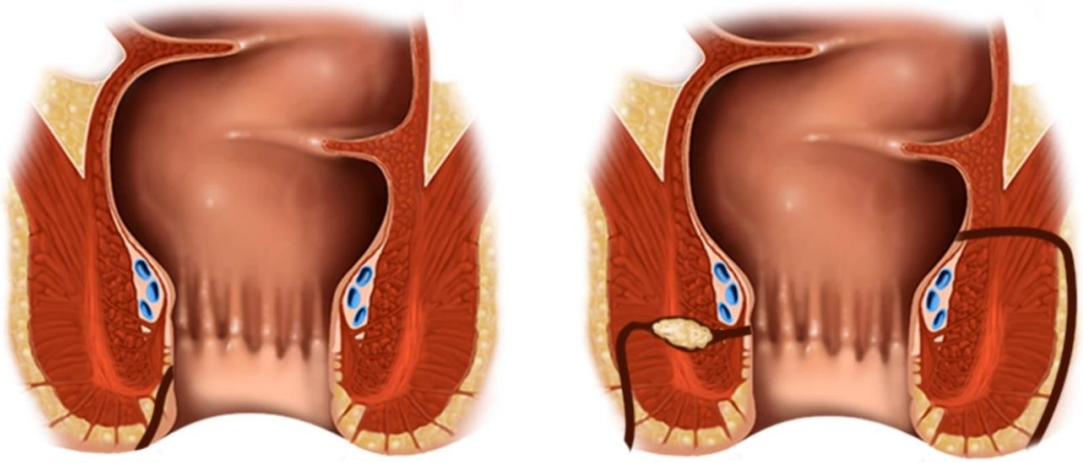
Simple

- Low

(superficial or low intersphincteric, low transphincteric origin) - low tract runs through lower 1/3 of external anal sphincter

- Single external opening
- No evidence of perianal abscess, rectovaginal fistula, anorectal stricture

Simple vs. Complex Fistulas



Simple Complex

Complex

- High

(high intersphincteric, transphincteric, extrasphincteric, suprasphincteric origin)

- Multiple external openings
- Associated perianal abscess, rectovaginal fistula or anorectal stricture

Pretreatment evaluation

- After the clinical assessment, further evaluation is required to
  - Define fistula anatomy
  - Exclude perianal abscess

- 3 options
  - **Examination under anaethesia (EUA)**
  - **MRI Pelvis**
  - **Endoscopic ultrasound (EUS)** – Endoanal/Endorectal

Depending on acuity of patient

Perianal abscess present

- Referral to surgeons for EUA
- *Imaging should not delay EUA if there is clinical evidence of perianal sepsis requiring immediate drainage*
- *Key to successful management is to establish adequate drainage of all abscesses and to control fistula healing*
  - *Imaging modality provides a virtual road map for this purpose*

- DRE done by experienced surgeon has accuracy of 62%
  - Scarring and induration with perianal CD

- EUA is accurate but has miss rate of 10% or greater

EUA

- Assess the anatomy of perianal fistulizing disease
  - ➢Number of tracks
  - ➢Anal canal involvement
    - **Stricture in the anal canal?**

- Assess the presence of **perianal abscess**
  - ➢If present in the setting of CD – usually an associated fistula present

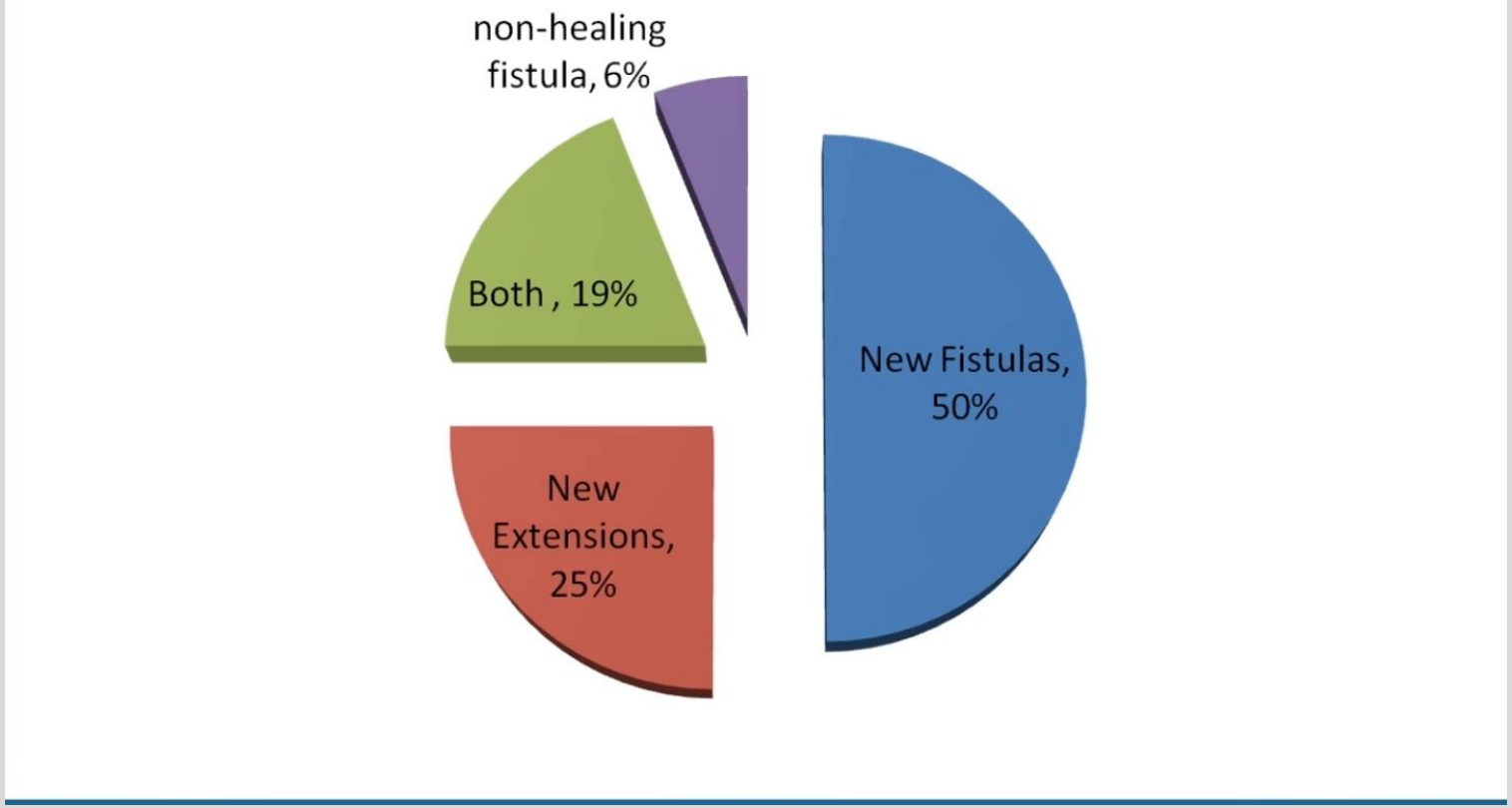
Initial surgical management at EUA

- Insertion of setons
- I&D of perianal abscess
- Fistulotomy
  - Only if a **simple fistula** is encountered

Fistulotomy

- Simple fistula with no proctitis
- Open fistula tract along its length
- Obliterate the epithelialized tract
- Healing = 80%
- Recurrence = 15%
- Risk of **incontinence** esp if
    - Short anal canal
    - Involvement of external sphincter
    - Persistent diarrhoea

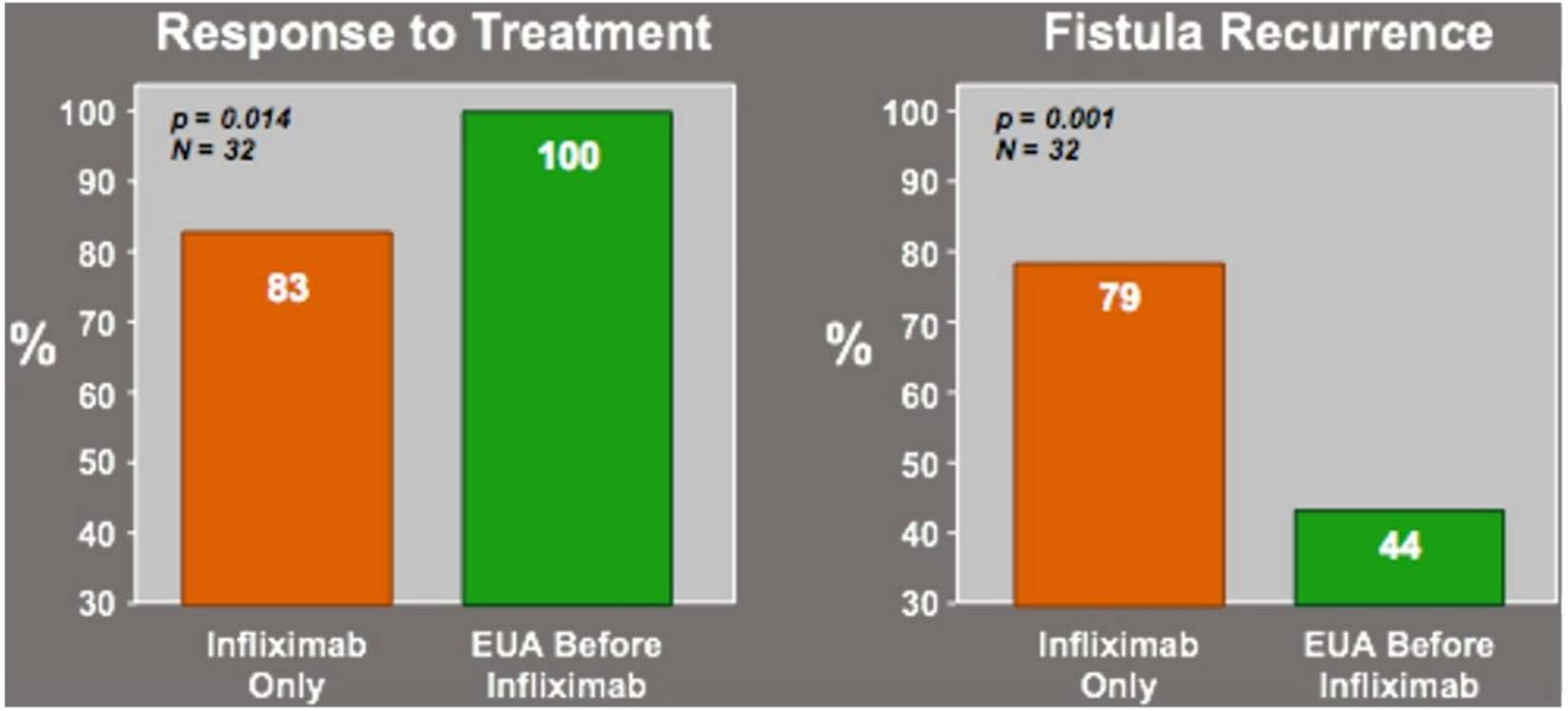
Fistulas missed at EUA



Fistula recurrence was always predicted by MRI

Buchanan et al Lancet 2002

EUA is beneficial



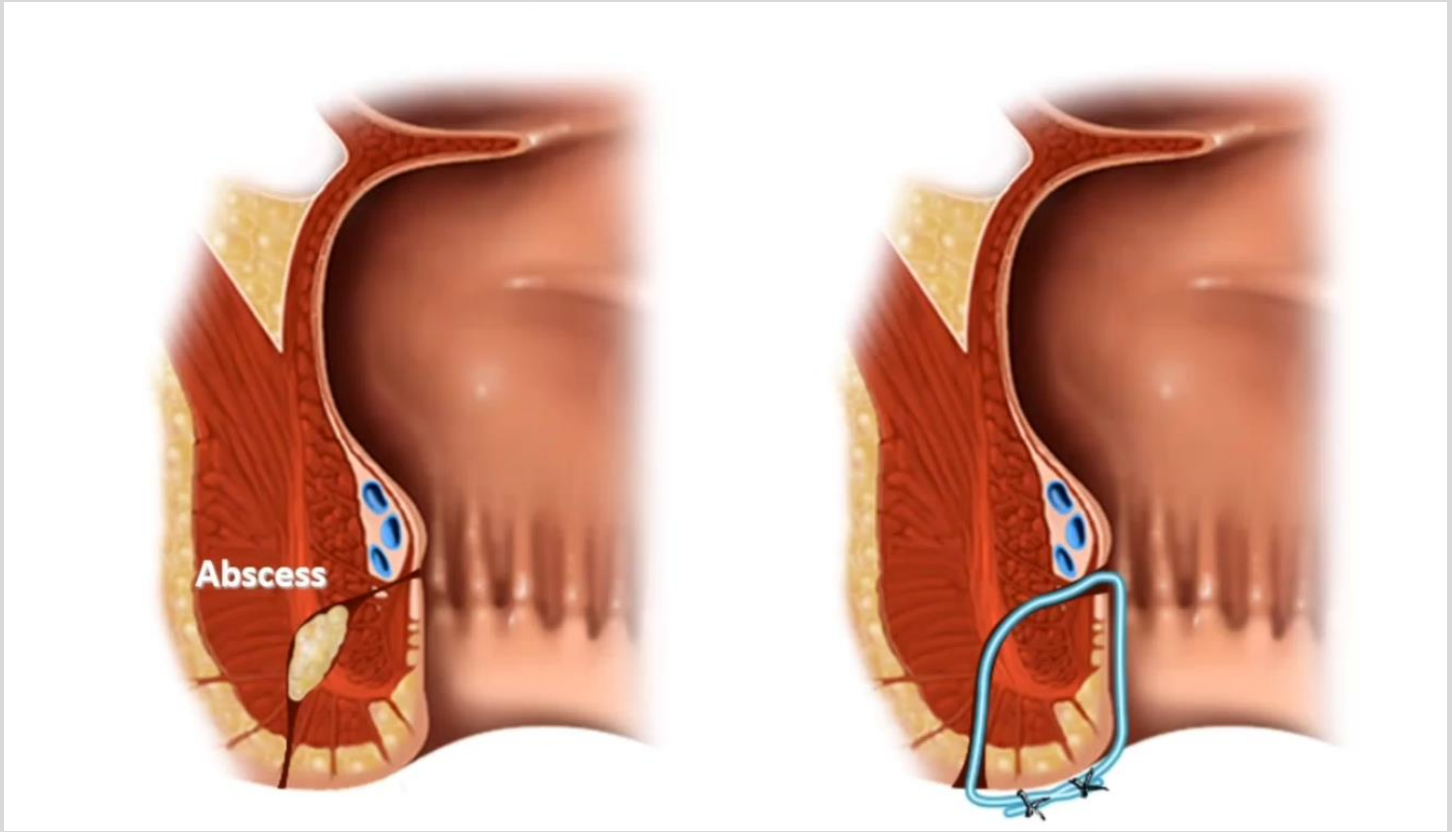
Mean time to recurrence:

IFX alone – 3.6 m

EUA before IFX – 13.5m

Regueiro et al IBD 2003

How setons help



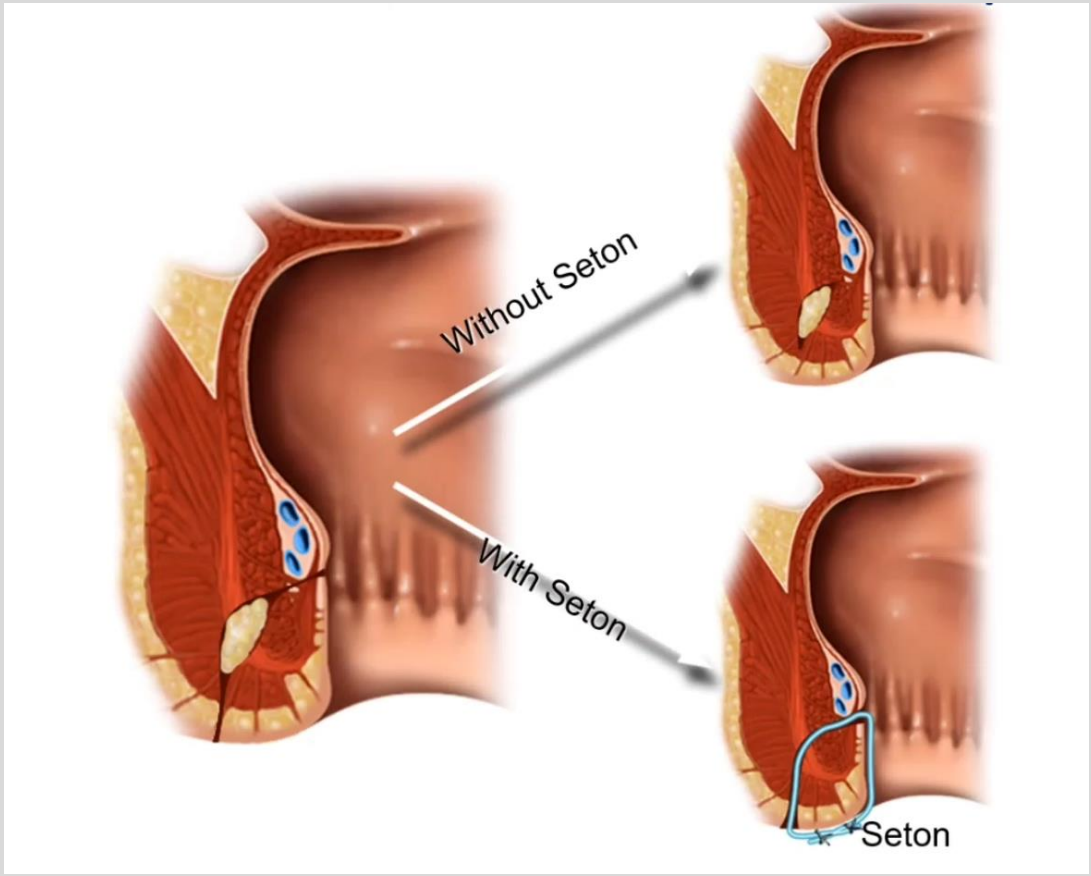
Non-cutting setons

Control perianal sepsis

↓ incidence of recurrent abscess formation

↓ New fistula tract formation

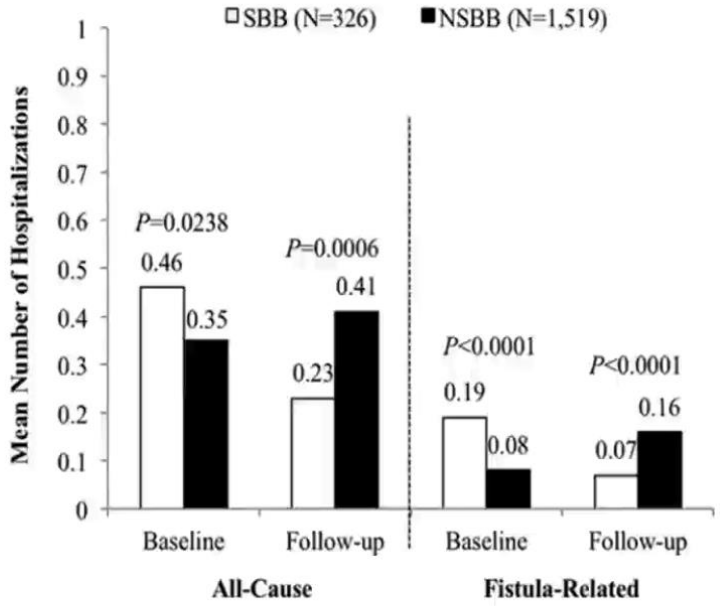
Improved efficacy and healing

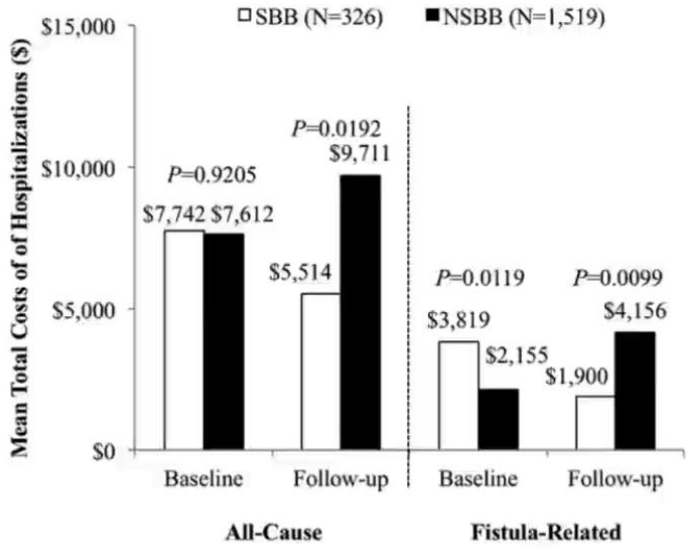


- Setons are easy on patient
- Easy to insert
- Sole use results in significant re-intervention rates
- *Dual usage with Biologics*

Seton reduce hospitalizations and costs

Comparison of Healthcare Utilization in Patients with CD Perianal Fistulas Treated with Biologics with or without Setons





Schwartz, IBD 2017

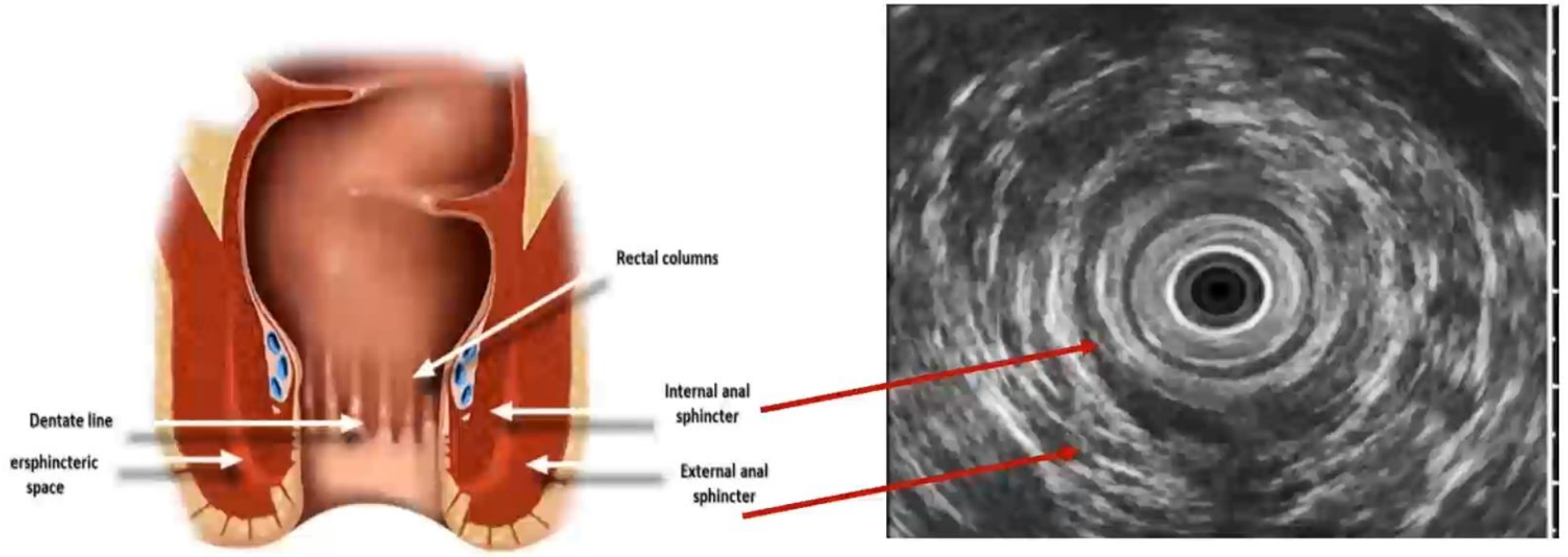
When to remove setons

- ✓**Collaborative discussion between gastroenterologist and colorectal surgeon**
- ✓Local infection has been fully treated
- ✓Drainage of all abscesses ensured
- ✓Follow-up imaging shows improvement in inflammation & sepsis
- ✓Pt well established on Biologics and immunomodulator
- ✓Good Biologic drug levels
- ✓Proctitis controlled

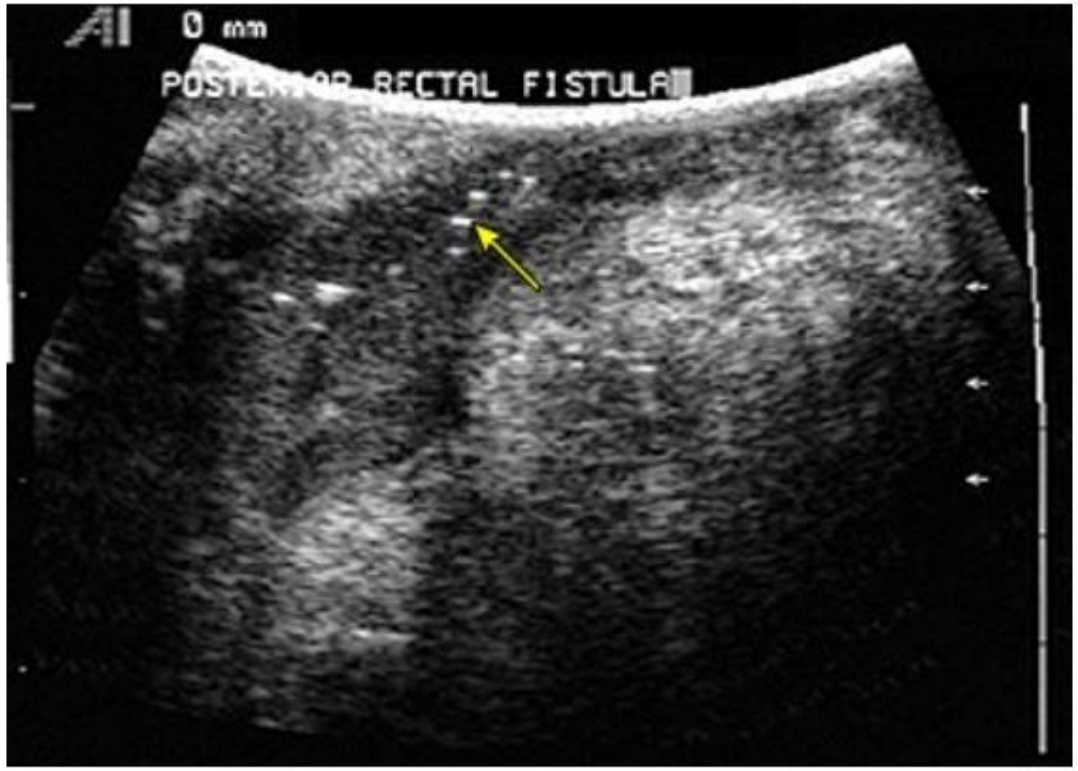
Endoscopic ultrasound (EUS)

- Ideally used when perianal pathology adjacent to anal canal
- Can be used in real-time intraoperatively
- Invasive
- Accurately identifies anorectal strictures
- Limited utility in presence of anorectal strictures

Normal Radial EUS Anatomy

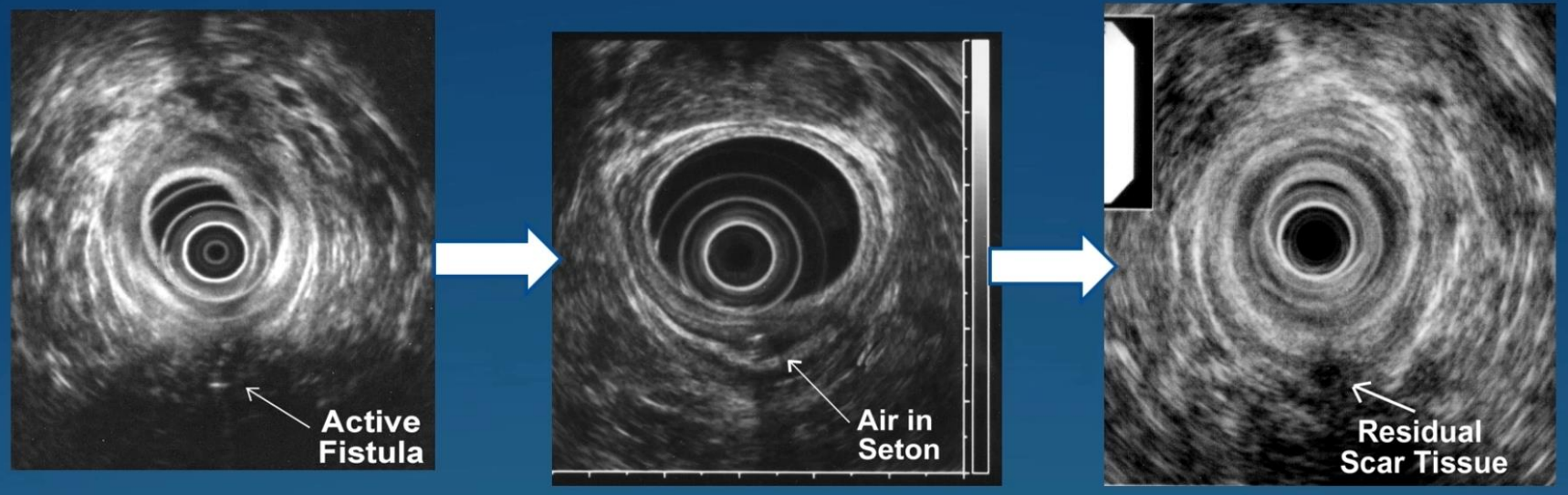


Air in fistula tract



Endoscopic ultrasound image showing air in a fistula tract (arrow).

Representative Patient – Initial EUS

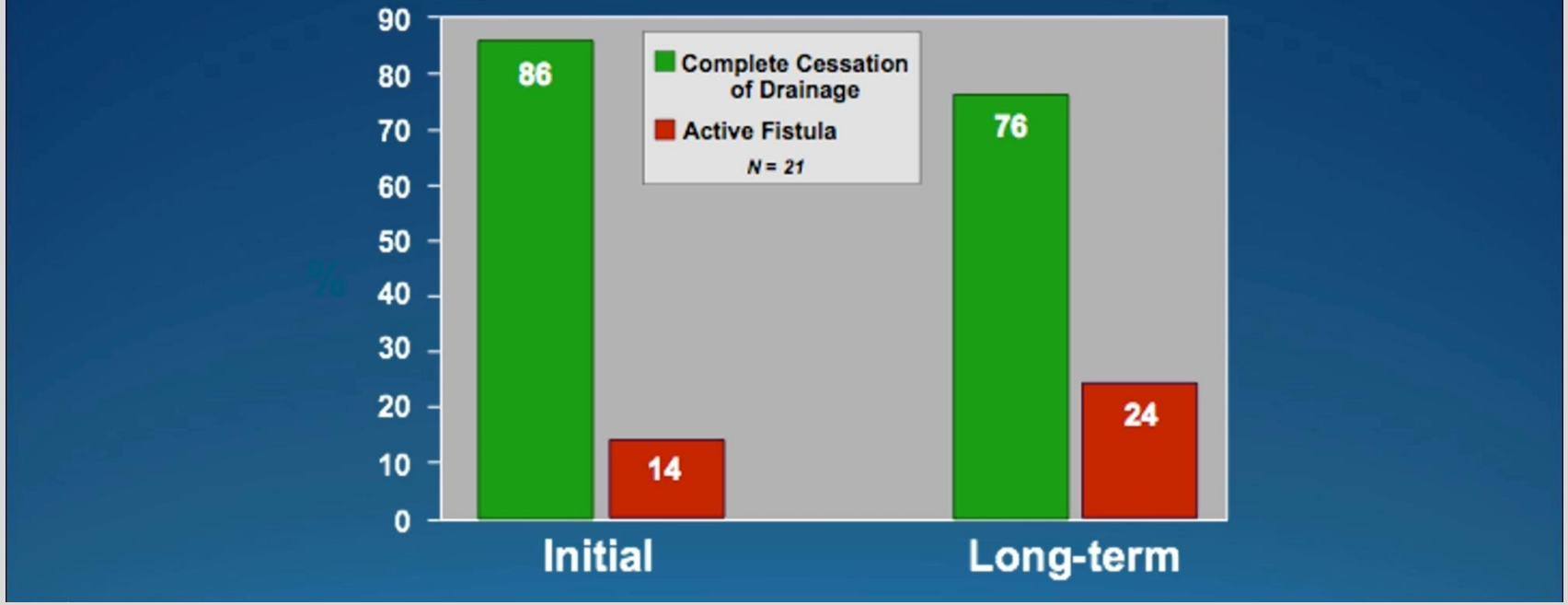


Initial Assessment

Week 16

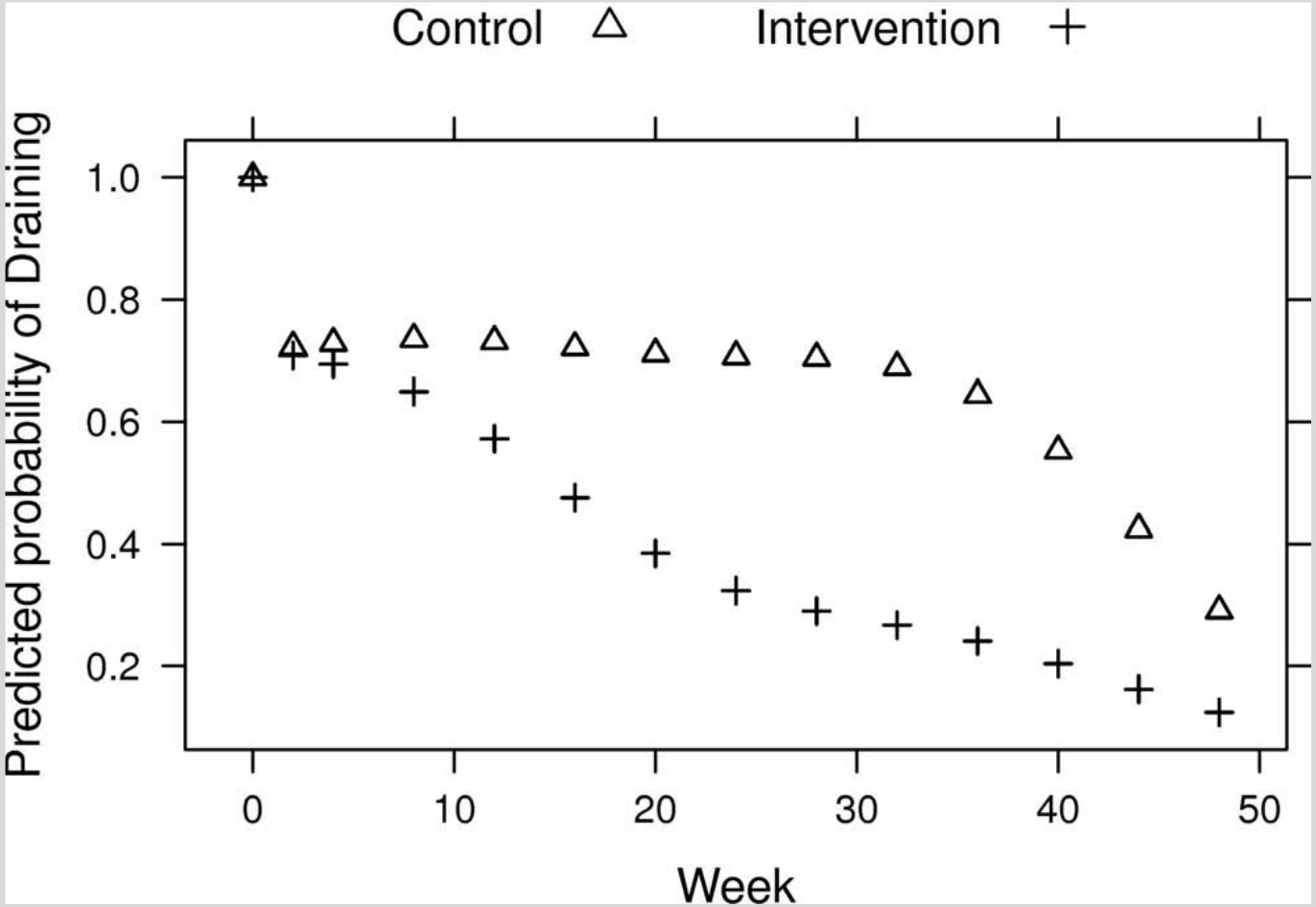
F/U – Wk 30

Utilizing EUS to Improve Fistula Healing



Schwatz et al IBD 2005

EUS improves patient outcomes



Prospective trial

All patients received I&D, setons, Adalimumab, antiobiotics (cipro or metro)

EUS in both groups at start

Intervention (9pts)– EUS @ 12 ; 48 wks (with treatment modification as per EUS)

Control (11 pts) – only surgeon opinion

Spradlin, Schwarz Am J Gastro (2008)

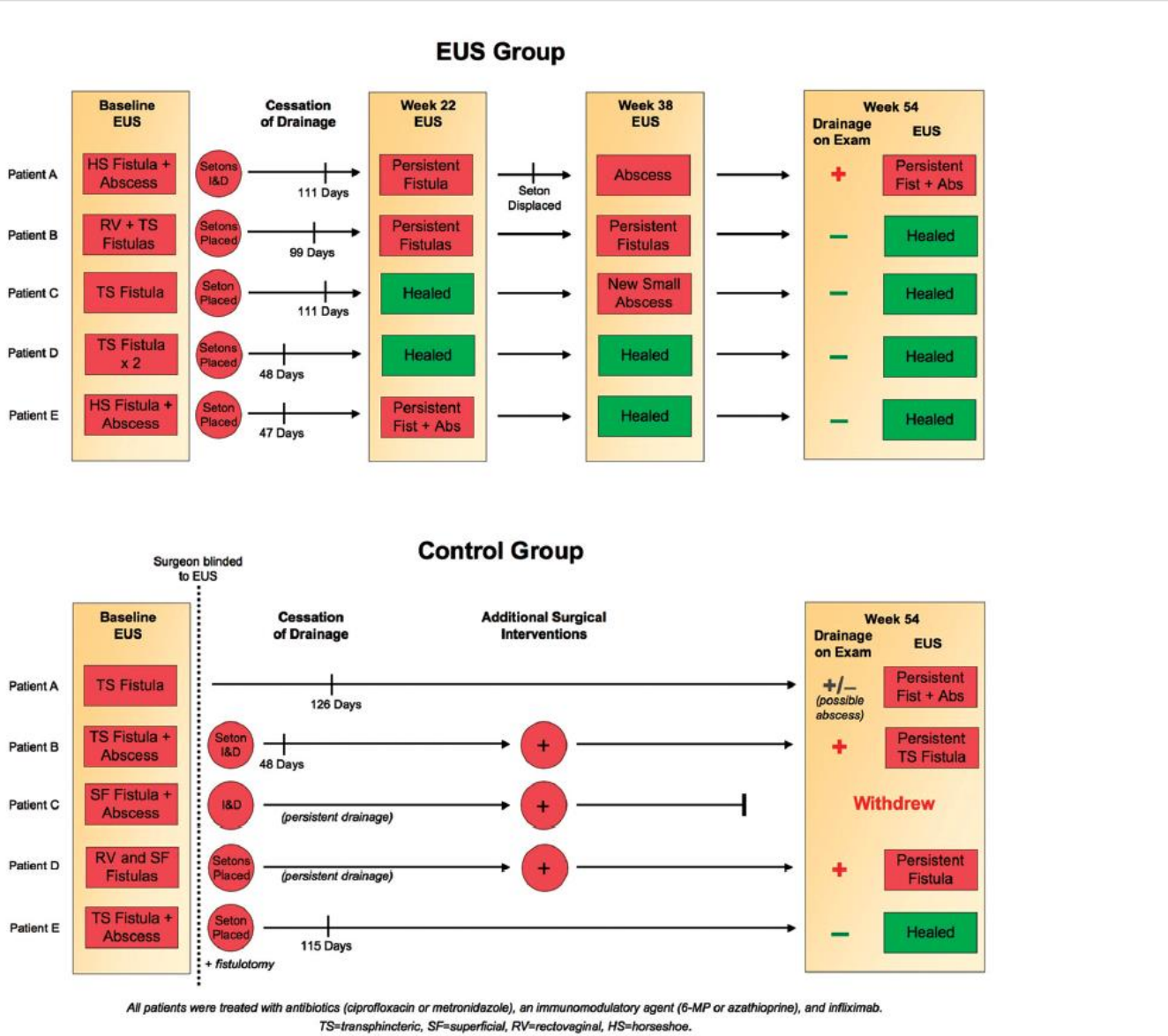


Figure 1. Flow diagram of outcomes in EUS and control group.

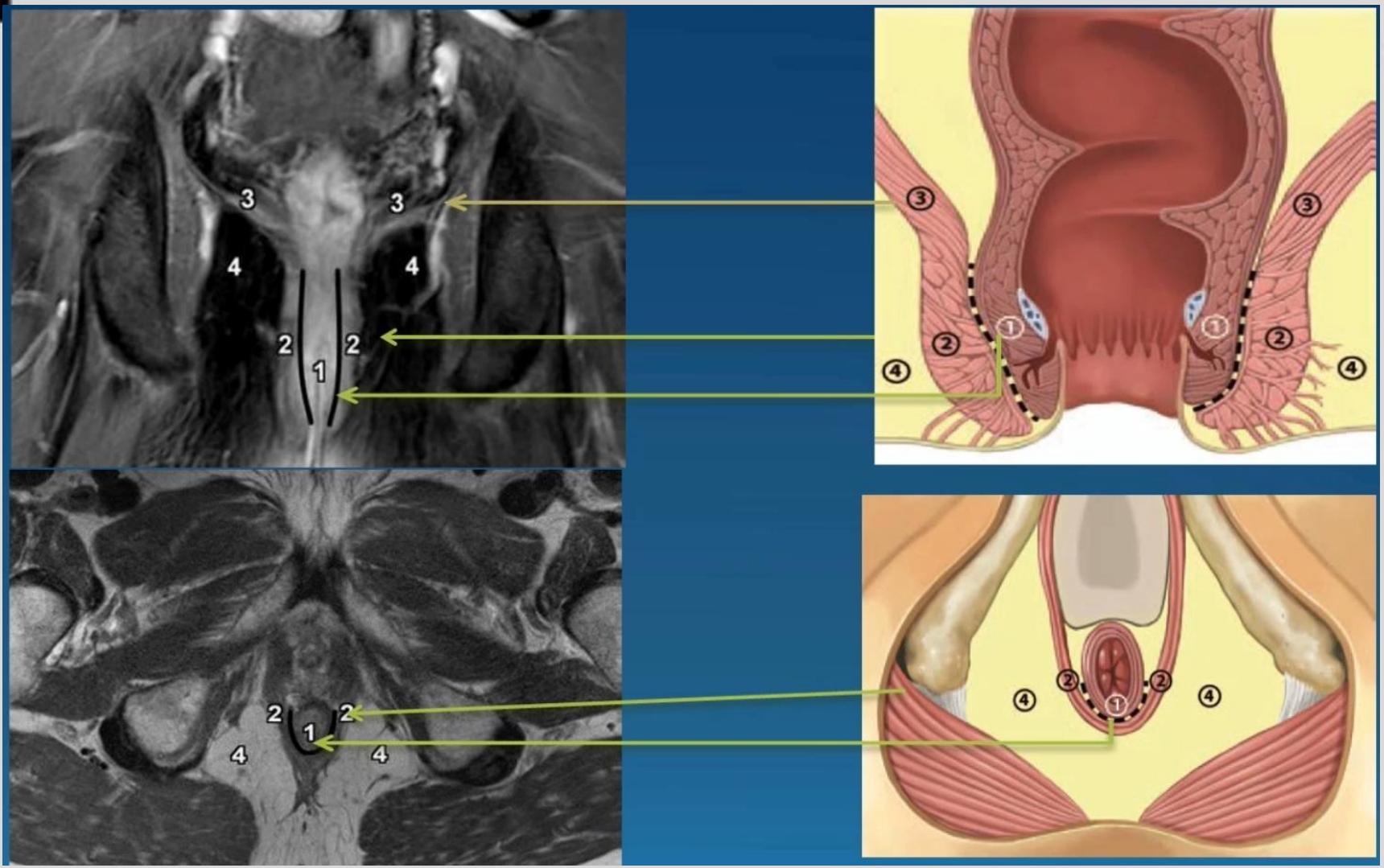
Prospective study
10pts
EUS at baseline &
Week 54 for all
EUS at 22 + 38 wks in Intervention group

Wiese, Schwarz
Am J Gastro 2011

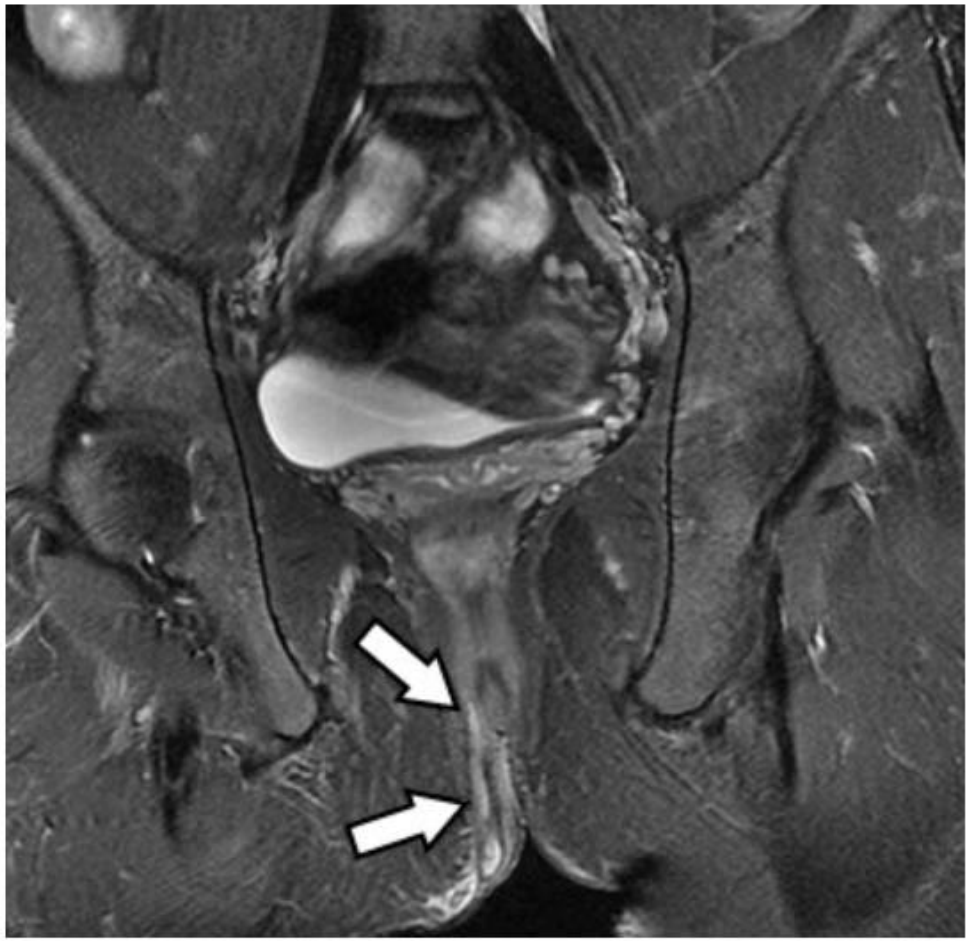
MRI Pelvis

- In comparison to surgery and endoscopy:
  - **Fistula** detection – Sensitivity 76%, specificity 96%
  - **Abscess** detection – Sensitivity 86 -100%, specificity 93-100%
- Gold standard of imaging
- Non-invasive
- Preferred to CT (no radiation)
- Most comprehensive of diagnostic modalities
- **T2 weighted imaging** – fluid in fistula tract and any abscess can be identified due to high signal
- **Contrast with Gadolinium** – identify areas of *neovascularization* indicative of fistula healing

Normal MRI anatomy

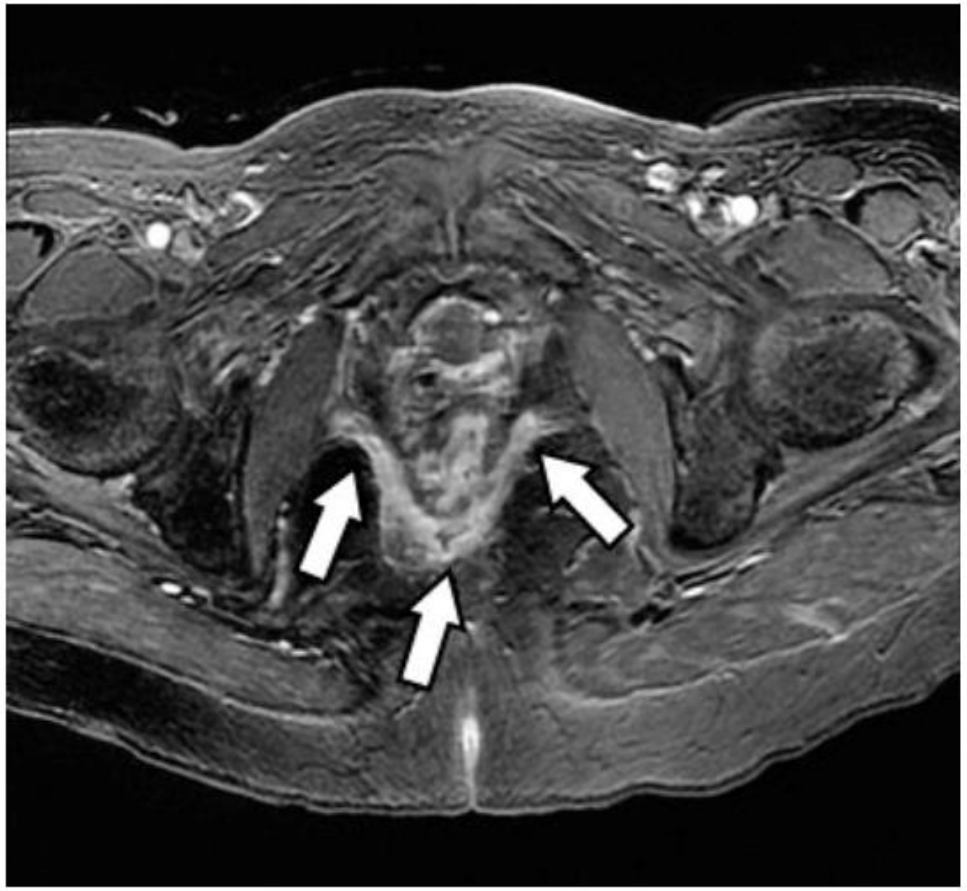


Perianal fistulas in Crohn disease



T2-weighted coronal magnetic resonance imaging (MRI) study showing a perianal fistula (arrows) in a patient with Crohn disease.

Perianal fistulas in Crohn disease



T2-weighted axial magnetic resonance imaging (MRI) study showing perianal fistulas (arrows) in a patient with Crohn disease.

Modified van Assche Index

Magnetic Resonance Imaging (MRI) Parametres

Points	1	2	3	4	5	6	7	8	0
Number of tracts									
Single, unbranched									
Single, branced									
Multiple									
Location									
Extra- or intersphincteric									
Transphincteric									
Suprasphincteric									
Extension									
Infralevatoria									
Supralevatoria									
Rectal wall involvement									
Hyperintensity on T2- weighted images									
Absent									
Mild									
Pronounced									
Hyperintensity on T1- weighted images									
Absent									
Mild									
Moderate									
Strong									
Normal									
Thickened									
Collections in tracts (cavities >3mm diatmeter)									
Absent									
Infiltrate									
Present									

Modified van Assche MRI score

Standardized assessment of perianal fistula severity and response following therapy

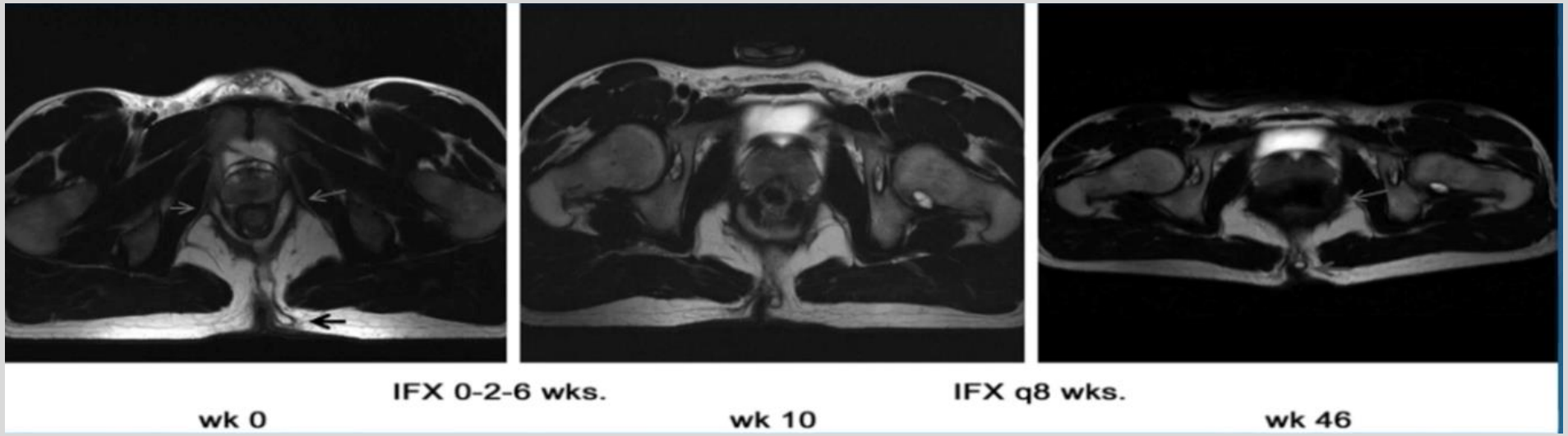
Assess fistula tract complexity, location, involvement of rectal wall and abscess formation

MRI response lags behind clinical response

- **1/3 of clinical responders may have no MRI response**

MRI to monitor therapy

- 59 pts with CD-PAF
- MRI at baseline – short – mid- and long-term
- MRI results coincided wth clinical improvement in **55% pts**
- No improvement seen between mid and long term MRI



Diagnostic evaluation

Prospective study comparing EUS, MRI and EUA
32 pts with suspected perianal CD
All 3 methods displayed good diagnostic accuracy

- EUS – 91%
- EUA – 91%
- MRI – 87&

Combining either increased diagnostic accuracy to 100%

Schwartz etal Gastro 2001

Colonoscopy

- To assess luminal disease esp degree of proctitis
- External fistula opening usually visible on the skin
- Internal fistula opening may be visible endoscopically

Differential diagnosis
(new presentation)

- STD
- HIV
- Hydradenitis suppurutiva
- Anal cancer
- TB
- Actinomycosis
- Haematological malignancy (leukemia, lymphoma, myeloma)

Perianal Biopsies

- Low sensitivity and specificity for CD
- 1/3 = granulomas
- Most useful for excluding **malignancy**
- Very difficult to interpret in the absence of luminal disease

Management principles

- Goals of therapy
- Sequence of therapies
- Peference for therapies
- Multidisciplinary approach

Goals of therapy

- Complete fistula closure is the primary therapeutic goal for most patients

- Complex perianal fistulas (closure may not be feasible)

➢ *symptomatic improvement*: ↓rectal pain ↓drainage

➢Improved *quality of life* but without complete fistula healing and closure

Sequence of therapies

- **Eradicate the infection**
  - ➢I&D, antibiotics, seton placement

- **Assess luminal CD and fistula tract (EUA/MRI/colo/EUS)**
  - in order to initiate medical therapy
  - intervene surgically if needed (eg non-healing fistula).

Preference for therapies

- no single preferred treatment strategy
- Important factors influencing decision making
  - severity of the clinical manifestations
  - anatomic complexity of the fistulas
  - Impact on quality of life
  - risk of adverse events
  - Presence/extent of luminal disease (esp degree of proctitis)
  - Response to medical and surgical treatment
  - patient preference

Multidisciplinary approach

- Requires input from the **MDT**
  - ✓Gastroenterologist
  - ✓Colorectal surgeon
  - ✓Radiologist
  - ✓Histopathologist

Medical therapy

- **Antibiotics**
  - metronidazole, ciprofloxacin
- **Immunosuppressives**
  - Azathioprine
  - 6-mercaptopurine
  - Cyclosporine
  - Tacrolimus
- **Biologic agents**
  - Infliximab
  - Adalimumab
  - Certolizumab
  - Vedolizumab
  - Ustekinumab
- **Novel agents**
  - Adipose derive stem cells

Antibiotics

- Metronidazole and ciprofloxacin most commonly used
  - Used separately or in combination
  - 1-2 weeks of Cipro; 1-2 months of metro
- Short-term benefit in fistula drainage
- Very few trials
- Monotherapy in simple fistula
- **Combination therapy for complex fistula**
  - Anti-TNF and thiopurine
- Topical therapy ineffective

Thiopurines

- Azathioprine and 6-MP evaluated in meta-analysis in 1995
  - 5 studies
  - Better than placebo
- Modest effect on fistula response
  - 54% compared to placebo (21%)
  - Started whilst awaiting biologic
  - High rate of recurrence
- Combination usage with antibiotics **better** than antibiotics alone
- Used as an adjunct to anti-TNF

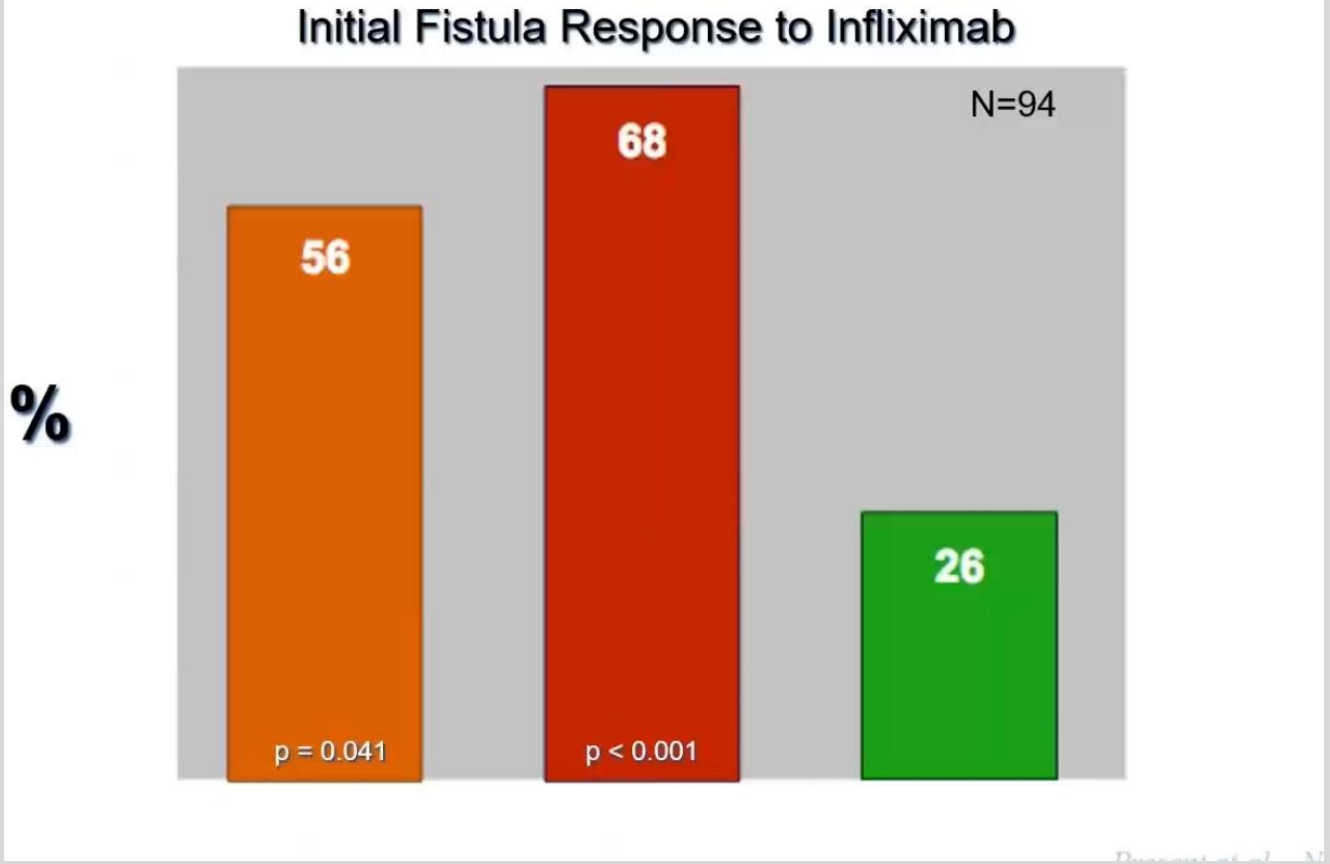

100 mg
Infliximab
Powder for
Concentrate for
Solution for Infusion
Schering-Plough

Anti-TNF therapy - INFLIXIMAB

- Infliximab is currently the mainstay of medical therapy in CD PAF
- Demonstrated efficacy in RCT
- Landmark studies (1999/2004)
  - Infliximab outperformed placebo for induction and maintenance of fistula healing
- **Induction studies** - Fistula healing
  - 68% of patients receiving 5mg/kg
  - 56% of patients receiving 10mg/kg
- **Maintenance studies (5mg/kg every 8 weeks)**
  - Extended time to recurrence to more than 40 weeks
  - Remission maintained in only 36% at week 54

Infliximab for Crohn's Perianal Fistulas

Primary endpoint; > 50% reduction in open fistulas



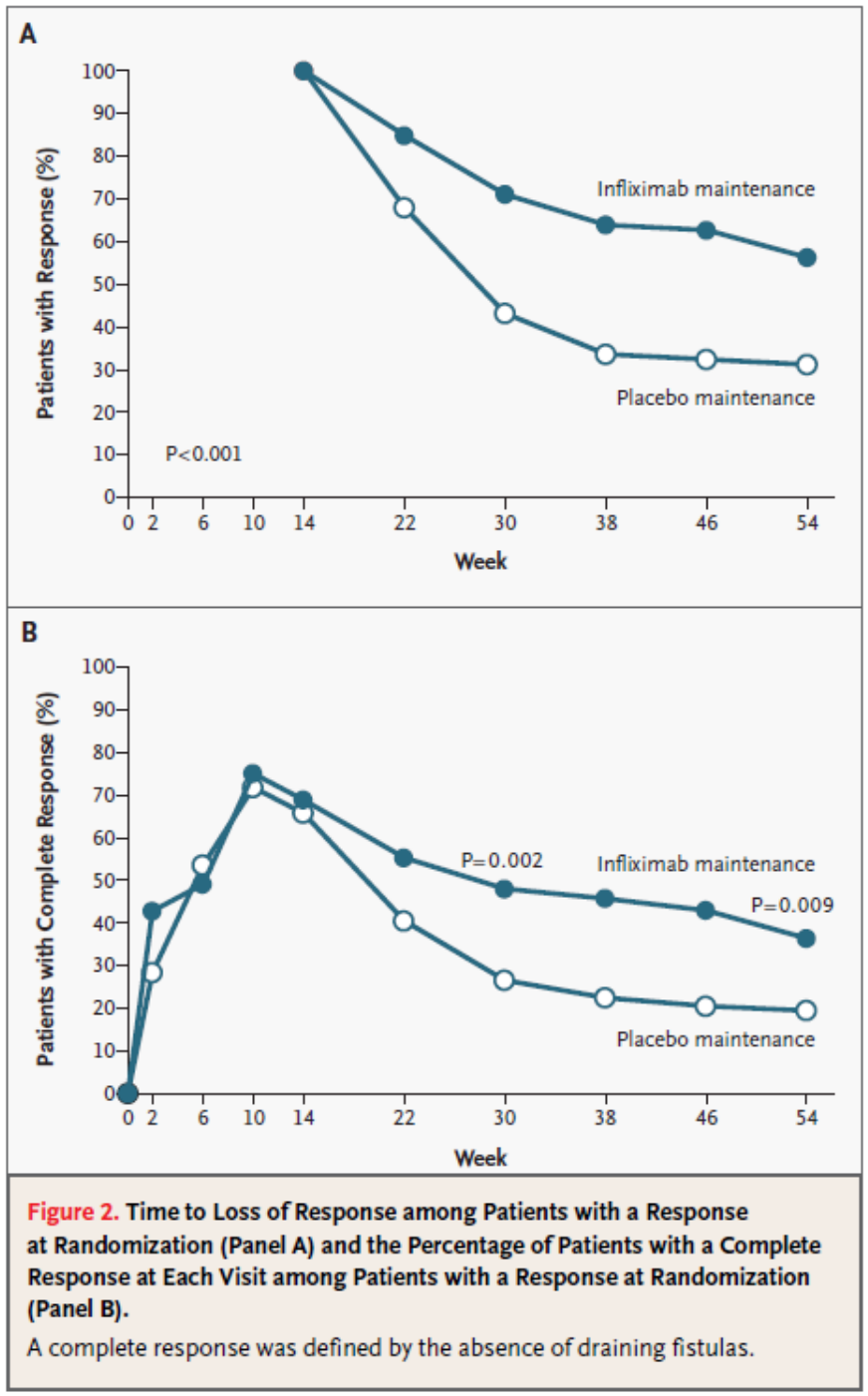


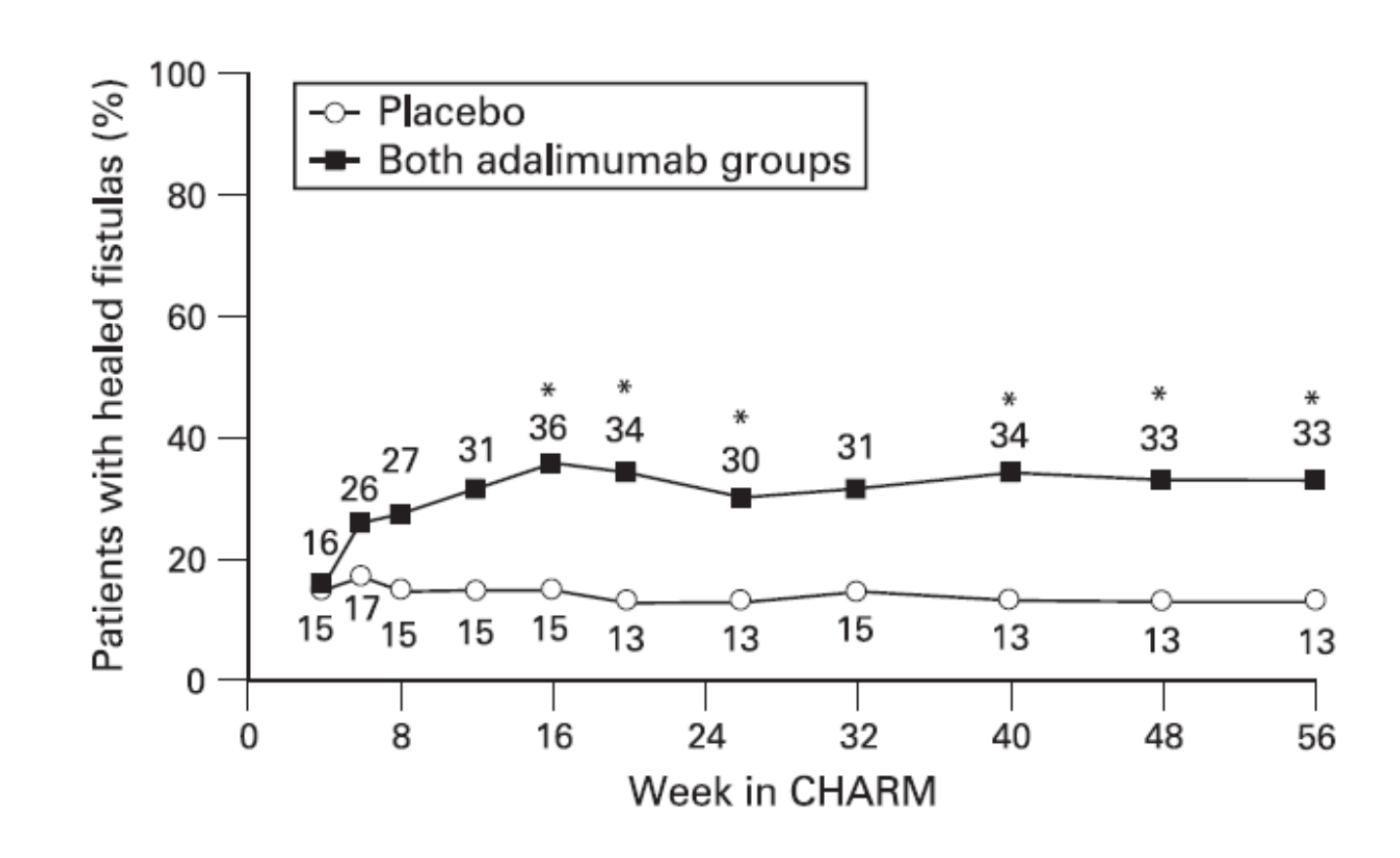
Figure 2. Time to Loss of Response among Patients with a Response at Randomization (Panel A) and the Percentage of Patients with a Complete Response at Each Visit among Patients with a Response at Randomization (Panel B).

A complete response was defined by the absence of draining fistulas.

Anti-TNF (ADALIMUMAB)

- Effective alternative to Infliximab
- Not evaluated in RCT
- **CHARM trial**
  - Higher rate of fistula closure (33%) compared to placebo (12%) at week 56
- **ADAFI trial**
  - Combination therapy with Ciprofloxacin and Adalimumab **better** than Adalimumab alone
  - Once antibiotics stopped – outcomes same at 6 months

CHARM trial


Placebo
Both adalimumab groups
Patients with healed fistulas (%)
100
80
60
40
20
0
0
8
16
24
32
40
48
56
Week in CHARM
16
26
27
31
36
34
30
31
34
33
33
15
17
15
15
15
13
13
15
13
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13
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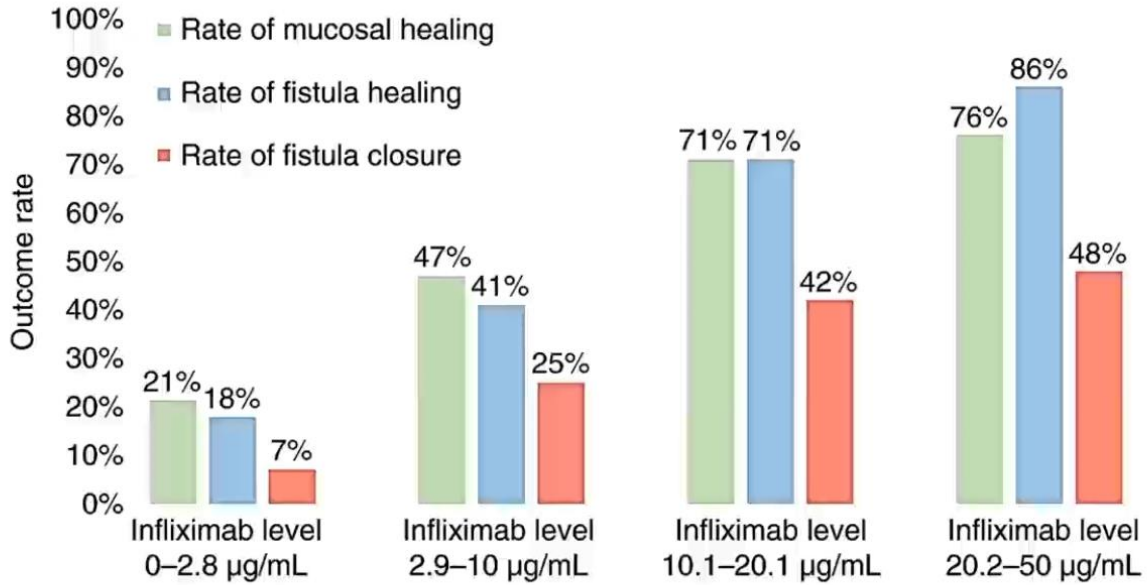
Higher IFX trough levels beneficial

Higher Infliximab Trough Levels are Associated with a Higher Rate of Perianal Fistula Healing



Yarur A., APT 2017

Early vs late Anti-TNF

- Early use of Anti-TNF in newly diagnosed CD associated with **59% risk reduction** of developing CD PAF

- General delay in starting anti-TNF in CD-PAF
  - Median of **6/12** between Dx of CD PAF and initiation of anti-TNF
  - Concern of worsening perianal infection

- **early initiation of anti-TNF should be considered following seton insertion**
  - Concomitant antibiotic usage
  - associated with lower rates of re-intervention compared to chronic fistula drainage alone
- **Combination of anti-TNF and thiopurine**
  - No difference in fistula outcomes but recent retrospective data associated with improved fistula outcomes
  - Prevent development of immunogenicity

Evaluation of a Seton Procedure Combined With Infliximab Therapy (Early vs. Late) in Perianal Fistula With Crohn Disease

Myunghoon Jeon[1], Kihwan Song[1], Jail Koo[1], Sohyun Kim[2]

[1]Department of Surgery, Goo Hospital, Daegu; [2]Department of Surgery, Yeungnam University Medical Center, Yeungnam University College of Medicine, Daegu, Korea

76 pts

Early < 30 days of seton insertion

Late > 30 days of seton insertion

Annals of Colproctology 2019

Evaluation of a S… With Infliximab Therapy (Ea… …ula With Crohn Disease

…iyun Kim[2]

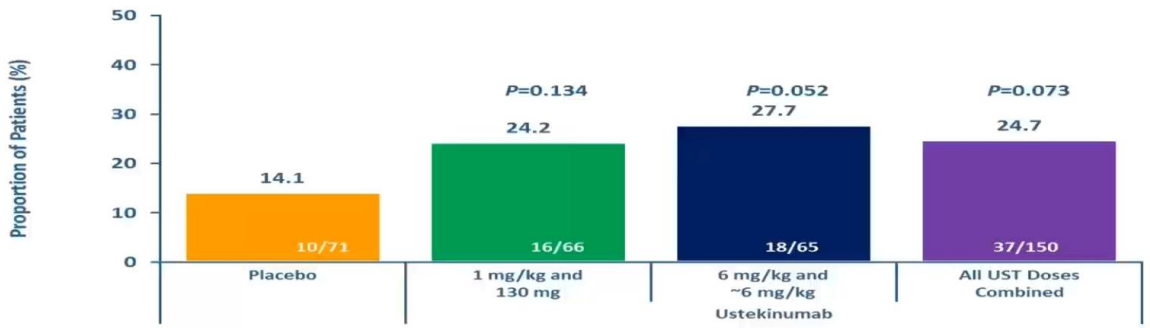
…ent of Surgery, Yeungnam University Medical Center, Yeungnam University College

No difference in fistula outcomes

Annals of Colproctology 2019

Post Hoc Analysis Suggests Ustekinumab Effective for Perianal Disease in Crohn's

Fistula Resolution at Week 8 - Pooled Data from CERTIFI, UNITI-1 and UNITI-2



What about Vedolizumab?

Clinical Gastroenterology and Hepatology 2022;20:1059–1067

Efficacy and Safety of 2 Vedolizumab Intravenous Regimens for Perianal Fistulizing Crohn's Disease: ENTERPRISE Study

David A. Schwartz,[*] Laurent Peyrin-Biroulet,[‡,§] Karen Lasch,[‖] Shashi Adsul,[¶] and Silvio Danese[#]

[*]*Inflammatory Bowel Disease Center, Vanderbilt University Medical Center, Nashville, Tennessee,* [‡]*Department of Gastroenterology, Nancy University Hospital, Nancy, France,* [§]*Inserm U1256 NGERE, Lorraine University, Nancy, France,* [‖]*Takeda Pharmaceuticals USA Inc, Lexington, Massachusetts,* [¶]*Takeda Pharmaceuticals International AG, Zurich, Switzerland, and* [#]*IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milano, Italy*

Results from ENTERPRISE, a randomized, double-blind, phase 4 trial

Enrollment and study population

N = 52 patients were screened:

moderately to severely active CD

draining perianal fistulae

inadequate response, loss of response, or intolerance to conventional therapy or anti-TNF

Treatment regimen (300 mg VDZ)

N = 34 randomized 1:1

n = 16

IV VDZ at weeks:

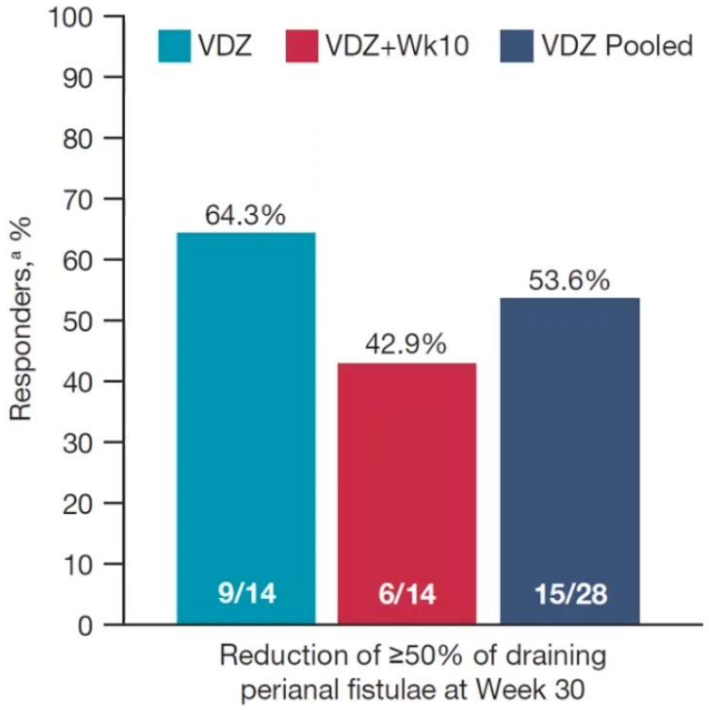
0 2 6 14 22

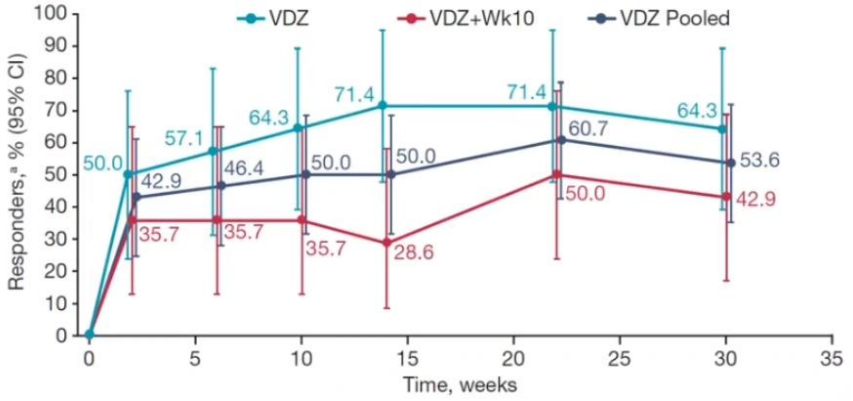
n = 18

IV VDZ at weeks:

0 2 6 10 14 22

Vedo promotes fistula closure





Schwartz et al. CGH 2022

Fistula response with VDZ (N = 28)

≥50% reduction in draining fistulae at weeks 22 and 30

100% fistulae closure at week 30

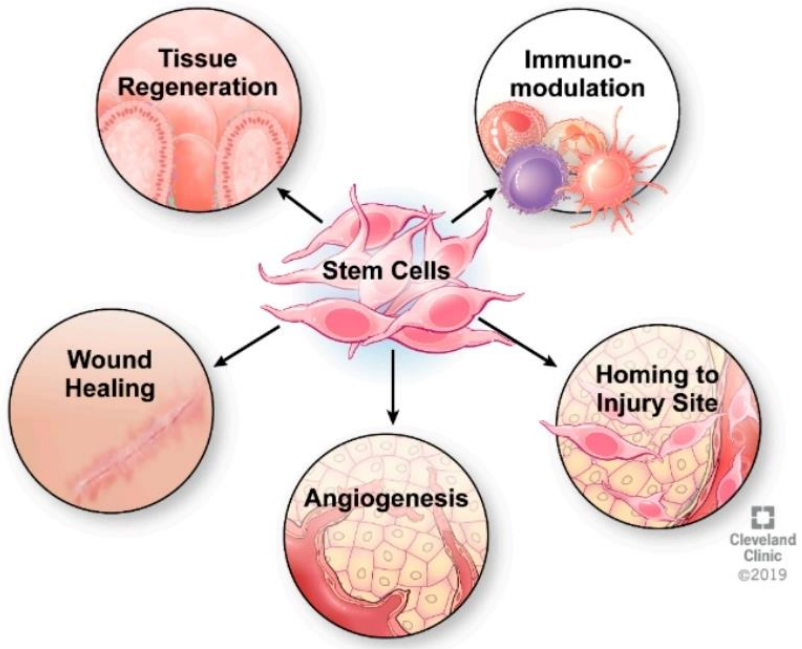


Figure 1. Mechanism of action of MSCs (courtesy of Cleveland Clinic, with permission).

Virtual Grand Rounds

universe.gi.org

Int J Colorectal Dis (2003) 18:451–454
DOI 10.1007/s00384-003-0490-3

CASE REPORT

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Autologous stem cell transplantation for treatment of rectovaginal fistula in perianal Crohn's disease: a new cell-based therapy

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Autologous stem cell transplantation for treatment of rectovaginal fistula in perianal Crohn's disease: a new cell-based therapy

- 33-year-old female
- Complex fistula with 5 perianal tracts which converged into rectovaginal fistula
- Infliximab
- Gracilis flap
- ***Injection of 9×10^6 MSCs → healed within 3 months***

Mesenchymal Stem Cells (MSCs) are safe

- No trial has reported systemic complications
- No trial has reported systemic infections
- Most frequent AE = pain at site of injection (12-15%)
- 2nd most frequent AE = perianal abscess at injection site (5-13%)
  - **same frequency in treatment and control*

	Cx601 (n=103)	Placebo (n=102)
Overall	68 (66%)	66 (65%)
TEAEs leading to study withdrawal	5 (5%)	6 (6%)
TEAEs in ≥5·0% of patients*		
Proctalgia	13 (13%)	11 (11%)
Anal abscess	12 (12%)	13 (13%)
Nasopharyngitis	10 (10%)	5 (5%)
Diarrhoea	7 (7%)	3 (3%)
Abdominal pain	4 (4%)	6 (6%)
Fistula†	3 (3%)	6 (6%)
Treatment-related adverse events	18 (17%)	30 (29%)
Treatment-related adverse events in ≥2·0% of patients*		
Anal abscess	6 (6%)	9 (9%)
Proctalgia	5 (5%)	9 (9%)
Procedural pain	1 (1%)	2 (2%)
Fistula discharge‡	1 (1%)	2 (2%)
Induration	0	2 (2%)
Serious TEAEs§	18 (17%)	14 (14%)
Serious TEAEs in ≥2·0% of patients*		
Anal abscess	9 (9%)	7 (7%)
Serious treatment-related adverse events	5 (5%)	7 (7%)
Anal abscess	5 (5%)	5 (5%)
Proctalgia	0	1 (1%)
Anal inflammation	0	1 (1%)
Liver abscess	0	1 (1%)

Cx601: allogeneic, expanded, adipose-derived stem cells. TEAE=treatment-emergent adverse event (MedDRA, version 17.0). *In either treatment group. †New fistula, reopening of closed fistula. ‡Fistula discharge in a closed fistula. §Defined as any adverse event that at any dose resulted in death, was life-threatening, caused permanent incapacity or disability, resulted in hospital admission or prolonged a hospital stay, was a medically significant event, or was a suspected transmission of an infectious drug.

Table 3: **Treatment-emergent adverse events up to week 24 in the safety population**

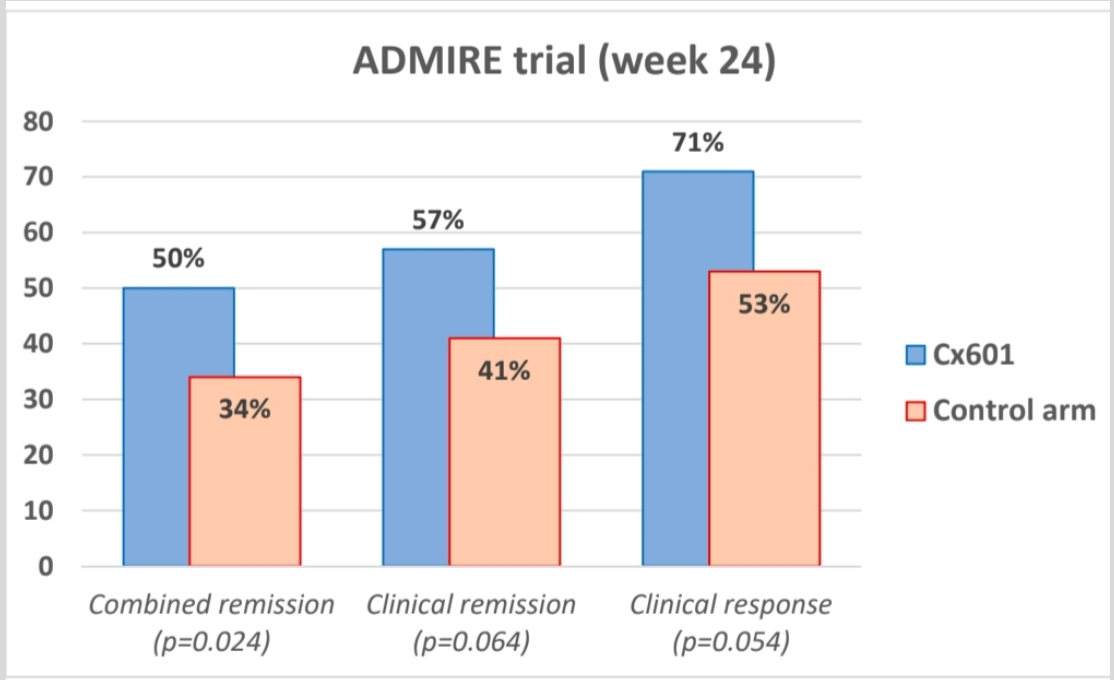


Figure 2. ADMIRE randomized trial results of efficacy at week 24.

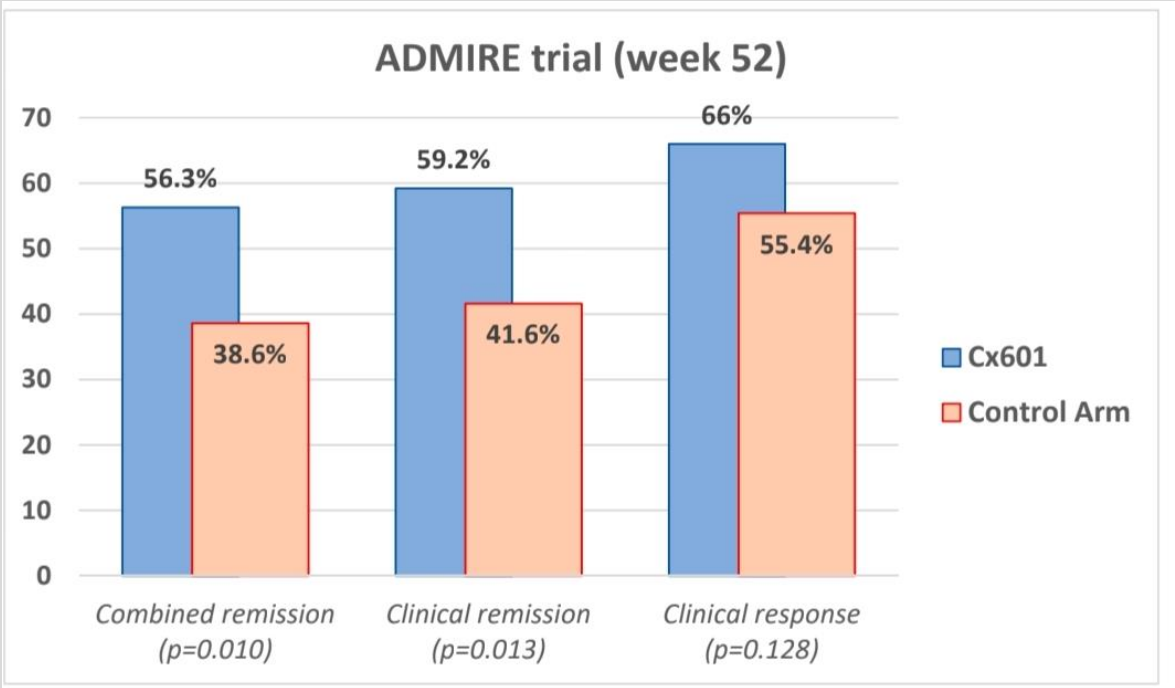
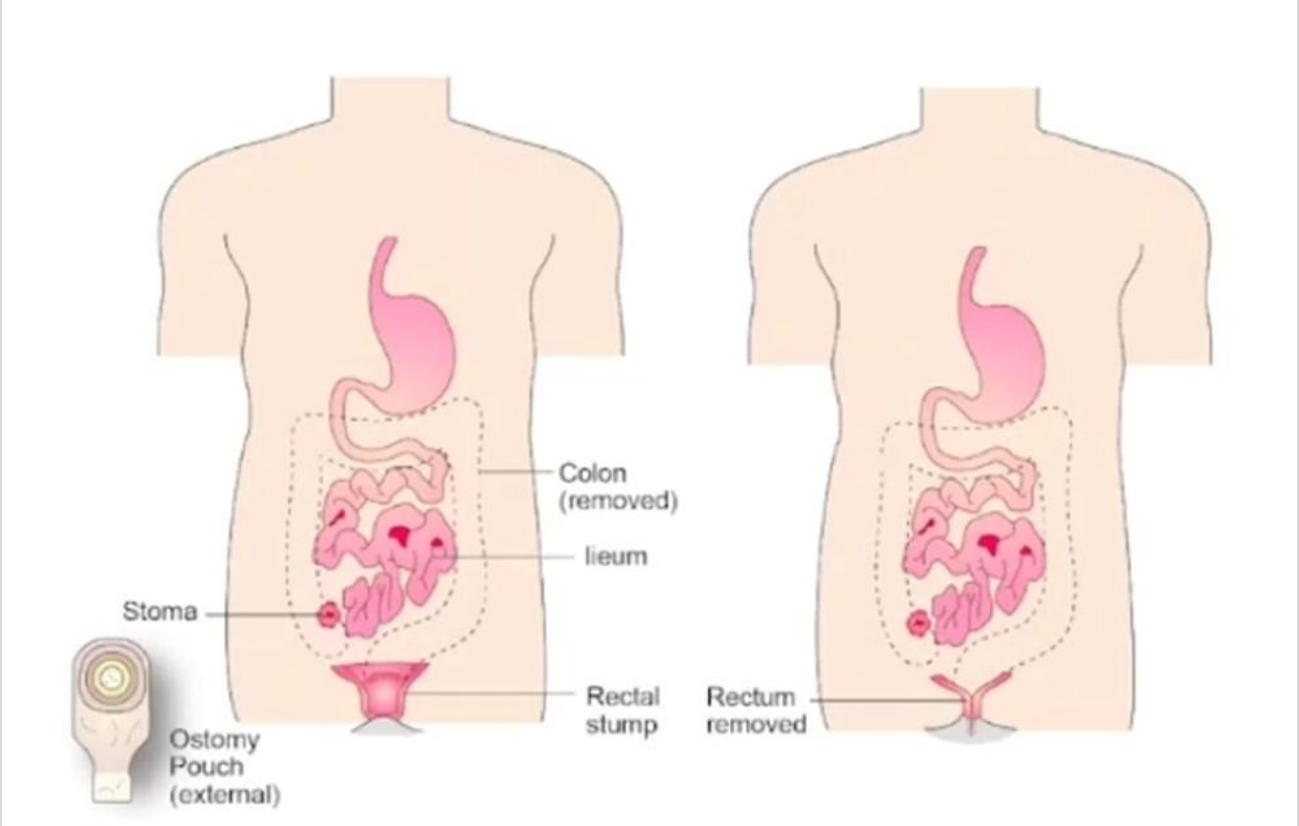


Figure 3. Long-term extension efficacy results of the ADMIRE randomized trial at week 52.

Diversion and proctectomy

- For severe, progressive and refractory disease
- 20% - temporary ileostomy or colostomy
  - Diversion of faecal stream improves fistulising disease
  - But often recurs when continuity restored
- 20% proctectomy



Conclusion

- CD PAF is a severe phenotype of CD with significant morbidity and impact on quality of life
- Difficult to treat
- Multidisciplinary management (esp gastroenterologist and colorectal surgeon)
- Early treatment of sepsis and insertions of setons in complex fistulas
- Use of imaging to provide a virtual roadmap and guide treatment
- Early use of Anti-TNF for complex fistulas
- Data emerging for newer treatments such as vedo and stem cells