Providence

The Role of Surgery in the Treatment of Inflammatory Bowel Disease

Who, When, and Where to Send to Surgery

September 2023

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Swedish Colon and Rectal Clinic

Disclosure

I do not have any relevant financial relationships with any commercial interest that pertains to the content of my presentation

I was an investigator in ADMIRE II

Who to Send to Surgery

- Penetrating Disease
- Cancer or Dysplasia
- Refractory to medical therapy
- Toxic Colitis
- Obstructing Disease

When to Send to Surgery

- Penetrating Disease
- Cancer or Dysplasia
- Refractory to medical therapy
- Toxic Colitis
- Obstructing Disease

Where to Send to Surgery

- High Volume/Experience
- Specialized Surgeons
- Multidisciplinary Access
- GI Pathologists

Focus on Challenging and Controversial Topics

Dysplastic Lesions in Ulcerative Colitis

Stricturoplasty vs Resection for Fibrostenotic Crohn Disease

Perianal Crohn Disease

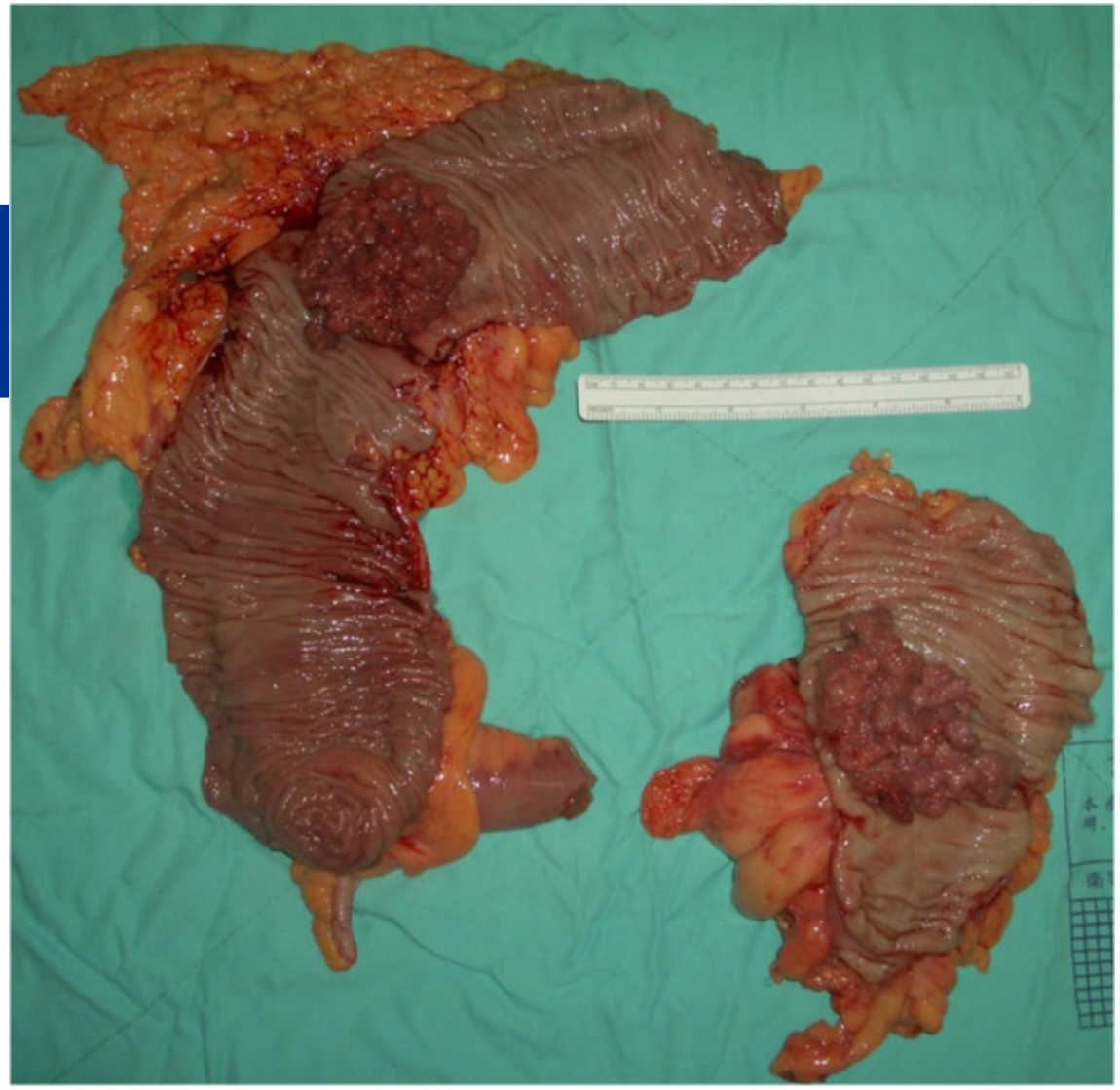
Focus on Challenging or Controversial Topics

Dysplastic Lesions in Ulcerative Colitis

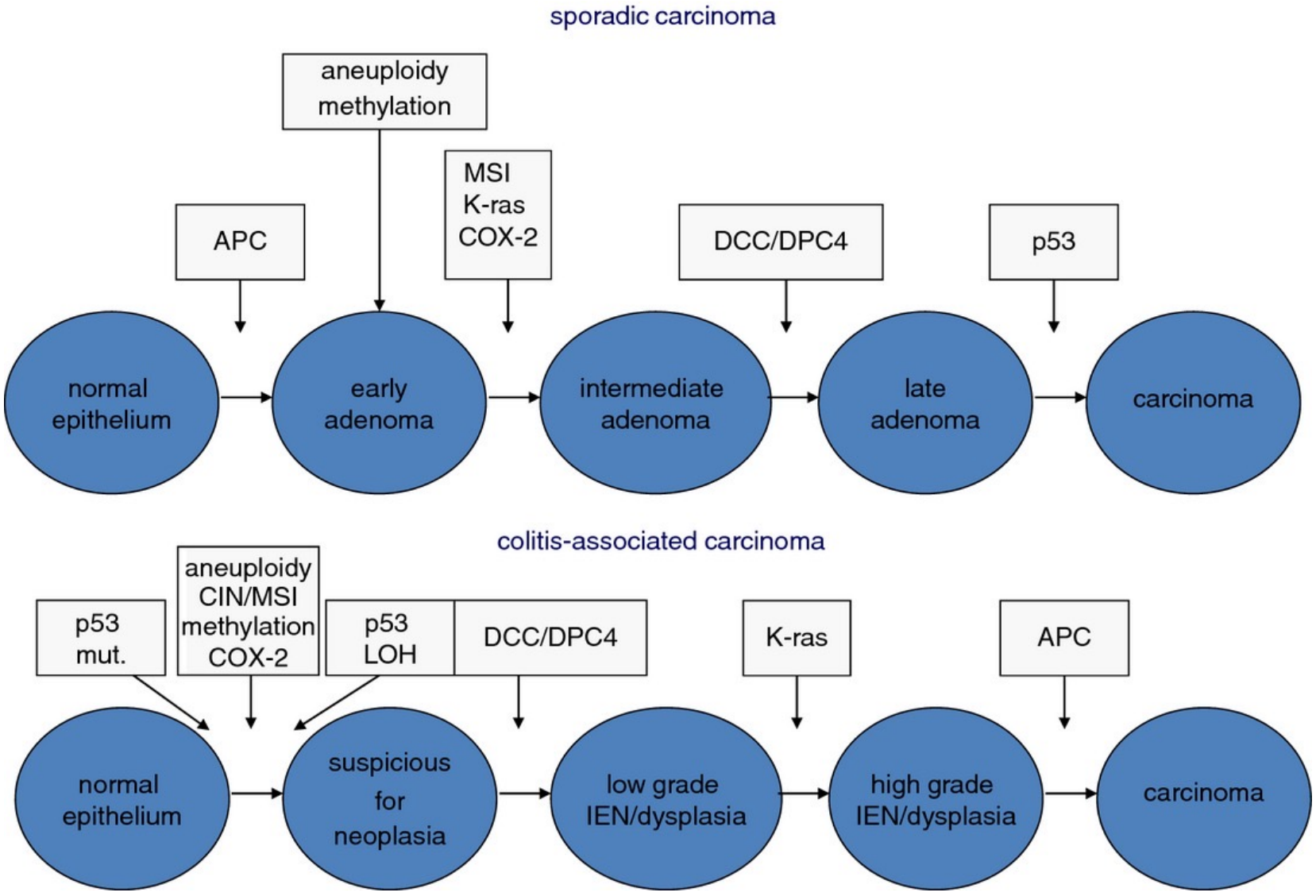
Carcinoma

Increased in UC and CD

- 95/100,000
- UC
  - 2% at 10 years
  - 8% at 20 years
  - 18% at 30 Years
- CD
  - 8% at 22 years

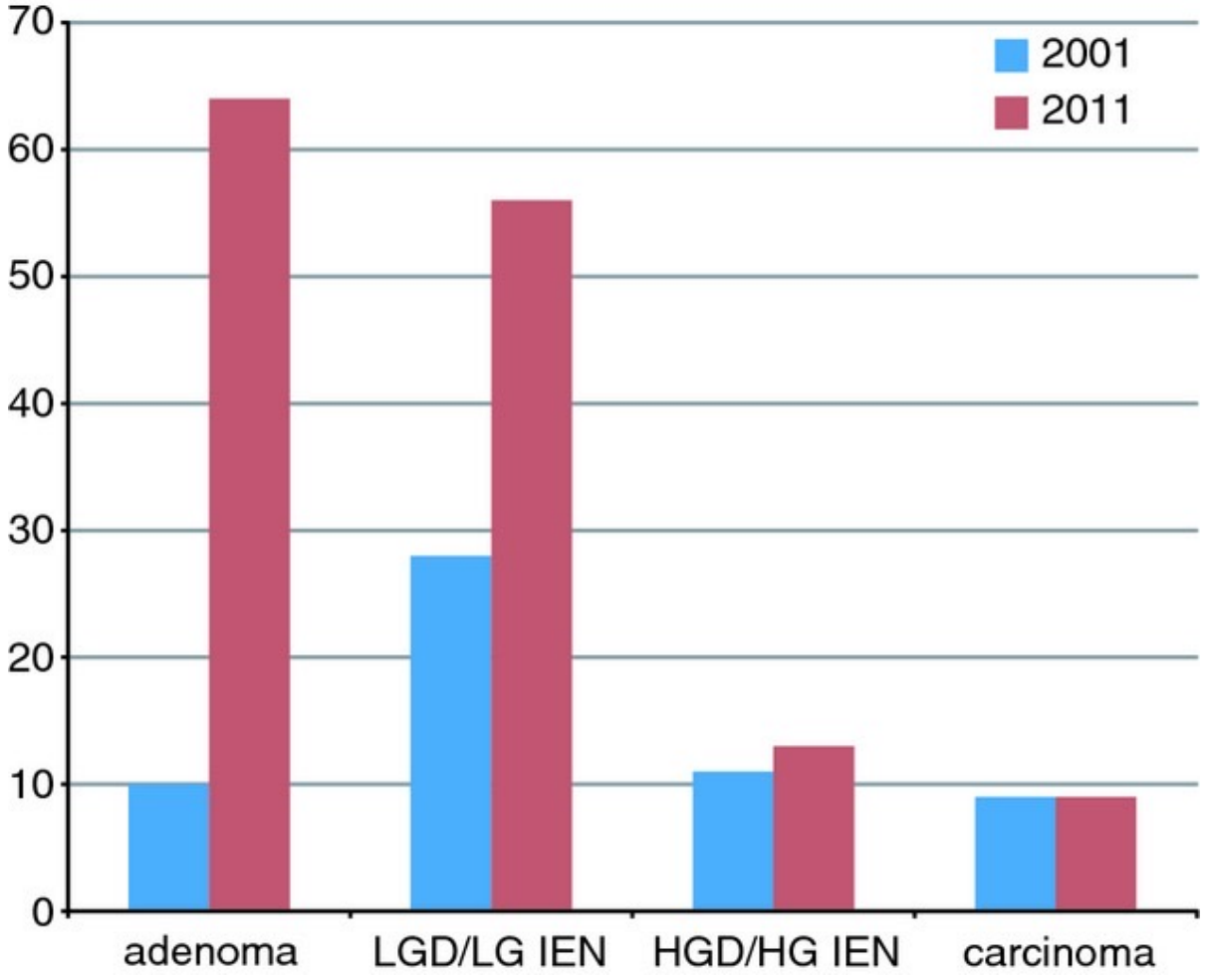


IBD Cancer pathway may be different from sporadic CRC



Histopathology 2015

Improved Detection with Improved Technology



Histopathology 2015

Evolution of dysplasia detection and management

Time period	Detection Strategy	Management Approach
Pre-colonoscopy (pre-1970) • CRC natural history of IBD	No strategy to detect dysplasia	Proctocolectomy with ileostomy
Early colonoscopy (1970s-90s)	Most dysplasia is “invisible” Random biopsies	Restorative proctocolectomy vs ileostomy
Early 2000s	Most dysplasia is visible Random biopsies	LGD→polypectomy vs colectomy HGD→laparoscopic restorative proctocolectomy
Present • High Definition endoscopy • Chromoendoscopy • EMR and ESD • High tech tools for resection	Most dysplasia is visible Targeted biopsies with improved visualization	Endoscopic resection of discrete lesions Surgery for select cases (MIS)

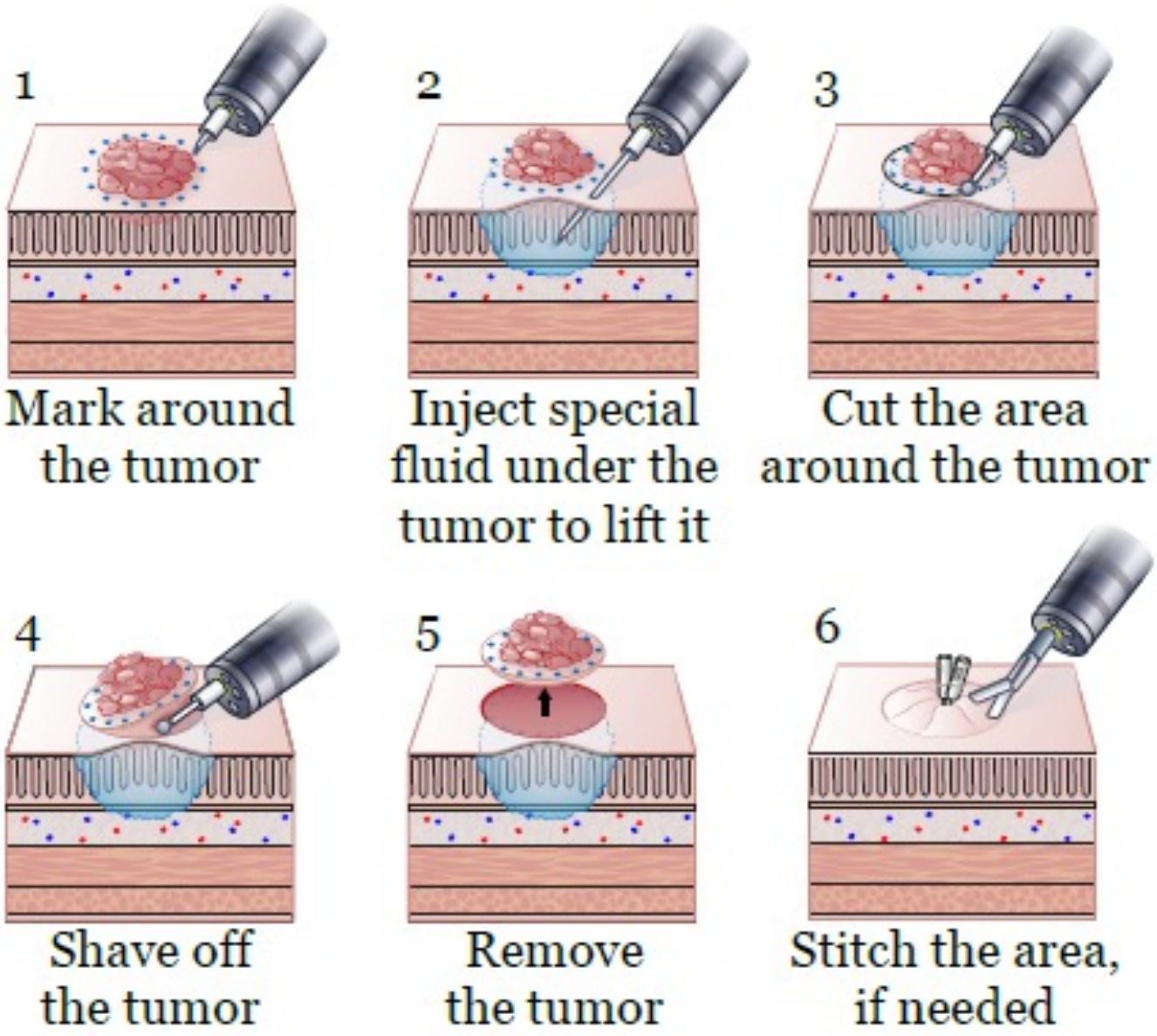
Visible Dysplasia

Resectable

- Distinct margin on endoscopy
- Lift and hot snare
- Complete removal
- Negative margins on histology
- Negative biopsies from the periphery and base

Non-resectable

- Large size (>2cm)
- Inability to lift
- Poorly delineated margins



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Visible Dysplasia

Colectomy

- HGD
- CRC
- Multifocal LGD
- Incompletely resected dysplasia
- Recurrent

Continued Surveillance

- Completely resected LGD
  - 6% annual incidence of any dysplasia
  - 0.5% annual incidence of CRC

Challenges in Management of Invisible Dysplasia

Uncertainty

Histological interpretation

Likelihood of progression to CA

Ability to do effective surveillance

Strategy to prevent progression

Lesions not seen

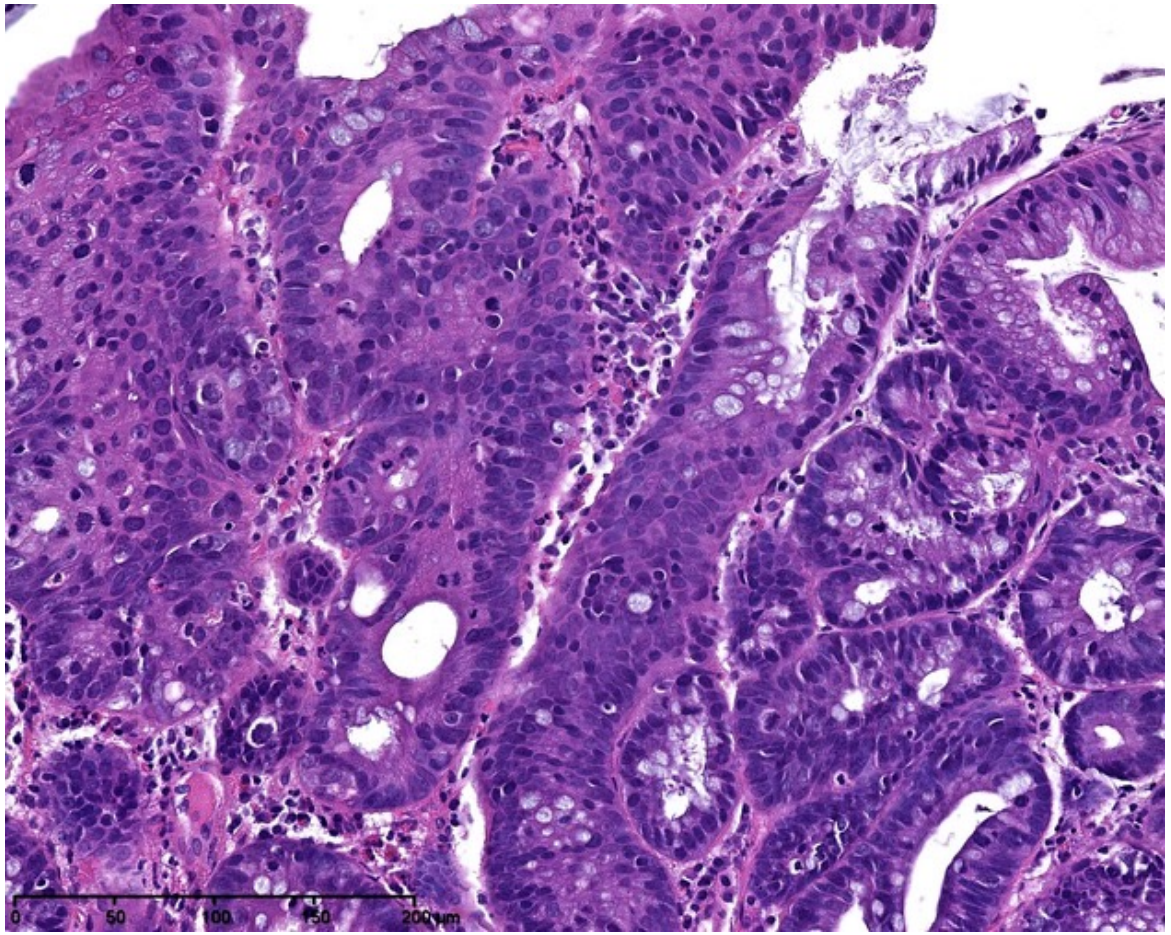
Treatment options

Colectomy

- What if pathologic interpretation was wrong
- What if lesion is small and endoscopically resectable?

Surveillance

- What if endoscopist can't find the lesion again and patient progresses to CA?
- Timing of interval frequency for surveillance



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A	Management of visible and invisible dysplasia within a colitis field*	
Endoscopic assessment	**Management**	**Next colonoscopy and comments**
• < 2cm + resectable (clear border, no features of submucosal invasion or fibrosis) + no histologic features of invasive cancer	Endoscopic resection with continued surveillance	• 3–6 months: high-grade dysplasia or incomplete resection • 12 months: > 1cm, low-grade dysplasia (LGD) • 24 months: < 1cm or pedunculated, LGD
• Large (≥ 2cm) • Complex (i.e. lateral spreading, highly irregular or indistinct border) • Incomplete resection after several attempts • Local recurrence	Endoscopic resection with intensive surveillance vs surgery	• Every 3–6 months for first year (if resect) • Decision to resect based on lesion details, local expertise, disease activity
• Unresectable due to size, location, features of invasive cancer or submucosal fibrosis • Invasive cancer on histology	Surgery	
• Invisible dysplasia (non-targeted biopsy) or subtle/ poorly delineated lesion (targeted biopsy)	• Confirm histology with second pathologist • Treat inflammation • Perform dye spray chromoendoscopy (DCE)	• Use DCE to unmask subtle lesions. If no lesion seen, take extensive non-targeted biopsies in area of prior dysplasia. Use box A or B to manage.

B	Management when no visible dysplasia is detected on DCE*	
Histologic assessment	**Management**	**Next colonoscopy and comments**
• Persistent high-grade or multifocal invisible dysplasia	Surgery	
• Persistent unifocal low-grade invisible dysplasia • No histologic dysplasia	Intensive surveillance with DCE **	• 3–6 months if prior high-grade or multifocal dysplasia; 6–12 months if prior low-grade dysplasia. Continue intensive surveillance until 2 consecutive negative high quality DCE exams.

*Consider expert opinion if uncertainty; ** Although intensive surveillance proposed, long-term management is uncertain. Discuss risks and benefits of surgery vs surveillance based on current and past inflammatory burden, quality of mucosal visualization, mucosal details from where dysplasia initially detected, and other CRC risk factors.

ECCO Guideline/Consensus Paper

Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery, and Ileo-anal Pouch Disorders

Fernando Magro,[a,†] Paolo Gionchetti,[b,†] Rami Eliakim,[c,#] Sandro Ardizzone,[d] Alessandro Armuzzi,[e] Manuel Barreiro-de Acosta,[f] Johan Burisch,[g] Krisztina B. Gecse,[h] Ailsa L. Hart,[i] Pieter Hindryckx,[j] Cord Langner,[k] Jimmy K. Limdi,[l] Gianluca Pellino,[m] Edyta Zagórowicz,[n] Tim Raine,[o] Marcus Harbord,[p#] Florian Rieder;[q] for the European Crohn's and Colitis Organisation [ECCO]

8.5.3. Management of endoscopically visible dysplasia

ECCO statement 8L

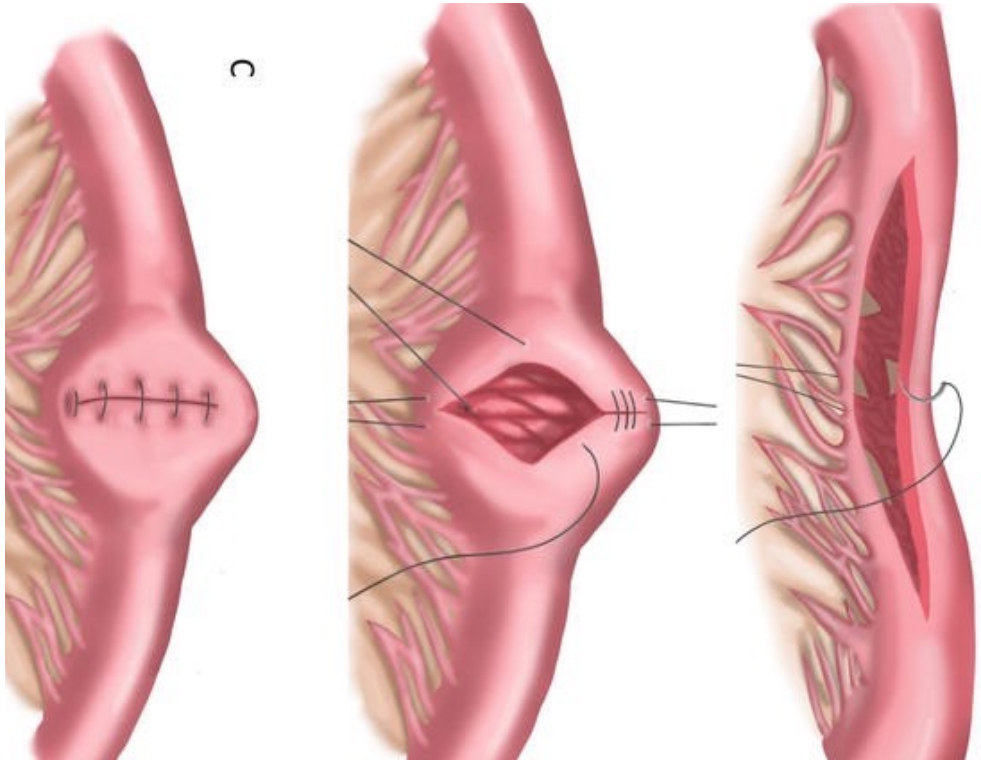
Polypoid dysplasia can be adequately treated by polypectomy provided the lesion can be completely excised, and there is no evidence of non-polypoid or invisible dysplasia elsewhere in the colon [EL 2]

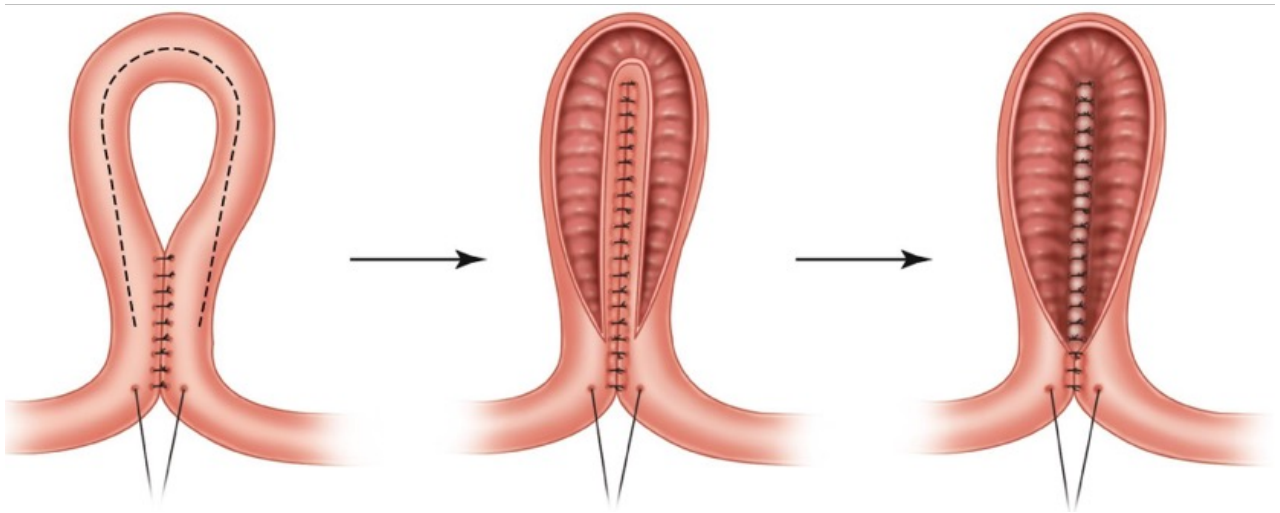
ECCO statement 8M

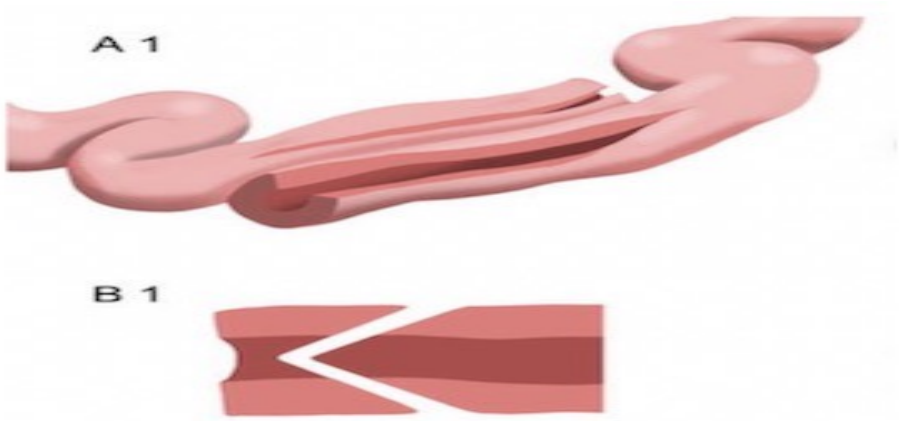
Non-polypoid dysplastic lesions can be treated endoscopically in selected cases. If complete resection can be achieved, with no evidence of non-polypoid or invisible dysplasia elsewhere in the colon, continued surveillance colonoscopy is reasonable [EL 5]. Every other patient with non-polypoid dysplasia should undergo colectomy, regardless of the grade of dysplasia detected on biopsy analysis [EL 2]

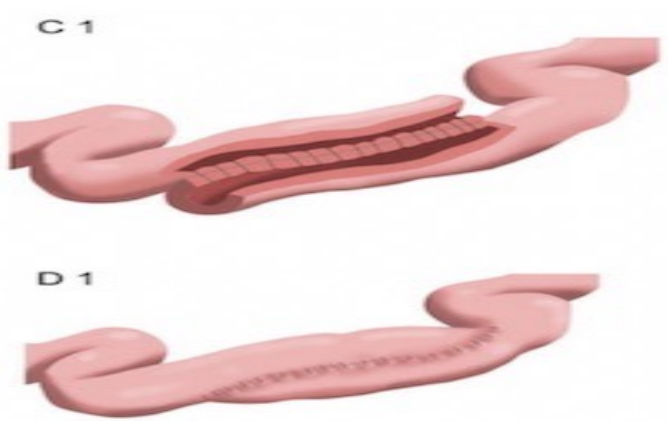
Focus on Challenging or Controversial Topics

Stricturoplasty vs Resection for Fibrostenotic Crohn Disease









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Strictureplasty versus bowel resection for the surgical management of fibrostenotic Crohn's disease: a systematic review and meta-analysis

Waqas T. Butt[1] · Éanna J. Ryan[1,2] · Michael R. Boland[1] · Eilis M. McCarthy[3] · Joseph Omorogbe[3] · Karl Hazel[3]
Gary A. Bass[1] · Paul C. Neary[1,4] · Dara O. Kavanagh[1,4] · Deirdre McNamara[3,4] · James M. O'Riordan[3,4]

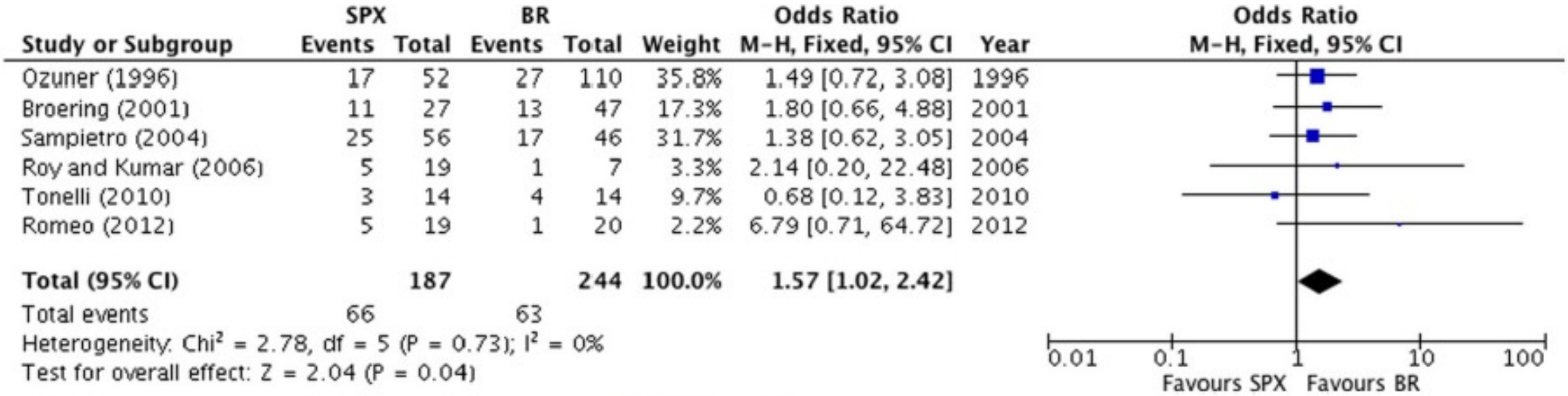


Fig. 2 Forest plot comparing overall recurrence in patients with SPX vs BR

Strictureplasty versus bowel resection for the surgical management of fibrostenotic Crohn's disease: a systematic review and meta-analysis

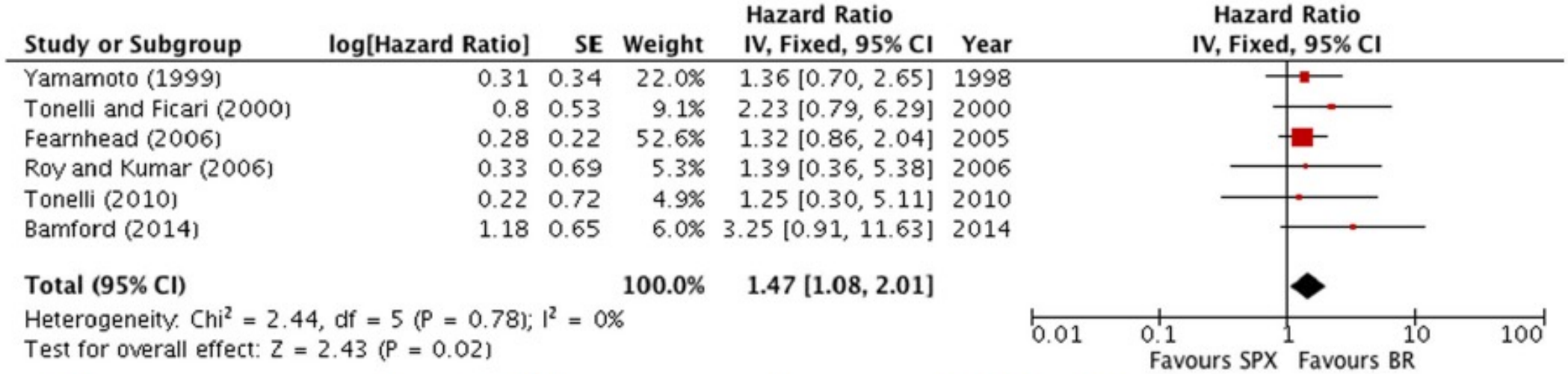


Fig. 3 Forest plot comparing recurrence-free survival (time to recurrence) in patients with SPX vs BR

Strictureplasty versus bowel resection for the surgical management of fibrostenotic Crohn's disease: a systematic review and meta-analysis

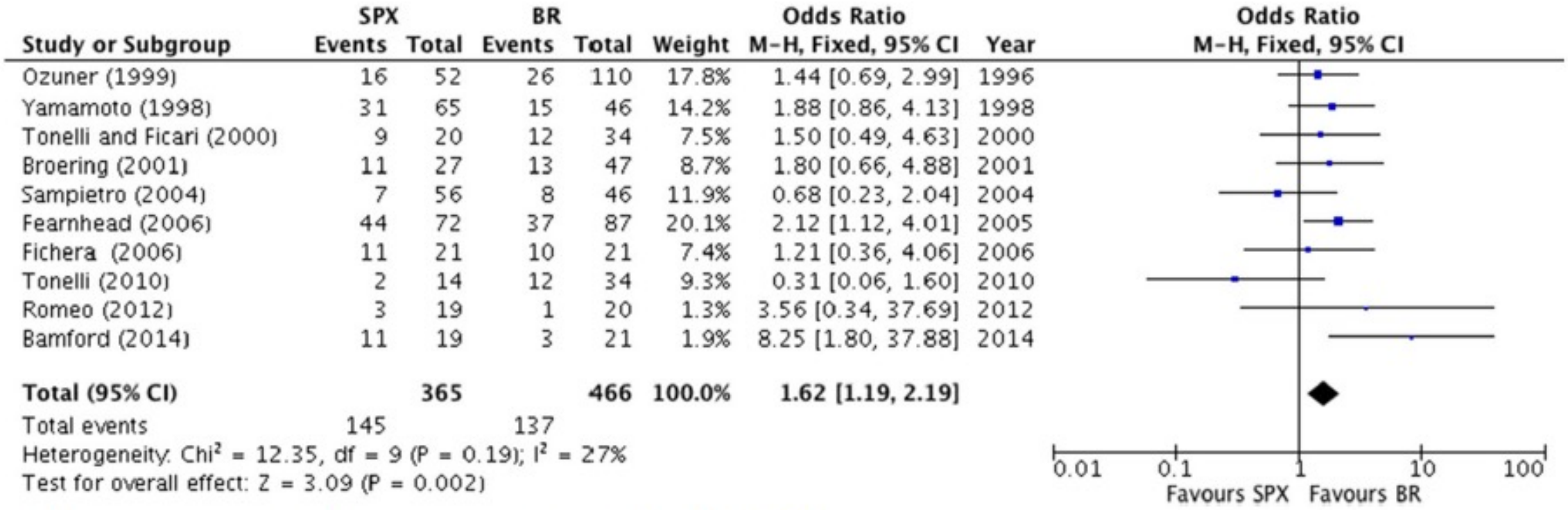


Fig. 4 Forest plot comparing surgical recurrence in patients with SPX vs BR

Strictureplasty versus bowel resection for the surgical management of fibrostenotic Crohn's disease: a systematic review and meta-analysis

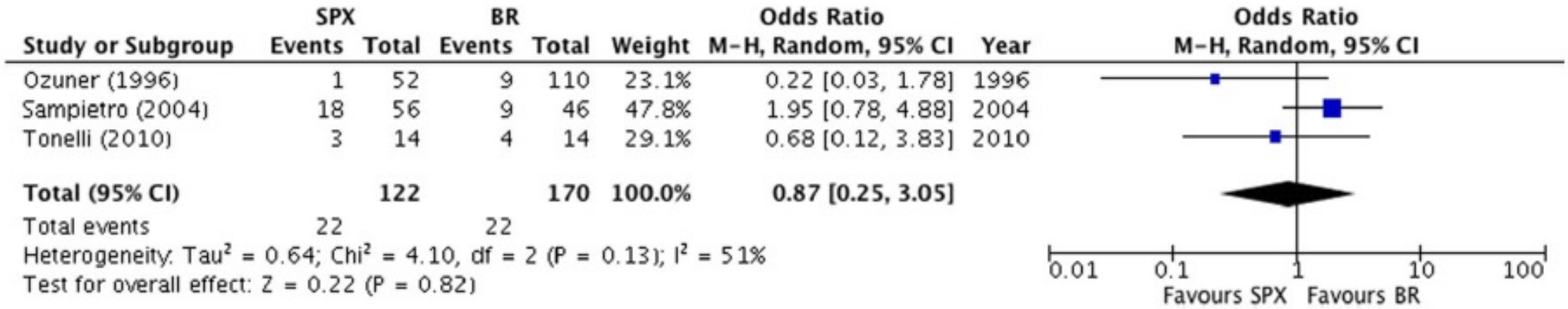


Fig. 5 Forest plot comparing medical recurrence in patients with SPX vs BR

Strictureplasty versus bowel resection for the surgical management of fibrostenotic Crohn's disease: a systematic review and meta-analysis

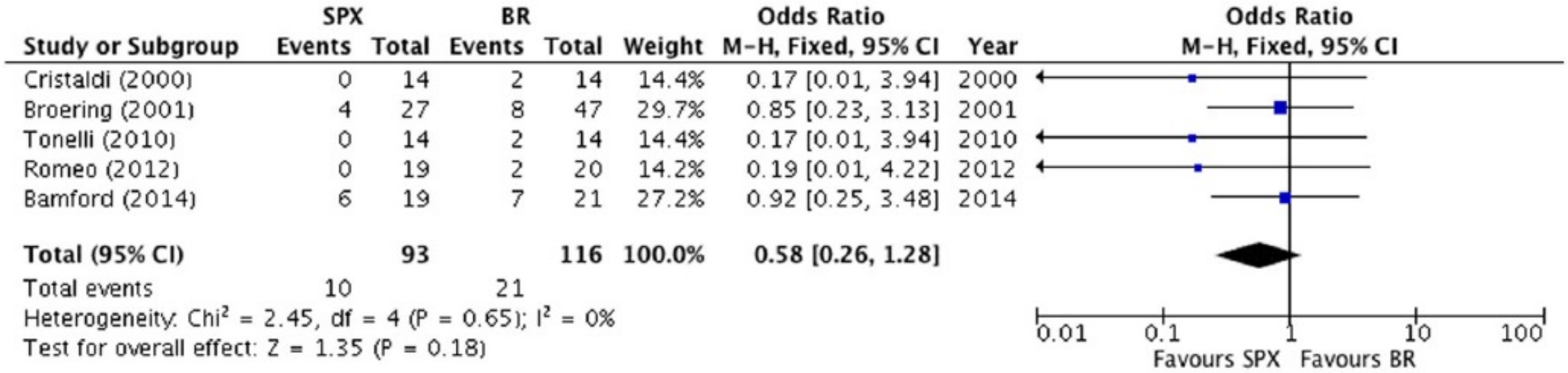


Fig. 6 Forest plot comparing overall morbidity in patients with SPX vs BR

Summary

Compared to strictureplasty, bowel resection for fibrostenotic crohn's disease results in improved

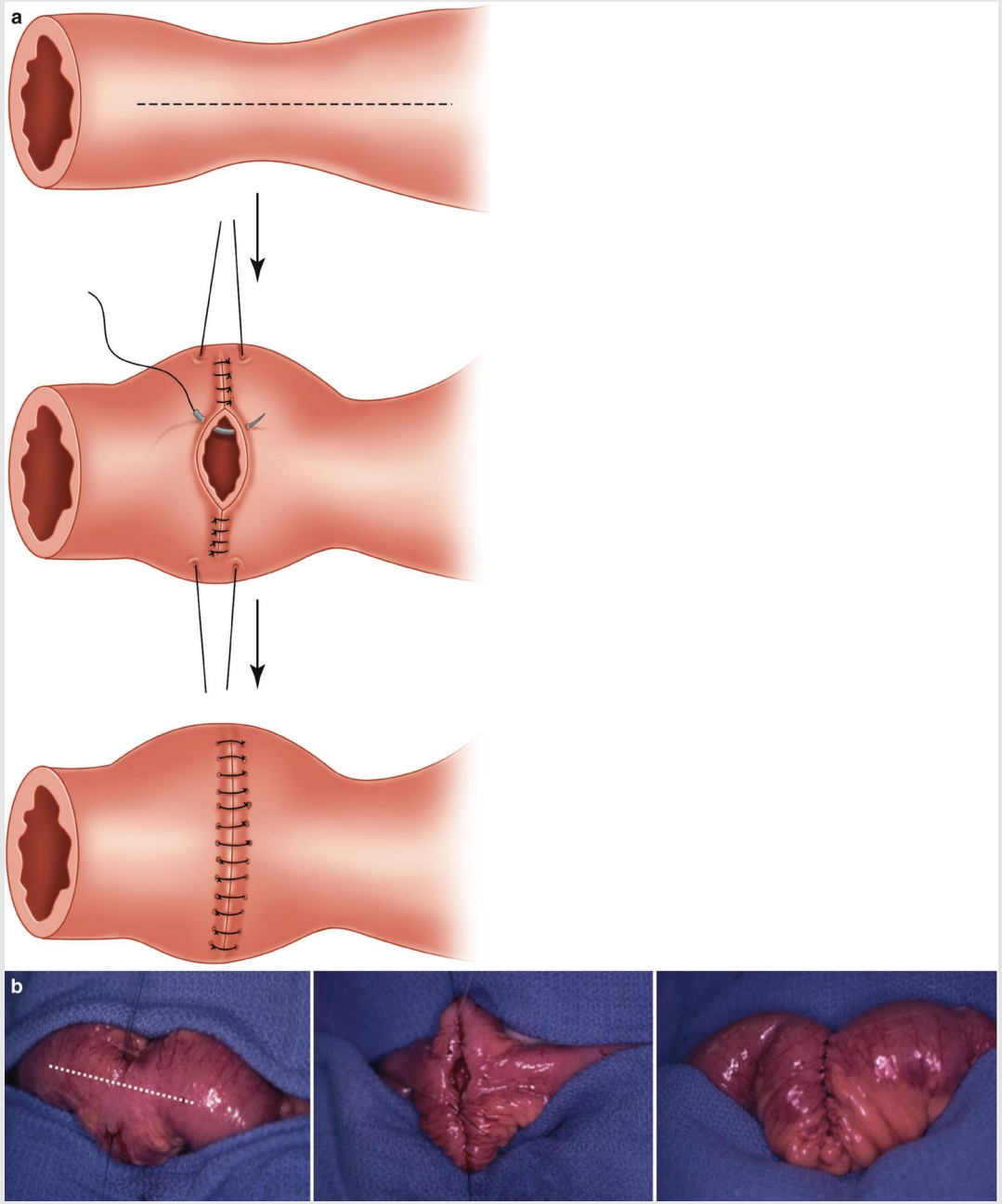
- Overall recurrence
- Recurrence free survival
- Surgical recurrence

But with

- Higher morbidity*

And

- No difference in medical recurrence



Focus on Challenging or Controversial Topics

Perianal Crohn Disease

20% of patients with CD will present with some anal or perineal involvement

Risk increases with time

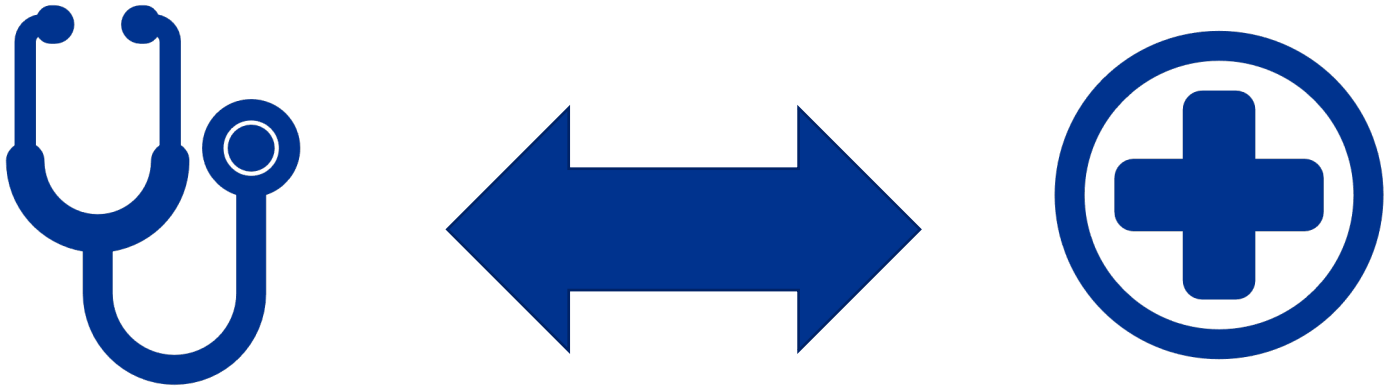
Anus or perineum eventually involved in 60 to 80% of patients

Fissure
Skin tag or hemorrhoid
Cavitating ulcer
Fistula
Abscess
Anorectal stricture
Carcinoma

Exam under anesthesia

Stages of Therapy

- **Control of the Acute Disease**
  - Drainage of abscess
  - Placement of non-cutting seton
- **Stabilization**
  - Antibiotics
  - Immunomodulators
- **Operative Management**
  - Risk of incontinence
  - Risk of recurrence



Medical

Surgical

CURE

CONTINENCE

Surgical Options

Drain Abscess

Seton
- Short term
- Long term

Fistulotomy

LIFT

Modified LIFT

Rectal advancement flap

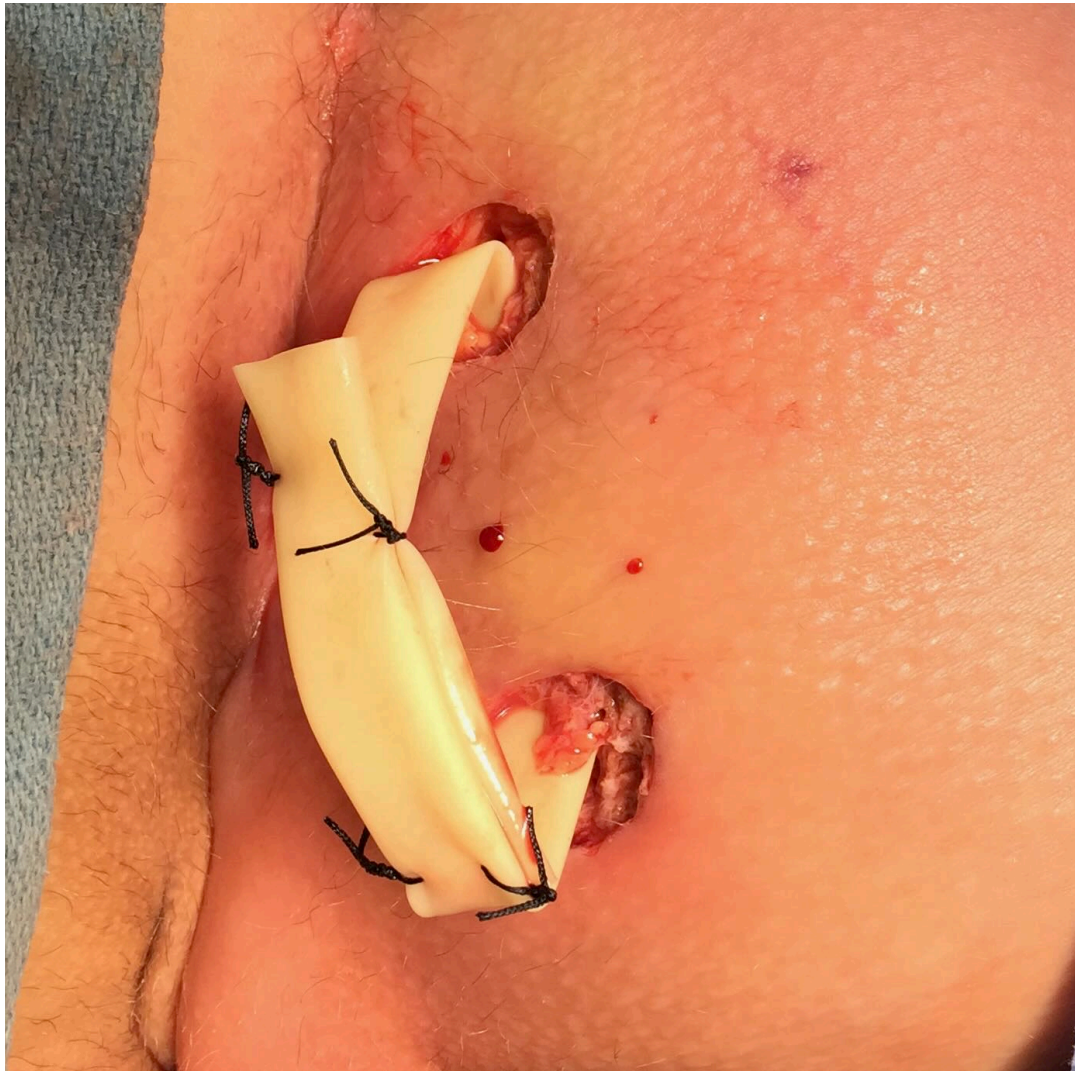
Dermal advancement flap

Stem cell injection

Stoma/APR

RVF
- Martius flap
- Gracilis muscle flap

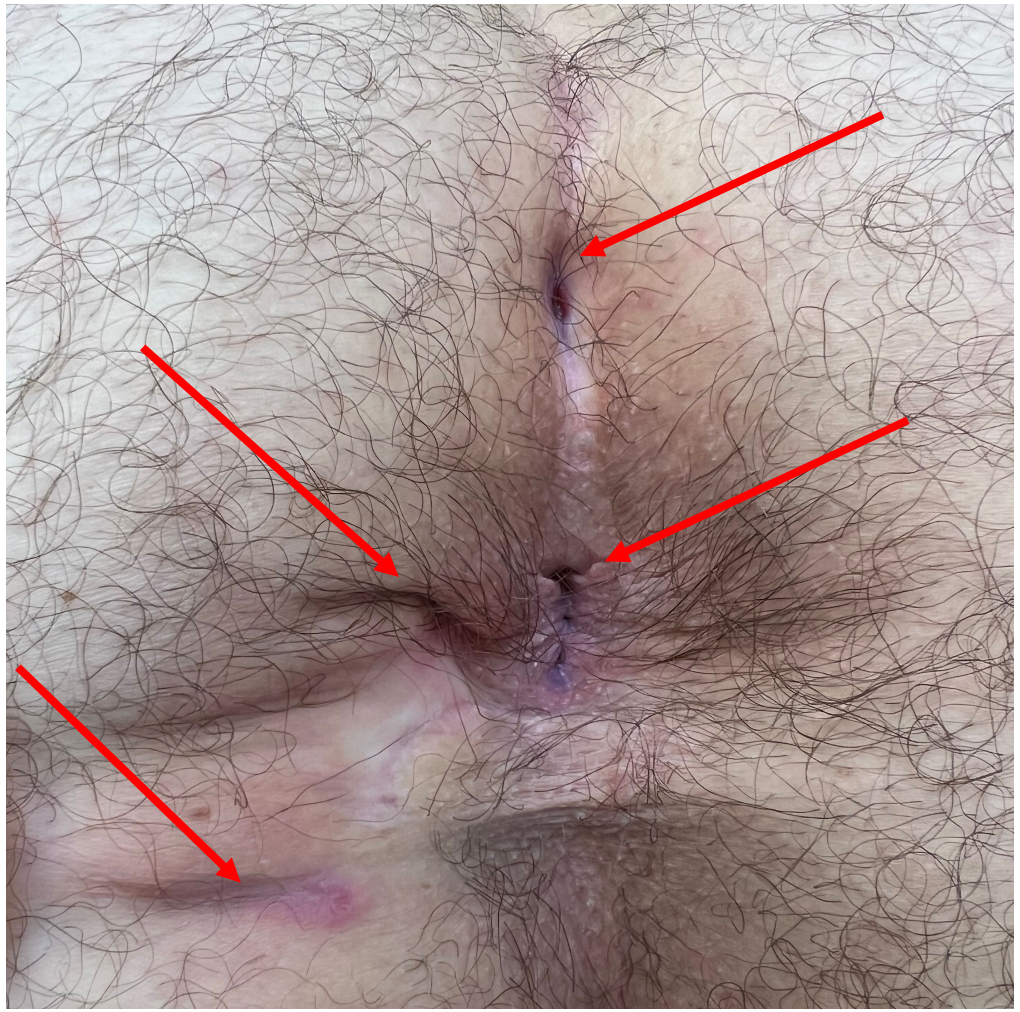
Drain Abscess



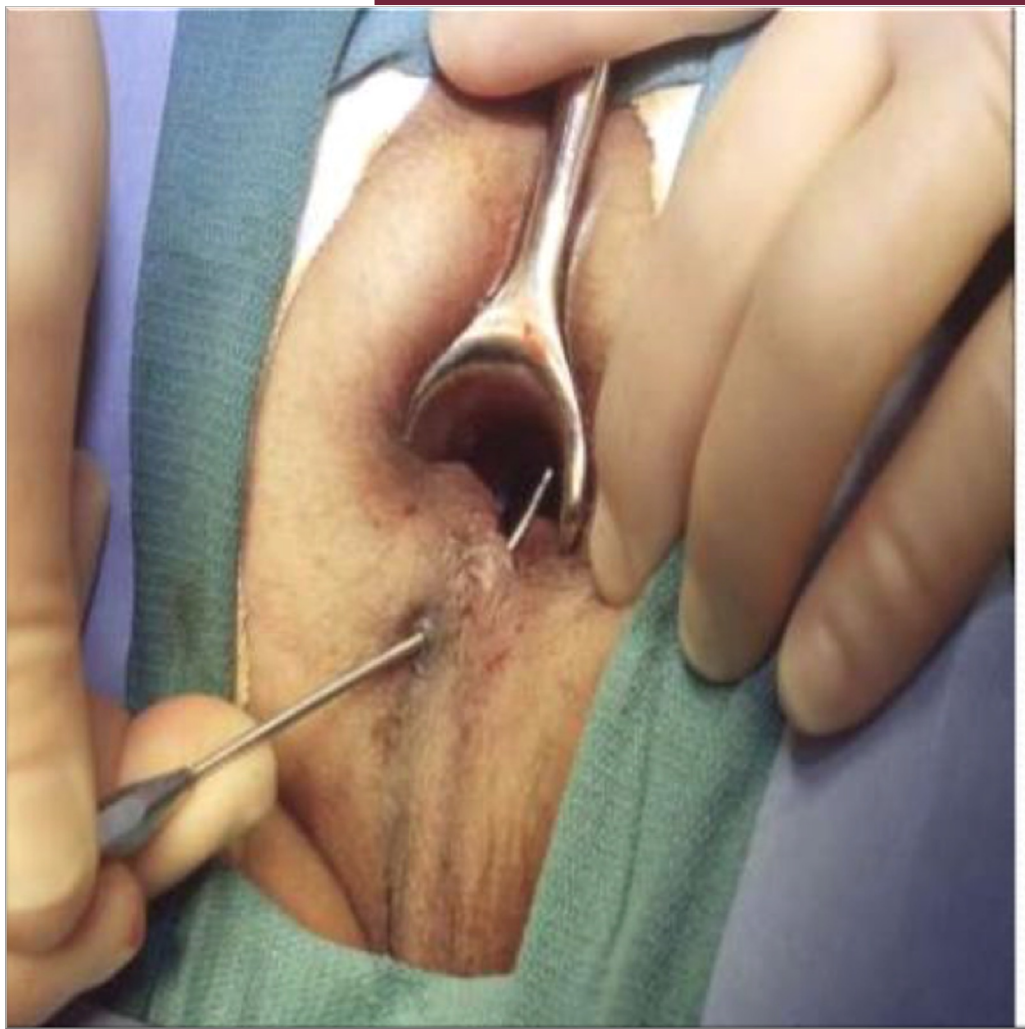
Seton

- Short term
- Long term

Chronic Fistulas, Recurring Abscesses

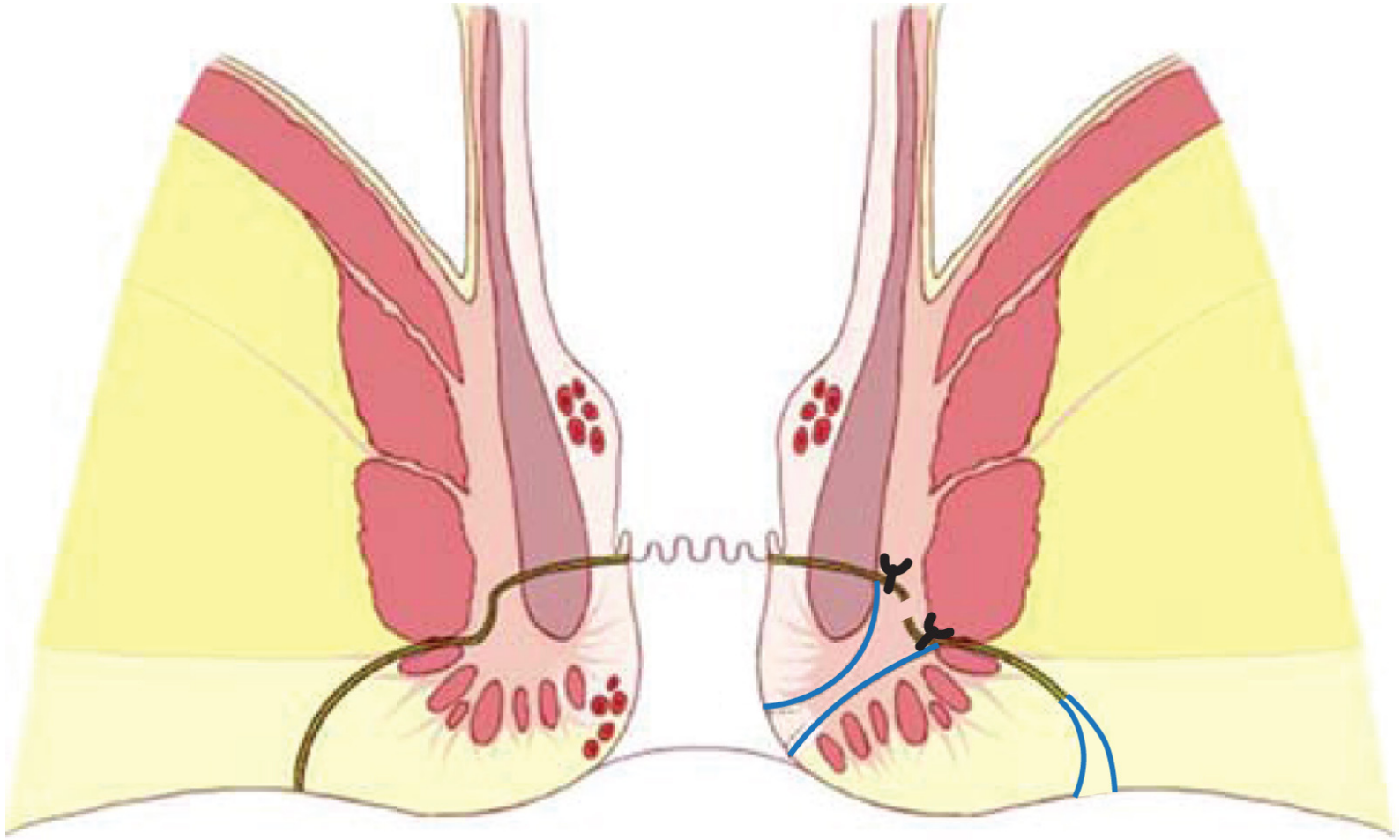


Fistulotomy



LIFT

Ligation Intersphincteric Fistula Tract (LIFT)



LIFT Procedure
(Ligation of the Intersphincteric Fistula Tract)

Disrupt the fistula (cure)

Don’t divide sphincter complex (continence)

Initial Results

- **Success >90%**

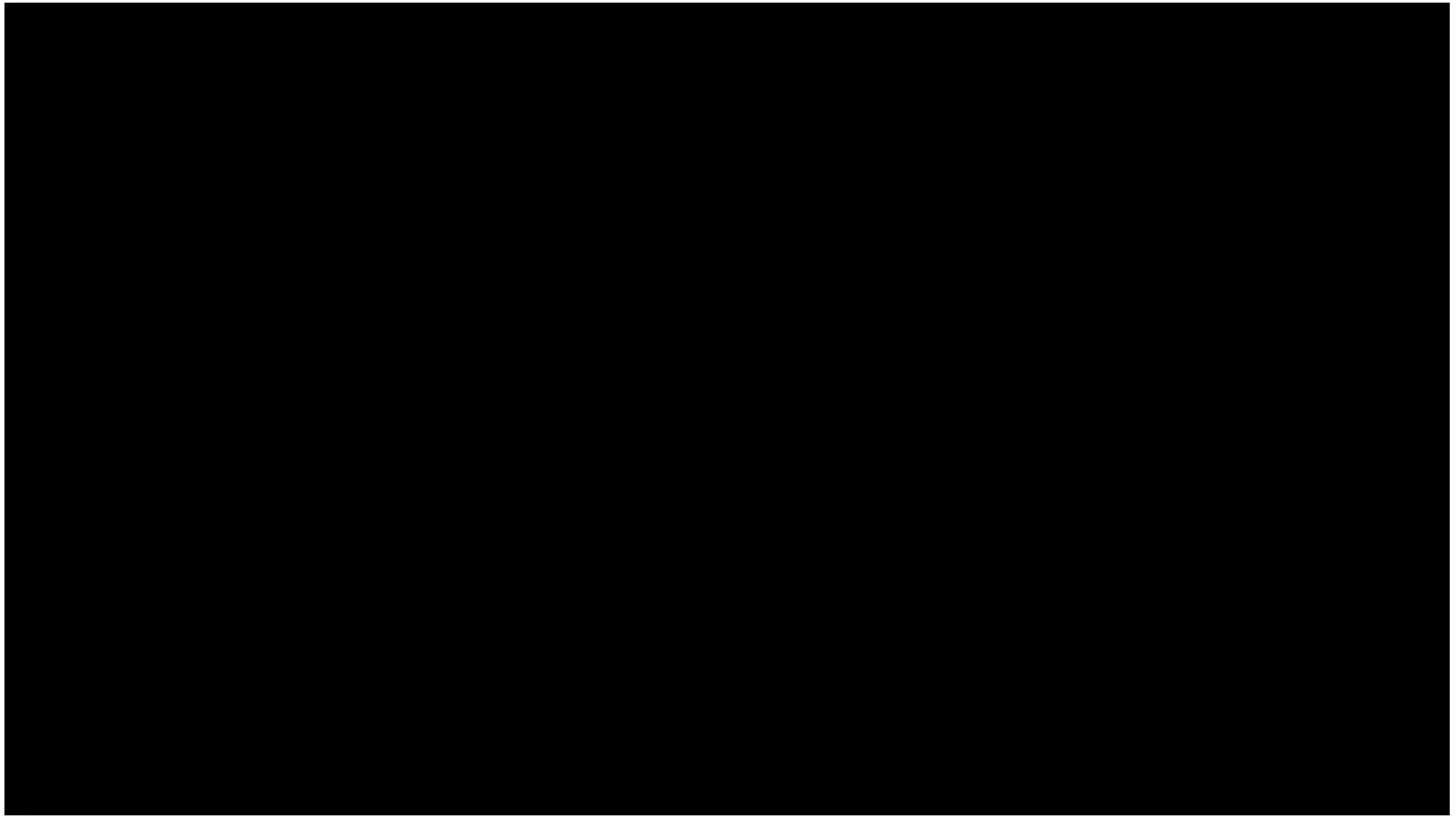
Long-term results

- **Success ~45%**

Challenging when:

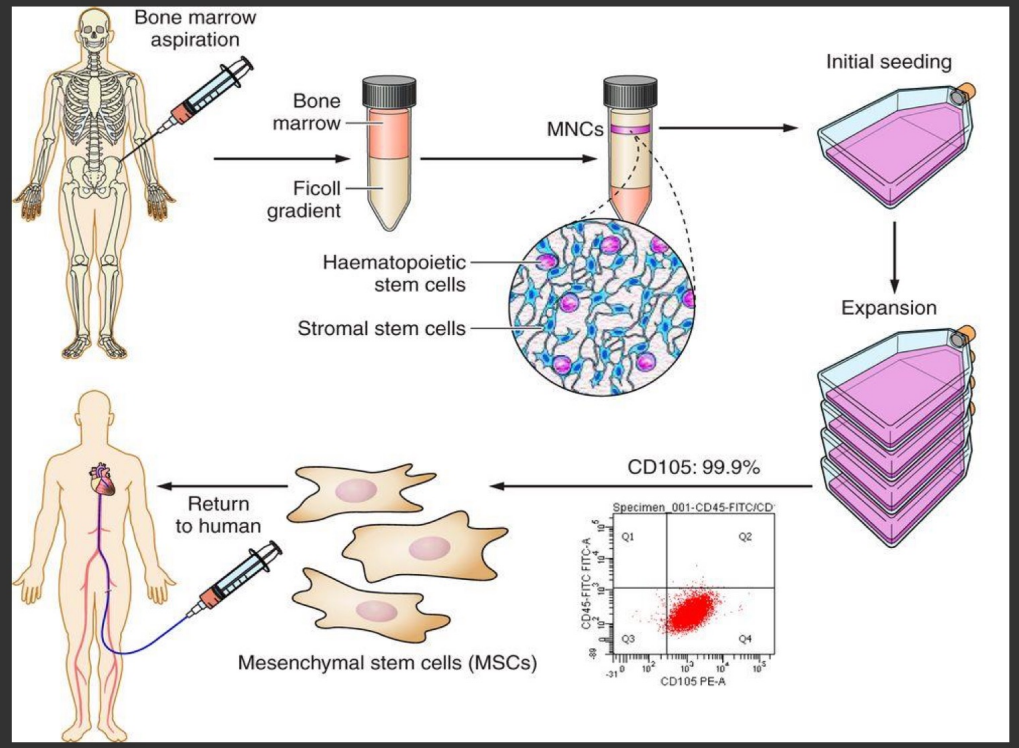
- **Multiple**
- **Deep**
- **Suprasphincteric/Extrasphincteric**
- **Bifurcated**
- **Abscess**
- **Recurrent**

LIFT

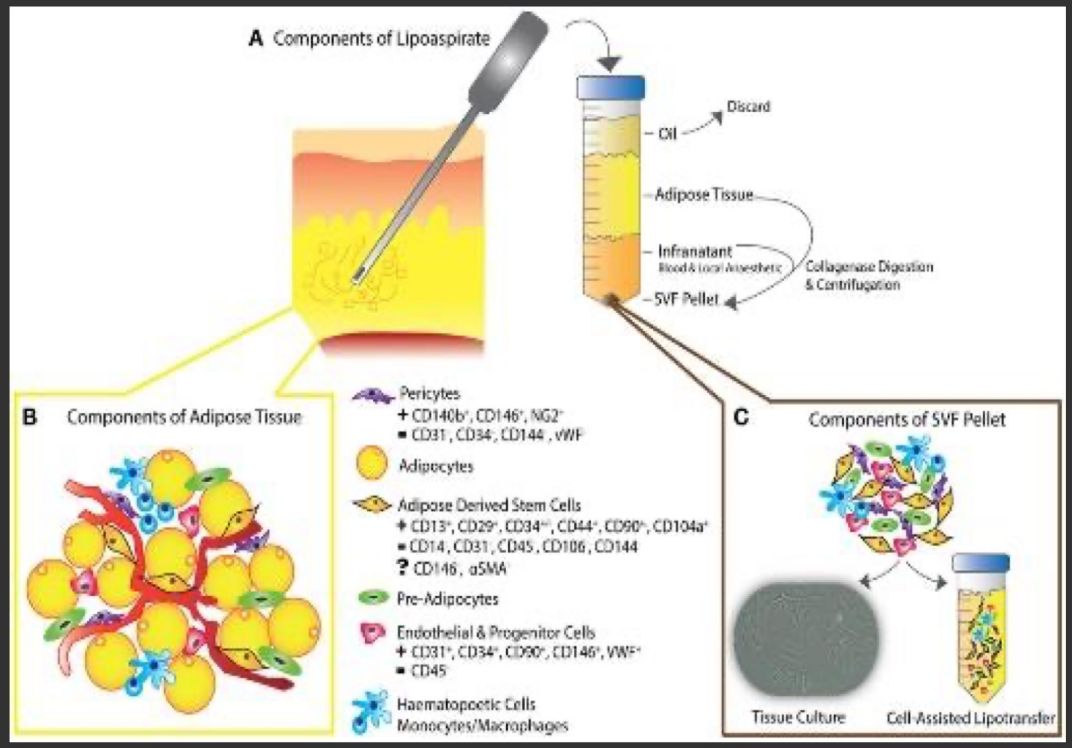


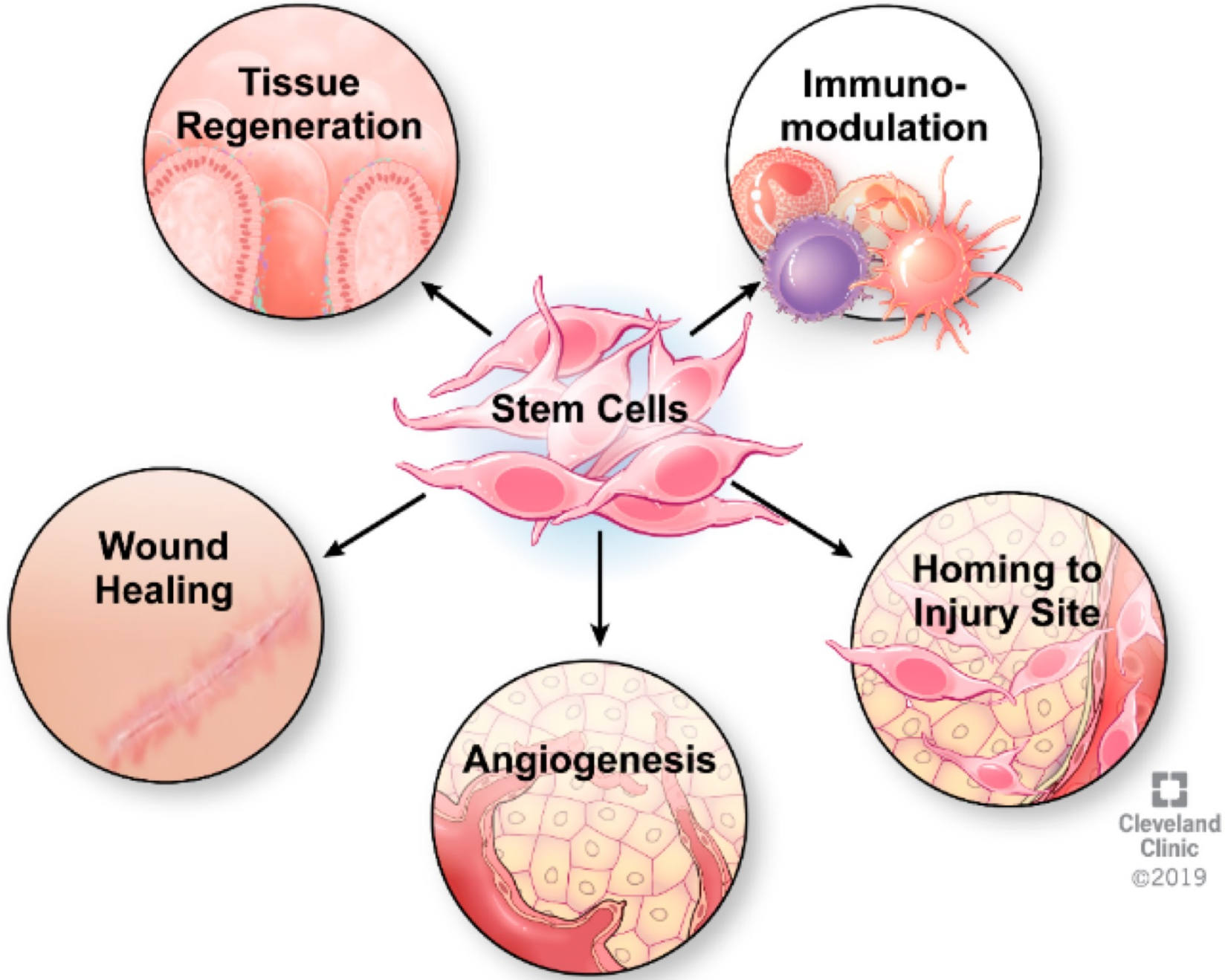
Stem cell injection

Bone marrow (mesenchymal)



Adipose tissue (Fat)




Tissue Regeneration
Immuno-modulation
Stem Cells
Wound Healing
Homing to Injury Site
Angiogenesis
Cleveland Clinic
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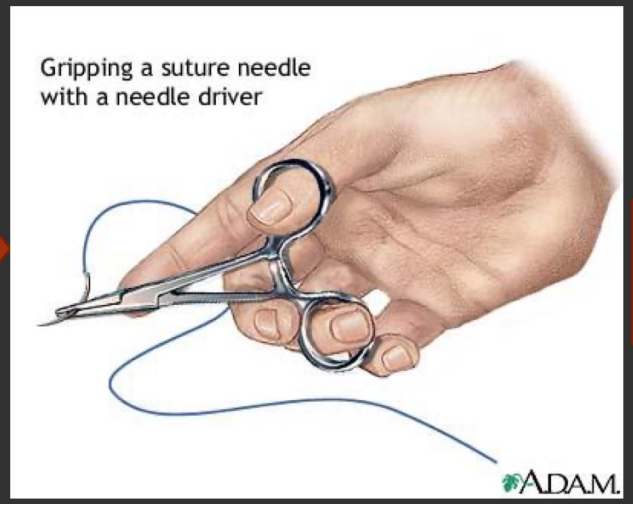
Curette and clean

Closure of Internal opening



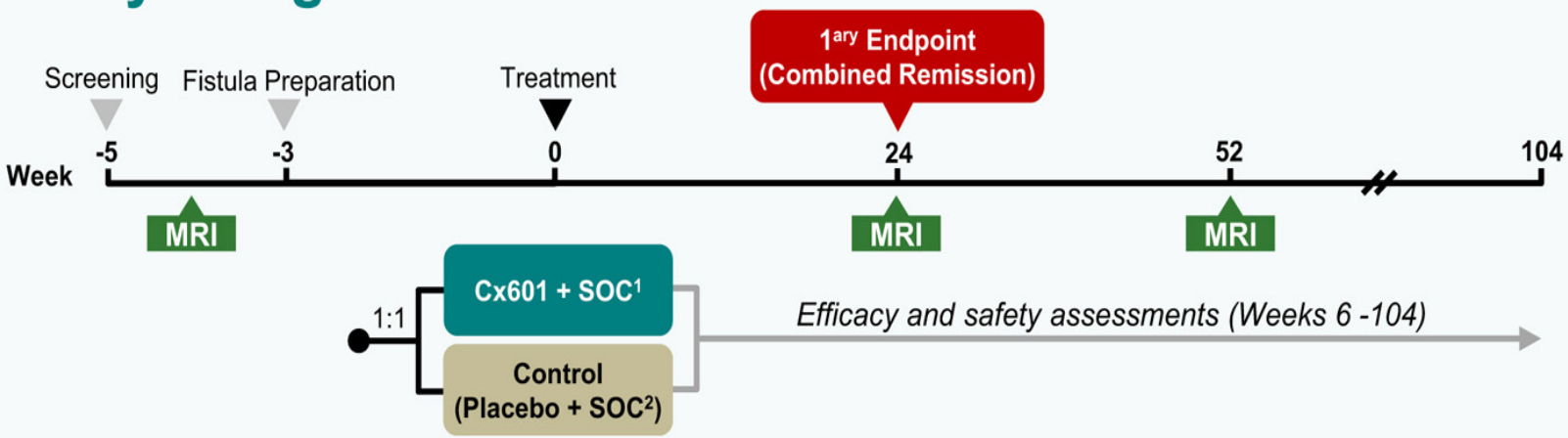
Injection of stem cells

ADMIRE CD Study: Cx601 for Complex Perianal Fistulas in Crohn's disease

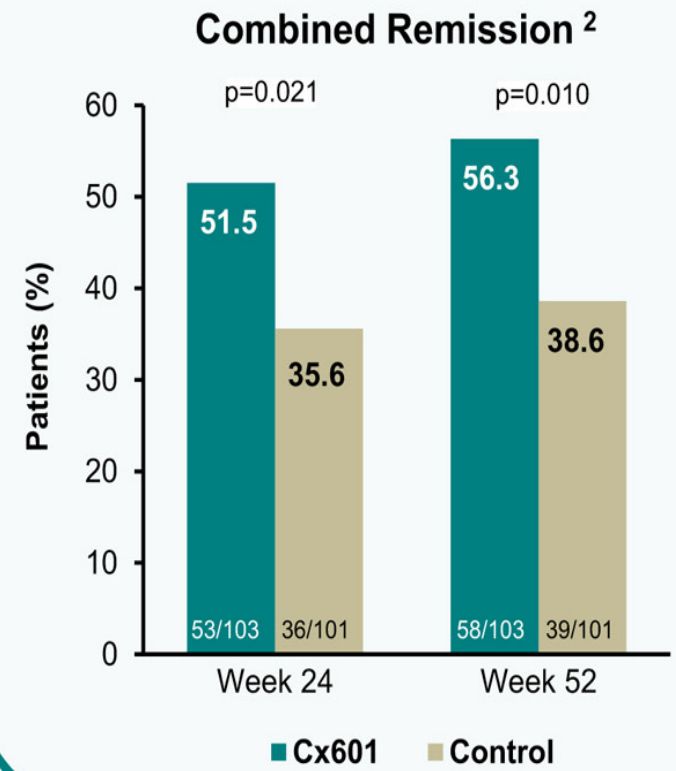
Treatment

Cx601 is a suspension of allogeneic expanded adipose-derived stem cells (eASC) injected locally, and has been shown to be efficacious and well tolerated in Crohn's disease patients with treatment-refractory complex perianal fistulas

Study design



Efficacy



1. Standard of care; 2. mITT population (modified intention to treat)

Gastroenterology

Efficacy of stem cells therapy for Crohn's fistula: a meta-analysis and systematic review

Yantian Cao[1], Qi Su[2], Bangjie Zhang[1], Fangfang Shen[3] and Shaoshan Li[2*]

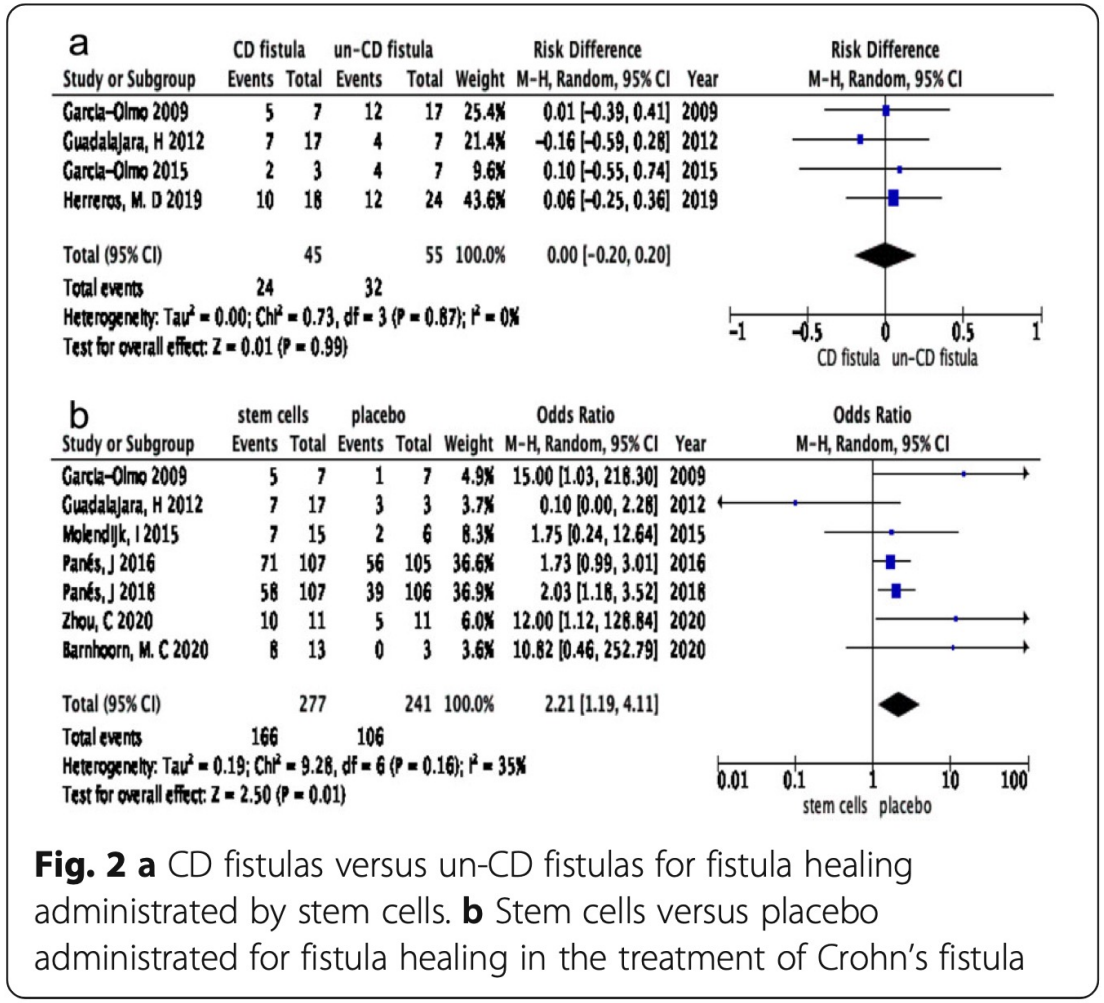
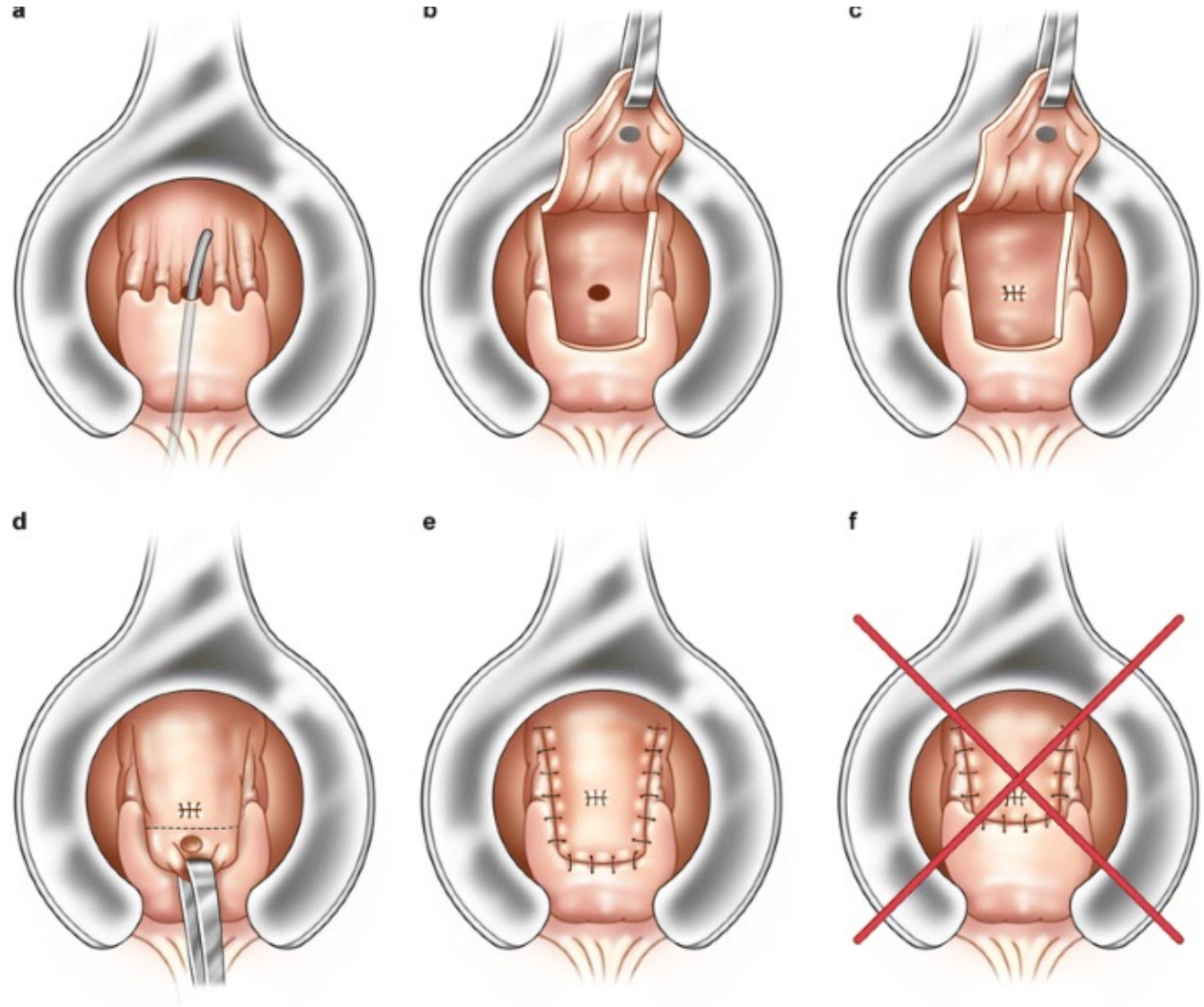


Fig. 2 a CD fistulas versus un-CD fistulas for fistula healing administrated by stem cells. **b** Stem cells versus placebo administrated for fistula healing in the treatment of Crohn's fistula

Rectal advancement flap



Stoma/APR

- If all else fails
- Often still anal leakage due to mucus
- Avoids a perineal stoma
- Not without its own problems

Summary: Surgical Treatment of Anal Crohn's Fistula

Complex Problem

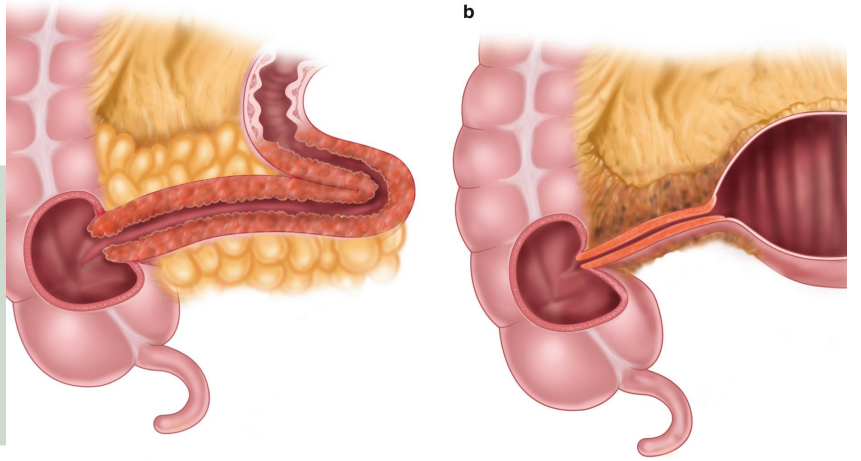
Coordinated care between GI and Surgery

Treat symptoms

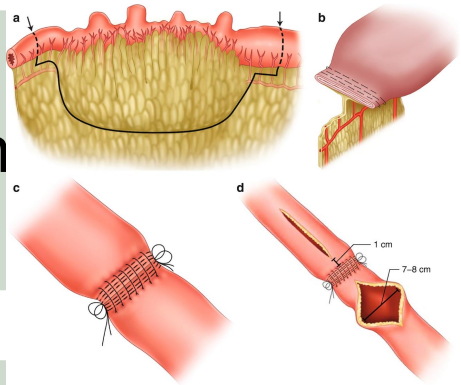
Preserve anal function, eye to future problems

Future controversial discussions

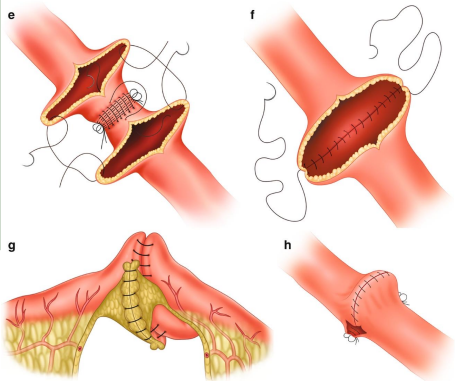
Primary surgery for terminal ileal CD



Kono-S or other configuration for ileocolic reconstruction



Mesenteric excision in CD recurrence



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September 2023

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