3rd IBDHORIZONS UPDATES FOR APP

IBDH

King Street Ballroom, October 29, 202

PREPPING PATIENTS WITH IBD FOR SURGERY

IBDH

ARS QUESTION 1

All of the following increase the risk of post-operative complications in Crohn's Disease **EXCEPT**:

A. High dose steroids
B. Tobacco smoking
C. Malnutrition
D. Infliximab

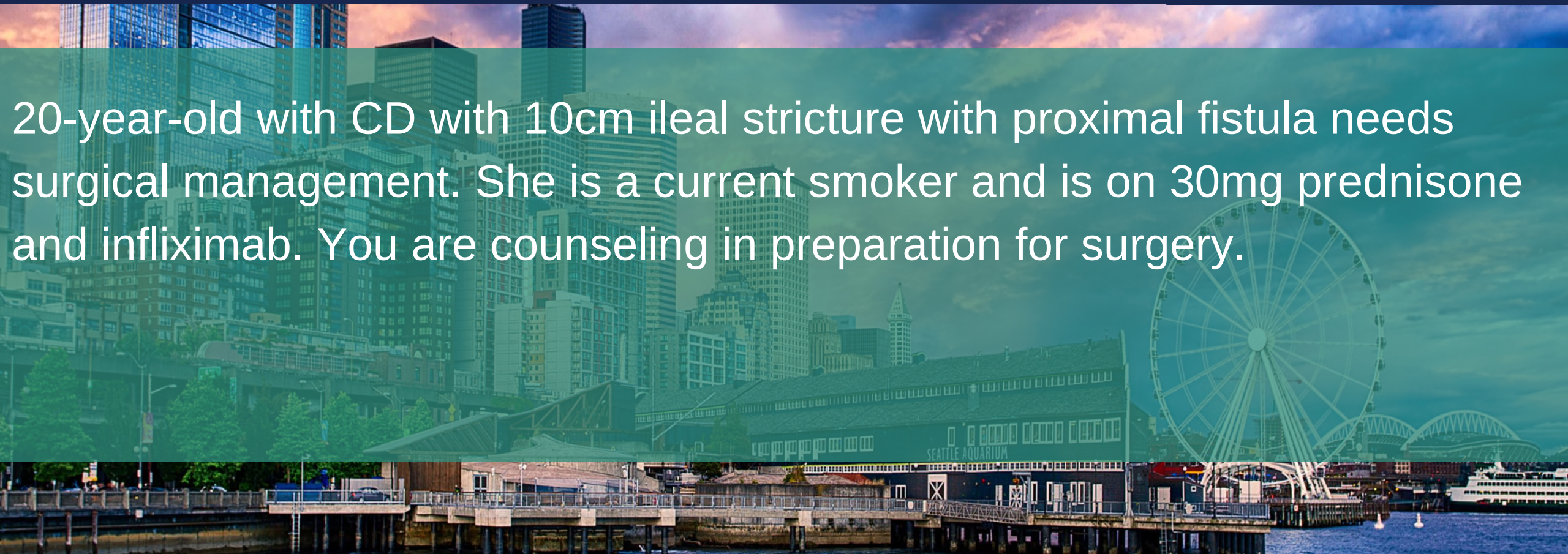
ARS QUESTION 2

Which of the following is **NOT** a high-risk factor for post operative disease recurrence in Crohn's disease:

A. Current tobacco smoking
B. Multiple prior resections
C. Cannabis use
D. Residual disease left in situ

CLINICAL CASE 6

IBDH



20-year-old with CD with 10cm ileal stricture with proximal fistula needs surgical management. She is a current smoker and is on 30mg prednisone and infliximab. You are counseling in preparation for surgery.

Prepping Patients with IBD for Surgery

Mitra Barahimi, MD

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IBDHORIZONS

DISCLOSURES

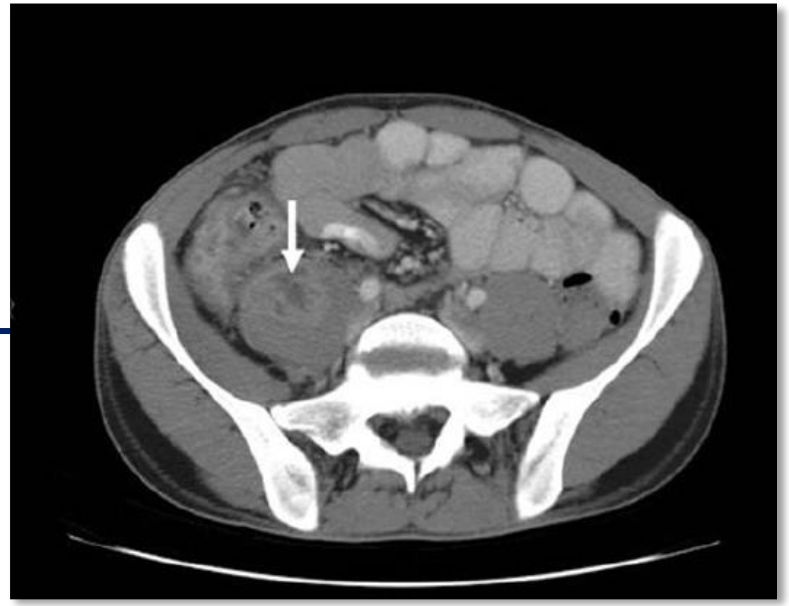
Consultant

- BMS, Janssen

Outline

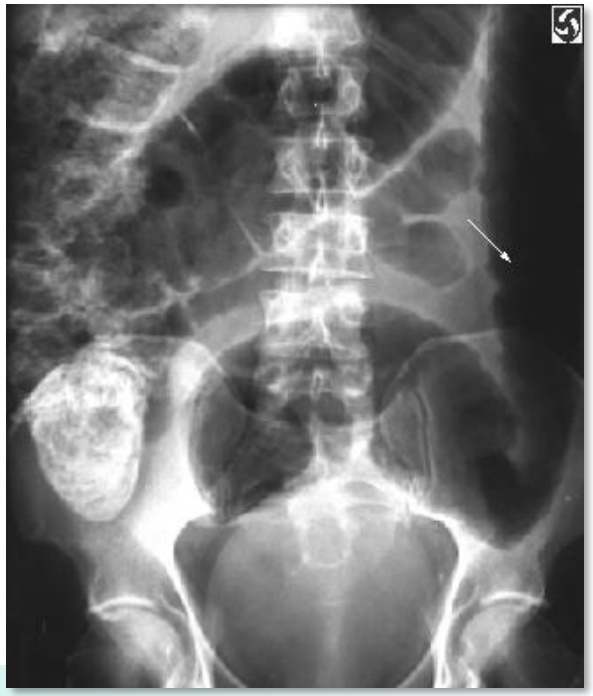
- When to refer to surgery
- Pre-operative Management
  - What to do with medical therapy before/after surgery (Crohn's disease)
- Post-operative Management
  - Disease management after surgery include medical therapy, endoscopic evaluation, labs
  - Risk Factors for post-operative recurrence
- Summary

Indications for surgery



Crohn's Disease

- **Bowel obstruction**
  - SBO or LBO
- **Abdominal Abscess**
  - Usually due to fistula
- **Perianal fistulizing disease**
  - Abscess, routine management in combination with medical therapy, complex refractory disease
- **Bowel perforation**
  - Penetrating disease, high grade obstruction, fistula w/abscess



Ulcerative Colitis

- **Fulminant colitis -> Toxic Megacolon**
  - Total colectomy followed later by IPAA (J pouch)
  - If concern for Crohn's disease, usually end ileostomy or ileorectal anastomosis after colectomy
- **Medically refractory disease**

Both UC and Crohn's disease

- Malignancy/high grade dysplasia

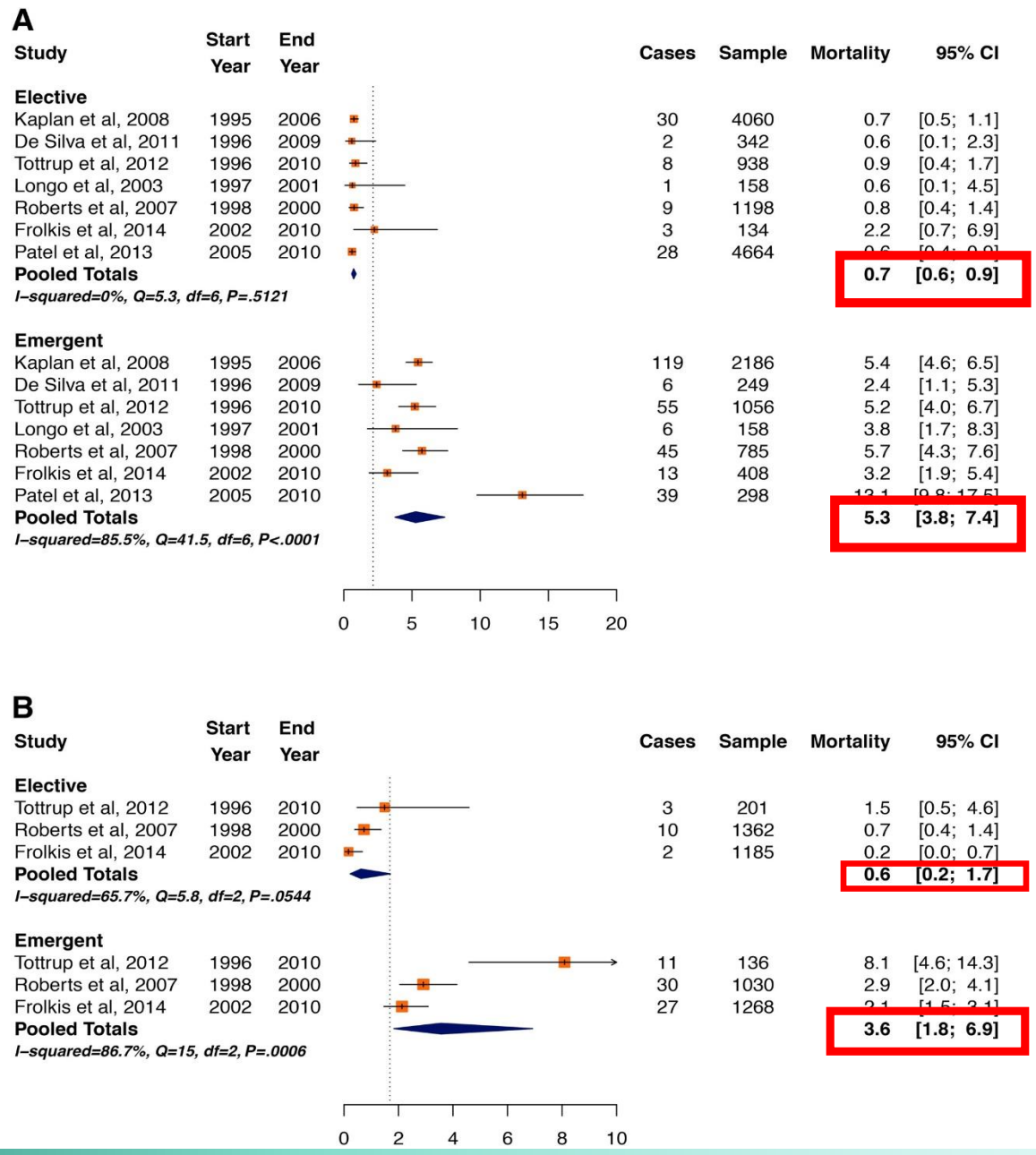
IBDHorizons

Emergent Surgery for Crohn's Disease Associated with Increased Mortality

- Many factors associated with increased mortality post intestinal resection, including age, comorbidities, and experience of the surgery center

- Singh et al. conducted meta-analysis of population-based studies
  - 75,971 patients who underwent intestinal resection for IBD related complications
  - Adjusted for time trends in surgical mortality

Kaplan et al. Gastroenterology 2008 Singh S et al., Gastroenterology 2015



Pooled results of meta-analysis for elective vs emergent surgery for:
A: Ulcerative Colitis
B: Crohn's disease

CD elective surgery mortality 0.6%

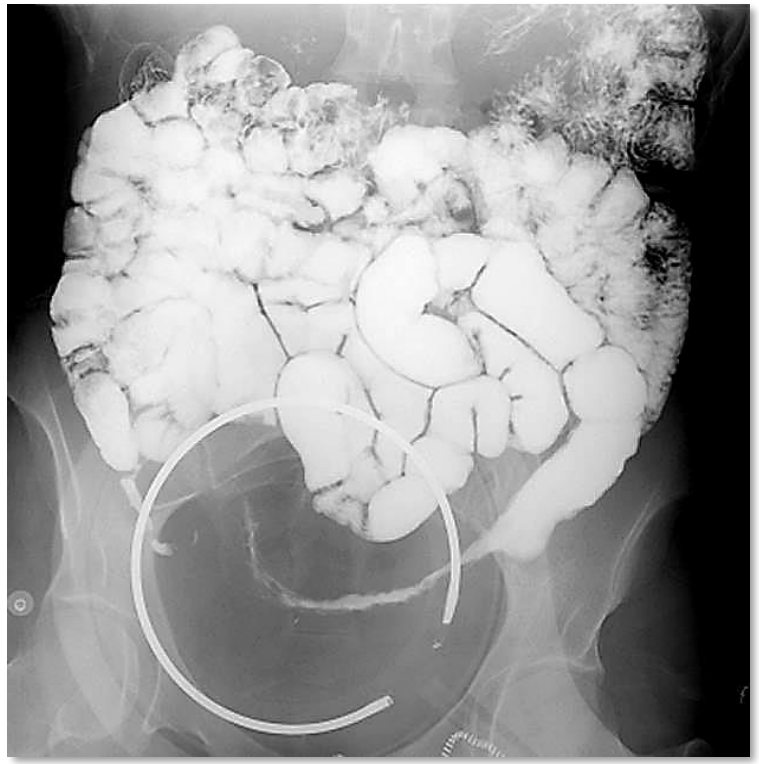
CD emergent surgery mortality 3.6%

Singh S, Gastroenterology 2015

Small Bowel Obstruction in Crohn's Disease

Most common indication for surgery in Crohn's

- ~ 30-54% with small bowel disease will develop obstruction
- Usually presents as recurrent partial SBOs



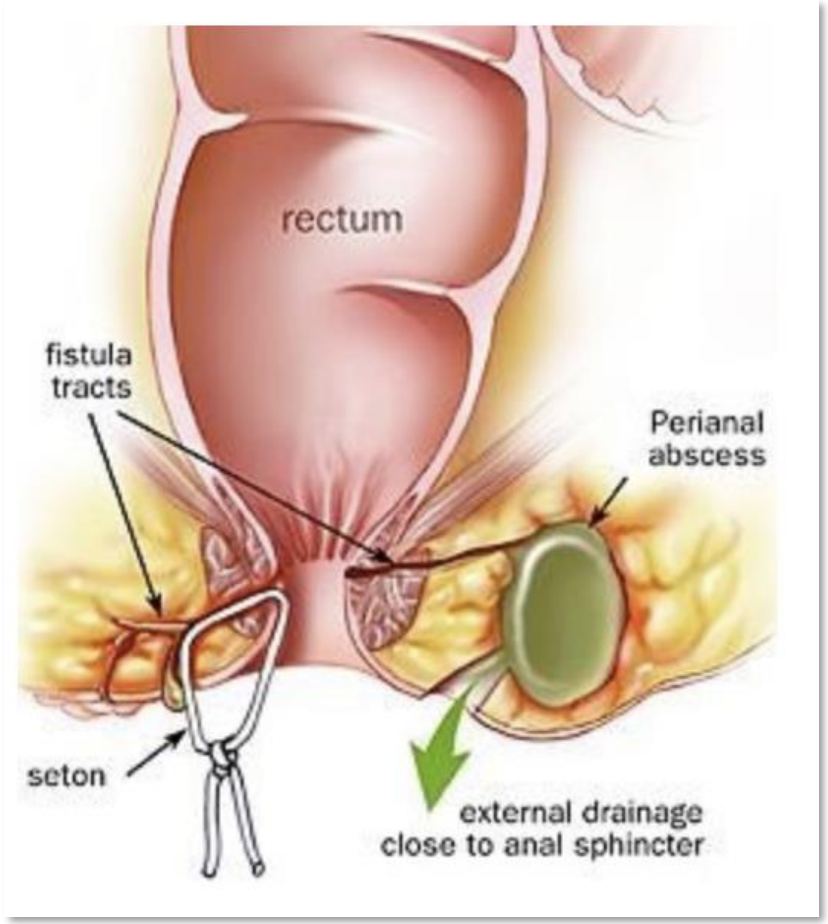
Differential diagnosis:

- Inflammatory stenosis
  - May be able to avoid surgery with a change in medical therapy
- Fibrostenotic Disease (stricture)
  - No medical therapy reverses fibrosis (not yet)
  - BUT often there is some acute inflammatory component
  - **Medical/nutritional optimization improves surgical outcomes**
- Adhesions
  - Discrete transition point, often in mid-small bowel
  - Patients with prior abdominal surgery

Perianal fistulizing Disease

- **EUA and drainage** – first line for treatment of acute abscess to control local sepsis prior to initiating medical therapy

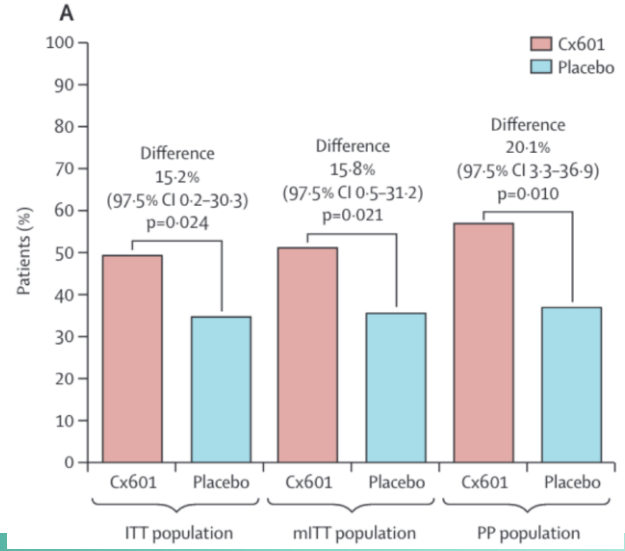
- **Definitive Surgical Options/"Curative" Procedures:**
  - **Advancement Flaps** – excise internal opening of fistula and using adjacent tissue flap to cover it
    - Can result in incontinence if involve the internal sphincter
  - **LIFT procedure -** involves ligation and excision of the fistula tract in the intersphincteric space
  - **In-fill materials – Fibrin glue, fistula plug**
    - **Fibrin glue** – seals the tract by activating thrombin to form fibrin clot - no impact on sphincter but very variable rates of success – limited studies with small number of patients, varying techniques
    - **Fistula plugs** – bioprosthetic device thought to promote wound healing. Also, variable healing rates owing to same issues as glue – no robust methodology, small numbers of patient's studies.
    - HOWEVER, in fill materials may serve as a scaffold for delivering stem cell therapy in the future (currently available in Europe)
  - **Fecal Diversion with or without proctectomy**
    - Healing rates variable and high rates of recurrence after ostomy takedown



Johnson et al. Inflammatory Bowel Disease, 2021. Adegbola et al. Annals of Gastroenterology, 2018.

Stem Cell Therapy for Complex Perianal Fistulizing Crohn's Disease

- Phase 3 study - Placebo controlled RCT
- Allogeneic Stem Cells for Complex Perianal Fistula in CD: Remission at Week 24
  - 50% of patients treated with an injection of Cx601 alone or added on to current medical treatment achieved combined remission (clinical + MRI) at week 24 compared with 34% of those who received placebo.



Panes J. et al. The Lancet. 2016.

Inflammatory Bowel Diseases, XXXX, **XX**, 1–4
https://doi.org/10.1093/ibd/izab276
Advance access publication 13 November 2021
Brief Report - Clinical

CROHN'S & COLITIS FOUNDATION

Treatment of Fistulizing Perianal Crohn's Disease by Autologous Microfat Enriched With Adipose-Derived Regenerative Cells

Karam Matlub Sørensen, MBChB,[*,†,] Charlotte Harken Jensen, PhD,[†,‡] Søren Paludan Sheikh, PhD,[†,‡] Niels Qvist, MD,[*,†] and Jens Ahm Sørensen, PhD[†,§]

From the [*]Research Unit for Surgery and IBD Care, Odense University Hospital, Odense, Denmark
[†]Clinical Institute, University of Southern Denmark, Odense, Denmark
[‡]Laboratory of Molecular and Cellular Cardiology, Department of Clinical Biochemistry and Pharmacology, Odense University Hospital, Odense, Denmark
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75% clinical healing and 67% radiological healing of the fistula at 6-month follow-up and no clinical sign of recurrence at 1-year follow-up!

Sørensen et al. Inflammatory Bowel Disease. 2021.

IBDHorizons

Pre-operative Management prior to Intestinal Resection Crohn's Disease:

- **If patient is on advanced therapy, should this be held before surgery?**
  - Puccini trial (2022) showed the pre-operative TNF antagonist therapy (within 12 weeks of surgery) did not increase risk of infection 30 days after intra-abdominal surgery (mostly Crohn's patients but UC included)
  - Similar smaller trials show that ustekinumab and vedoluzimab do not increase risk of post-op complications
  - Surgeon's preference matters
- **Should medical therapy be started ahead of surgery?**
  - If treatable active disease and surgery is not urgent then yes!
- **What about steroids ?** – can impair wound healing and impair HPA axis so taper if you can. If patient is steroid dependent, then surgery may temporarily divert to allow anastomosis to heal
- **Smoking** – increases the risk of post-op Crohn's recurrence and post operative complications (wound healing, infection etc)
- **Nutrition:**
  - Poor preoperative nutrition increases postoperative morbidity rates and intra-abdominal septic complications.
  - Postoperative complications following anastomotic leaks may be devastating. There are numerous studies evaluating anastomotic leaks and hypo-albuminemia, with anastomotic dehiscence consistently associated with a serum albumin levels below 3.5 g/dL in elective colorectal resections

Cohen et al. Gastroenterology, 2022.

Post-operative Disease Management- Medical Therapy:

- If on no medical before surgery who should start after surgically induced remission of CD?
  - Active disease seen intra-operatively and not resected
  - Surgical pathology shows active inflammation with involved margins
  - Risk Factors for post-op Recurrence in the absence of intervention:

Table 4. Illustrative Risk Groups for Recurrence of CD After Surgical Resection in the Absence of Any Intervention

Illustrative risk groups	Typical patient characteristics corresponding to risk category	Illustrative risk of clinical recurrence (>18 mo after surgery)	Illustrative risk of endoscopic recurrence (>18 mo after surgery)
Lower risk	Older patient (older than 50 y) Nonsmoker First surgery for a short segment of fibrostenotic disease (<10 to 20 cm) Disease duration >10 y	20%	30%
Higher risk	Younger patient (younger than 30 y) Smoker, ≥2 prior surgeries for penetrating disease, with or without perianal disease	50%	80%

Nguyen et al. Gastroenterology, 2017.

IBDHorizons

Post-operative Disease Management- Medical Therapy:

- If high risk for post op recurrence based on clinical factors, then treat
- If low or intermediate risk or patient declines treatment, then perform colonoscopy 6-12 months after surgery to assess neo-TI

Rutgeerts grade	Endoscopic finding	Risk of symptomatic recurrence at 5 years	Probability of absence of symptoms at 5 years
i0	No lesions in the distal ileum	6%	94%
i1	Not more than 5 anastomotic aphthous lesions in the distal ileum	6%	94%
i2	More than 5 aphthous lesions with normal mucosa between the lesions, or skip areas of larger lesions or ulcers up to 1 cm confined to ileocolonic anastomosis	27%	73%
i3	Diffuse aphthous ileitis with diffusely inflamed mucosa between the multiple aphthae	63%	37%
i4	Diffuse inflammation, with larger lesions: large ulcers and/or nodules/cobble and/or narrowing/stenosis	100%	0%

Rutgeerts et al. Gastroenterology, 1990.

IBDHorizons

Post-operative Disease Management What therapy is best?

- **TNF inhibitor most well studied and still preferred**
  - Data supports its superiority to non-biologics – (5-ASA, antibiotics, immunomodulator)
  - PREVENT trial teaches us that infliximab is more effect than placebo in reducing risk of endoscopic recurrence
- **Paucity of data with other biologic therapies including vedoluzimab, ustekinumab, and newer therapy risankizumab**
  - HOWEVER, should not be barrier to initiating treatment in TNF failures

2. In patients with surgically induced remission of CD, the AGA suggests using anti-TNF therapy and/or thiopurines over other agents. *Conditional recommendation, moderate quality of evidence.*
Comments: Patients at lower risk for disease recurrence or who place a higher value on avoiding the small risk of adverse events of thiopurines and/or anti-TNF treatment and a lower value on a modestly increased risk of disease recurrence may reasonably choose nitroimidazole antibiotics (for 3–12 months).

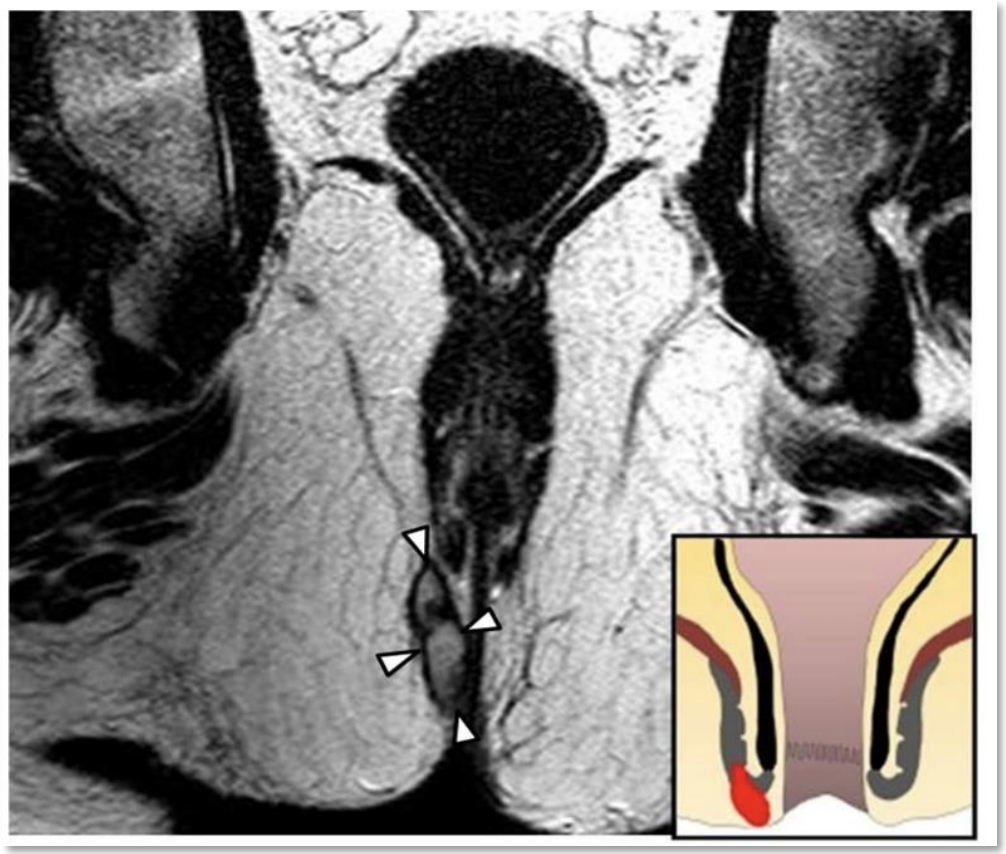
Nguyyen et al. Gastroenterology, 2017.

Regueiro et al. Gastroenterology, 2016.

Singh et al. Gastroenterology, 2015.

Post-operative Disease Management- What about labs and imaging?

- Labs – CBC, CMP, CRP - start with 6-8 weeks after surgery then every 3-4 months thereafter
- Routine MR enterography (MRI abdomen with oral and IV contrast) not necessary after ileocolonic resection but can be performed as needed in conjunction with colonoscopy (for ex. recurrent pSBO)
- MR pelvis helpful for re-evaluating perianal Crohn's disease after I&D with seton placement and initiation of medical therapy - if MR pelvis shows resolution of abscess and colonoscopy shows mucosal healing can refer for seton removal.



MR image of perianal abscess from Rev. Argent. Radiol. 2017.

Post-operative Disease Management After Colectomy

Ulcerative colitis - colectomy

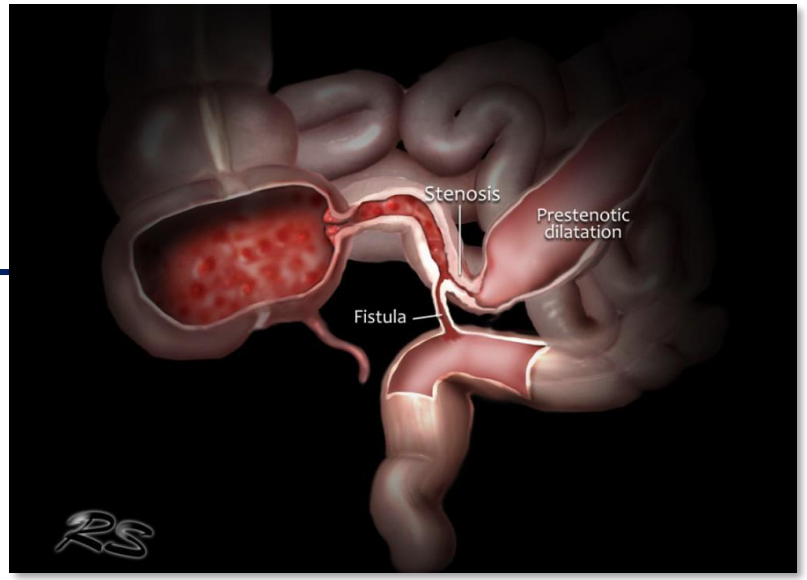
- After colectomy with Hartmann's, can discontinue therapy and discuss IPAA vs permanent end ileostomy
  - IPAA does reduce fertility in female patients so may want to wait until after childbearing or pursue egg retrieval
  - Make sure you're not missing Crohn's disease – EGD, capsule, colonoscopy and even IBD serologies

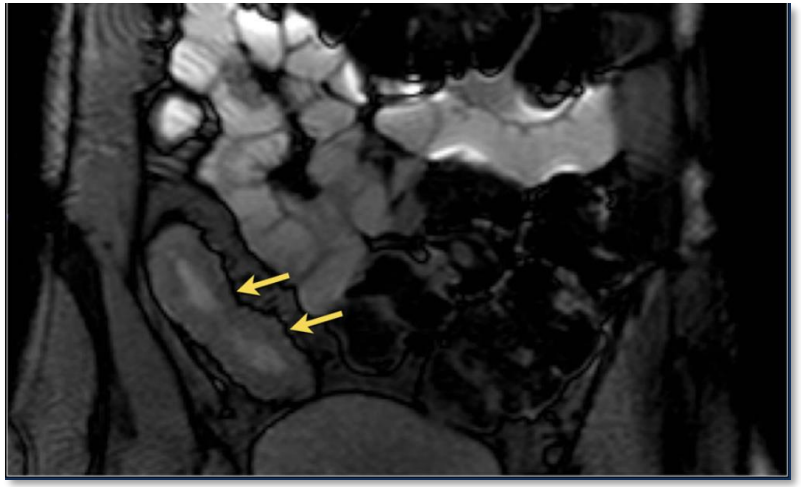
Crohn's – Colectomy

- Permanent end ileostomy vs ileorectal anastomosis if no h/o perianal and rectal disease involvement.
- IPAA contra-indicated given high rates of pouch complications/failure

Summary

- Most common indication for surgery in Crohn's disease is SBO – other indications include abscess, perianal disease
- Elective surgery in Crohn's disease associated with decreased mortality compared to emergent/urgent surgery!
- Surgery for UC indicated for toxic colitis, medically refractory disease, dysplasia/cancer
- Perianal Crohn's disease - current surgical options have low rates of efficacy and durability – stem cell therapy shows promise
- Prior to Crohn's surgical resection – important to start medical therapy if active disease, counsel on smoking cessation, optimize nutrition (TPN)
- After Crohn's surgery – start medical therapy if high risk of disease recurrence (young age, long disease duration, active smoker, 2 or more prior surgeries)
- If you don't start medical therapy after surgery, then 6-month post op colonoscopy and use Rutgeert's score to guide decision to start therapy





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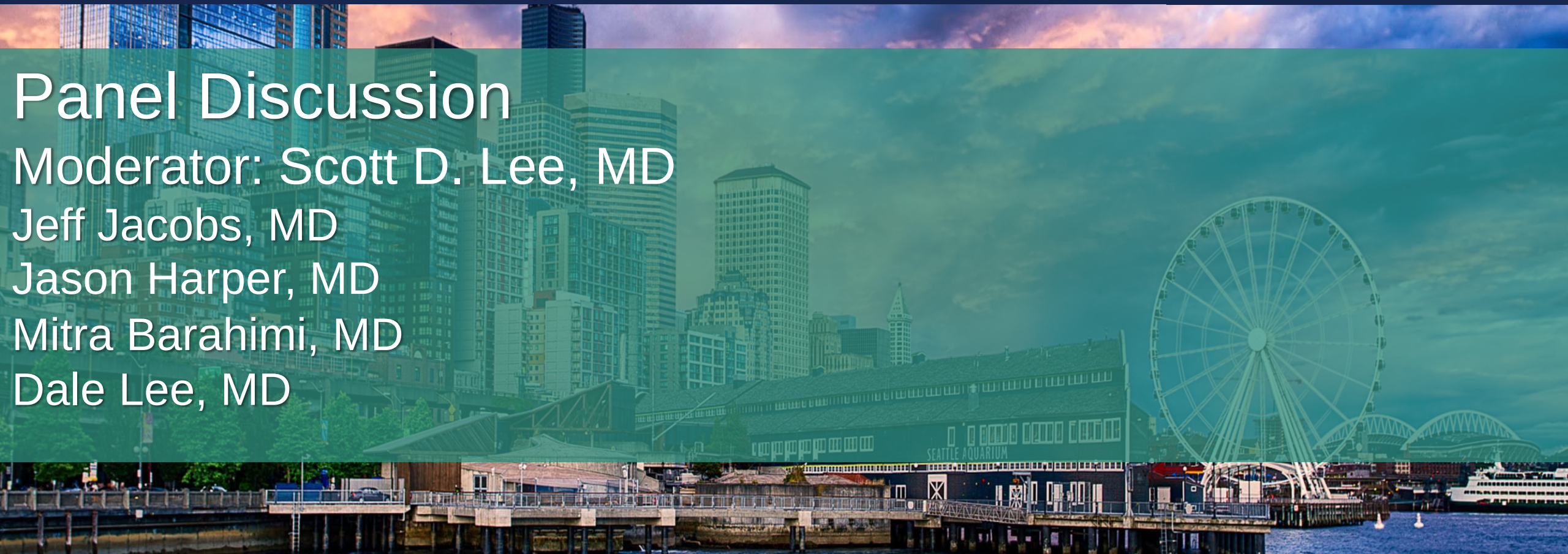
IBDHORIZONS

PANEL DISCUSSION

IBDH



Panel Discussion

Moderator: Scott D. Lee, MD

Jeff Jacobs, MD

Jason Harper, MD

Mitra Barahimi, MD

Dale Lee, MD

CLINICAL CASE 6

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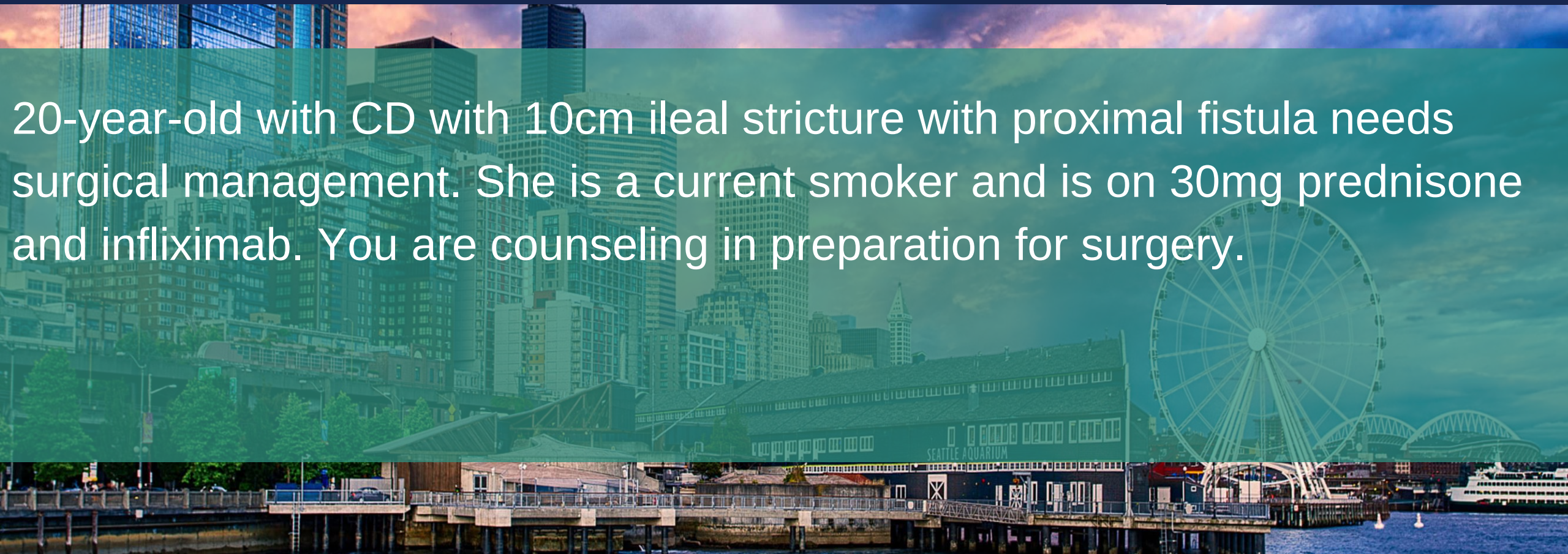

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