COLITIS

Suzana Buac, PGY3
Dr. Nawar Alkhamesi

October 14th, 2015.
Objectives

- Anatomy and embryology of colon
- Differential diagnosis and investigation of acute colitis
- Presentation, diagnosis and management of infectious colitis
- Presentation, diagnosis and management of ischemic colitis
- Review of some of the most recent seminal papers on topic
- Epidemiology and etiology of ulcerative colitis
- Pathology and histology of ulcerative colitis
- Clinical presentation, investigation and extra-intestinal manifestations of ulcerative colitis
- Medical management of ulcerative colitis (role of steroids, 5-ASA, immuno-modulators, biologics)
- Screening and risk of malignancy, management of dysplasia
- Elective indications for surgery in ulcerative colitis
- Emergent indications for surgery in ulcerative colitis
- Surgical options in ulcerative colitis
Embryology

- 3 weeks
  - Foregut
  - Midgut
  - Hindgut
  - Physiologic herniation
  - Return to the abdomen
  - Fixation
- Six weeks
  - Urogenital septum migrates caudally
  - Separates GI and GU tracts
Anatomy

- 150cm
- Terminal ileum → ileocecal valve → cecum
  - Appendix
    - 3 cm below ileocecal valve
    - Retrocecal (65%), pelvic (31%), subcecal (2.3%), preileal (1.0%), retroileal (0.4%)
- Ascending colon
- Hepatic flexure
- Transverse colon
- Splenic flexure
- Descending colon
- Sigmoid colon
- Rectum
Arteries

- SMA
  - Ileocolic
  - Right colic
  - Middle colic

- IMA
  - Left colic
  - Sigmoid branches
  - Superior rectal artery

- Redundancy/communication between the SMA and IMA territories
  - Marginal artery
  - Arc of Riolan
Arteries

- SMA
  - Ileocolic
  - Right colic
  - Middle colic
- IMA
  - Left colic
  - Sigmoid branches
  - Superior rectal artery
- Redundancy/communication between the SMA and IMA territories
  - Marginal artery
  - Arc of Riolan
Veins

- SMV
- IMV
- Mirrors arterial blood supply
Lymphatics

- mirrors arterial blood supply
- epicolic nodes
- paracolic nodes
- intermediate nodes
- primary nodes
- para-aortic nodal chain
- cisterna chyli
Nerves

- T6-T12 sympathetic nerves → preaortic ganglia → right and transverse colon
- Right vagus nerve → parasympathetic fibers along SMA → right and transverse colon
- L1-L3 sympathetic lumbar splanchnics → preaortic plexus → along branches of IMA → left colon, sigmoid, rectum
Differential diagnosis of colitis

- Infectious
  - Viral
  - Bacterial
  - Protozoan
  - Fungal
- Inflammatory
  - UC
  - Crohn’s disease
  - Microscopic
  - Indeterminate
- Ischemic
- Radiation
- Diversion
Ischemic colitis

- “Ischemic colitis” defined in 1963 and described as “reversible component to colonic ischemia”
- Most common form of injury to the gut
- Focal, non-occlusive, transient, usually resolves spontaneously
- Incidence 4.5-44 per 100,000 person-years
- Most between 6th and 9th decade of life
  - Slightly more common in men
- Precipitating cause found in <20%
- May be associated with aortic surgery, arteriosclerotic disease, conditions causing transient hypotension, oral contraceptives, cocaine, coagulopathies, CMV and E. coli O157:H7.
- Typically involves “watershed” area
Etiology

- Not usually associated with major vascular occlusion
- Typically segmental
- Two anatomically vulnerable areas of the colon
  - “Griffith’s point” at splenic flexure (SMA and IMA junction)
  - “Sudeck’s critical point” (IMA and middle rectal junction)
- Perfusion between these areas may be inadequate during hemodynamic insult
- Severity depends on duration of decreased blood flow, caliber of vessel, metabolic requirements of bowel, and associated conditions like distension, collateral circulation, colonic bacteria.
- Spectrum between transient ischemia, chronic ischemia, and gangrene
Clinical presentation

- Dependent on severity
- Mild crampy abdominal pain associated with tenesmus
- Hematochezia, Diarrhea
- Nausea, vomiting, distension
- In gangrenous ischemia – peritonitis on physical exam
- Investigations:
  - Leukocytosis on laboratory studies
  - Metabolic acidosis
  - Elevated lactate
Imaging studies

- Xrays are non-specific
  - May show ileus, distended colon
  - Thumb-printing – intestinal wall edema or submucosal hemorrhage
  - Free air – rare
- Barium enema is obsolete in acute setting
  - Risk of perforation
  - Useful for chronic strictures
- CT scan with IV contrast is useful
  - Visualize entire arterial supply
Endoscopy

- Direct visualization of colonic mucosa
- Can take bacterial cultures to rule out infection
- Can take biopsies
  - Mostly non-specific
- Hemorrhagic dusky mucosa
- Unable to distinguish between mucosal and transmural gangrene
Treatment
Surgical intervention

- Uncommon
- Subtotal or total colectomy +/- end ileostomy
- Revascularization procedures not indicated

Acute Indications:
- Perforation
- Fulminant colitis or megacolon
- Massive hemorrhage
- Persistent symptoms with pain, bleeding, diarrhea, recurrent sepsis, 2-3 weeks with no improvement

Chronic Indications:
- Stricture formation – obstruction, diagnostic uncertainty (?cancer)
Infectious colitis

- Colitis defined as >3 unformed stools/day with evidence of colonic inflammation
  - Fecal markers – leukocytes, lactoferrin (more sensitive than WBC) or calprotectin
    - Lactoferrin and calprotectin – constituents of PMN
    - Passage of small volumes with gross blood and mucus
    - Endoscopic evidence of mucosal inflammation
  - Assume infectious if:
    - Microorganism linked with mucosal inflammation or
    - Toxin identified epidemiologically (known outbreak) or
    - Microbiologically diagnosed
Etiology

- Nosocomial – C. difficile colitis
- International traveller
  - Shigella
  - Campylobacter
  - Salmonella
  - Enteroaggregative Escherichia coli
  - Enteroinvasive Escherichia coli
  - Aeromonas (tropical and semitropical)
  - Noncholera Vibrio (watery diarrhea/dysentery assoc. with shellfish/seafood)
  - Yersinia (watery diarrhea, fever, dysentery – appendicitis-like)
- Foodborne associated dysentery with hemolytic uremic syndrome
- STEC – Shiga toxin-producing Escherichia coli (EHEC)
C. Difficile

- Gram-positive, anaerobic, spore forming bacteria
- Produces enterotoxin
  - Toxin A
  - Toxin B
- Mucosal disruption
C. diff associated diarrhea (CDAD)

- Acute watery diarrhea, mild to severe colitis
- Suspect in hospitalized patients with recent antibiotics, immunocompromised, inflammatory bowel disease
- Stool for C. Diff Toxin
- CT
- Endoscopy for pseudomembranes (pathognomonic)
C. difficile common antigen (Glutamate Dehydrogenase): Positive by Enzyme Immunoassay.

C. difficile toxin: Negative by Enzyme Immunoassay.

C. difficile toxin gene: Detected by molecular method.

Molecular testing only detects the C. difficile toxin gene and will not detect active toxin production. This result must be interpreted in the context of the clinical history, signs and symptoms of the patient. A repeat test will not be performed within 14 days of a positive result.

Gene testing 98% specific
C. difficile common antigen (Glutamate Dehydrogenase): Positive by Enzyme Immunoassay.

C. difficile toxin: Negative by Enzyme Immunoassay.

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This result must be interpreted in the context of the clinical history, signs and symptoms of the patient.

A repeat test will not be performed within 14 days of a positive result.
Pseudomembranes
Management

- Discontinue offending antibiotic
- Avoid/Discontinue PPIs


Administration of proton pump inhibitors in critically ill medical patients is associated with increased risk of developing Clostridium difficile-associated diarrhea.

Buendgens L¹, Bruensing J¹, Matthes M¹, Dückers H¹, Luedde T¹, Trautwein C¹, Tacke F², Koch A¹.
Management

First episode

1\textsuperscript{st} line
- Metronidazole 500mg PO TID x 10-14 days
- Metronidazole 250mg PO QID x 14 days
- Metronidazole 500 mg IV q8hr

2\textsuperscript{nd} line
- Vancomycin 125mg PO QID x 14 days

3\textsuperscript{rd} line
- Vancomycin 125mg PO/PR QID x 14 days
- Metronidazole 500mg IV q8hr

No role for f/u stool culture within 6 weeks of treatment completion
Management

First recurrence

1\textsuperscript{st} line
- Vancomycin 125mg PO QID x 14 days

2\textsuperscript{nd} line
- Metronidazole 250/500mg PO TID/QID x 14 days
Management
Subsequent recurrence

1\textsuperscript{st} line
• Tapering vancomycin

2\textsuperscript{nd} line
• Fidaxomicin 200mg po bid
• Rifamixin

3\textsuperscript{rd} line
• Fecal bacteriotherapy
• Probiotics
<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
<th>Medication</th>
<th>Dosage and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/Moderate Disease</td>
<td>Mild to moderate defined as: diarrhea plus leukocytosis with a White Blood Cell Count 15 or lower and a serum Creatinine level less than 1.5 x pre-morbid level</td>
<td>metroNIDAZOLE</td>
<td>500 mg, tab, ORAL, q8 hours, order duration: 14 day First dose must be given STAT</td>
</tr>
<tr>
<td>Severe Disease</td>
<td><strong>UNCOMPPLICATED</strong>: White Blood Cell Count greater than or equal to 15 or Creatinine greater than or equal to 1.5 x baseline</td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, q6 hours, order duration: 14 day First dose must be given STAT</td>
</tr>
<tr>
<td></td>
<td><strong>COMPLICATED</strong>: toxic megacolon, ileus, or shock</td>
<td>vancomycin</td>
<td>500 mg, liquid, ORAL, q6 hours, order duration: 14 day, ... First dose must be given STAT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>metroNIDAZOLE</td>
<td>500 mg, injection, IV, q8 hours, order duration: 14 day, P... First dose must be given STAT</td>
</tr>
<tr>
<td>Tapering Dose Optional</td>
<td>For second recurrence of C-difficile</td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, q6 hours, order duration: 14 day, Requested Start Date/Time T:N</td>
</tr>
<tr>
<td></td>
<td>For second recurrence of C. difficile follow tapering dose schedule for vancomycin and select all medication orders below.</td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, q12 hours, order duration: 7 day, Requested Start Date/Time T+15;N</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, daily, order duration: 7 day, Requested Start Date/Time T+22;N</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, q48 hours, order duration: 7 day, Requested Start Date/Time T+30;N</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vancomycin</td>
<td>125 mg, liquid, ORAL, q72 hours, order duration: 7 day, Requested Start Date/Time T+38;N</td>
</tr>
</tbody>
</table>
Severe CDAD

- No consensus on definition

- SHEA/IDSA CPG
  - WBC ≥ 15
  - Serum Cr > 1.5x baseline
  - Hypotension/shock
  - Ileus
  - Megacolon

Severe, uncomplicated

Severe, complicated
Severe, complicated CDAD

- Requires surgical intervention for source control
- Indications for OR are ill-defined
  - Toxic megacolon
  - Perforation
  - MODS
Impact of Emergency Colectomy on Survival of Patients With Fulminant *Clostridium difficile* Colitis During an Epidemic Caused by a Hypervirulent Strain

François Lamontagne, MD,* Annie-Claude Labbé, MD,† ‡ Olivier Haeck, MD, † Olivier Lesur, MD,* Mathieu Lalancette, MD,* Carlos Patino, MD, † Martine Leblanc, MD, † Michel Laverdière, MD, † and Jacques Pépin, MD*

*Annals of Surgery* • Volume 245, Number 2, February 2007

• Survival benefit with subtotal colectomy for patients with:
  • Age \( \geq 65 \)
  • WBC \( \geq 20,000 \)
  • Lactate 2.2-4.9
Meta-analysis

Systematic review and meta-analysis of outcomes following emergency surgery for Clostridium difficile colitis

A. Bhangu, D. Nepogodiev, A. Gupta, A. Torrance and P. Singh, on behalf of the West Midlands Research Collaborative*

- Total/subtotal colectomy and end ileostomy was primary surgical intervention in 89% of patients
- 30-day post-operative mortality rate was 41.3% (19% to 71%)
- In-hospital mortality rate was 41.6% (25% to 80%)
Diverting Loop Ileostomy and Colonic Lavage

An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium difficile Associated Disease

Matthew D. Neal, MD, * John C. Alverdy, MD, † Daniel E. Hall, MD, *‡ Richard L. Simmons, MD, * and Brian S. Zuckerbraun, MD *‡

Annals of Surgery • Volume 254, Number 3, September 2011

1. Creation of diverting loop ileostomy.
2. Intraoperative antegrade colonic lavage with 8 liters of warmed PEG3350/electrolyte solution via ileostomy.
3. Postoperative antegrade colonic enemas with vancomycin (500 mg in 500 mL X 10 days) via ileostomy.
Diverting Loop Ileostomy and Colonic Lavage

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Annals of Surgery • Volume 254, Number 3, September 2011

• 19% (8 of 42) mortality versus 50% (21 of 42) mortality of a historical control

• 19% of surviving patients had ileostomy reversed

• Termed “Pittsburgh Protocol”
The London Protocol

1. Insertion of NJ tube
2. Confirmation with AXR
3. Insertion of Flexiseal
4. Colonic lavage with PEG 8L NJ over 2 days
5. Vancomycin 500 mg NJ/PO q6h x 14 days
6. Metronidazole 500 mg IV q8h x 14 days
Ulcerative colitis
Epidemiology

- Developed countries
  - Northern latitudes
- Seasonal variation
- Stable incidence
  - 4-6/100,000
- Prevalence 40-100/100,000
- Age<30
  - Small secondary peak 6th decade
- Equal among genders
- White, Jewish, northern European

Prevalence of Ulcerative colitis in the United States.

<table>
<thead>
<tr>
<th>Region</th>
<th>Prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast</td>
<td>255 (248–263)</td>
</tr>
<tr>
<td>South</td>
<td>209 (202–216)</td>
</tr>
<tr>
<td>Midwest</td>
<td>234 (227–241)</td>
</tr>
<tr>
<td>West</td>
<td>263 (253–273)</td>
</tr>
</tbody>
</table>

Etiology

◦ Cause is unknown
  ◦ Environmental
  ◦ Dietary
  ◦ Infectious
  ◦ Drugs
  ◦ Genetic
  ◦ Altered immunologic response

◦ Smoking may confer a protective effect

◦ Appendectomy may confer a protective effect
Pathology

- Mucosa and submucosa
- Rectal involvement (proctitis)
  - Extends proximally
  - May involve entire colon
  - No TI
- Continuous inflammation
- Pseudopolyps
- Strictures (5-12%)
<table>
<thead>
<tr>
<th>Colonoscopic Features</th>
<th>Ulcerative Colitis</th>
<th>Crohn's Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distribution</td>
<td>Continuous</td>
<td>Discontinuous</td>
</tr>
<tr>
<td>Rectal disease</td>
<td>4+</td>
<td>1+</td>
</tr>
<tr>
<td>Friability</td>
<td>4+</td>
<td>1+</td>
</tr>
<tr>
<td>Aphthous ulcers</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>Deep longitudinal ulcers</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>Cobblestoning</td>
<td>0</td>
<td>4+</td>
</tr>
<tr>
<td>Pseudopolyps</td>
<td>2+</td>
<td>2+</td>
</tr>
</tbody>
</table>
Histology

- Inflammation of mucosa and submucosa
  - Crypt abscesses
  - Vascular congestion
  - Crypt branching
- Sparing of muscularis
  - Except in megacolon
- pANCA in 86% patients with UC
Clinical presentation

- Gradual onset over weeks
- Diarrhea and mucus
- Urgency, tenesmus, incontinence
- Rectal bleeding
- Abdominal discomfort
- Fever, fatigue, weight loss
- Often similar presentation to Crohn’s disease
  - Less urgency in Crohn’s
  - Less bleeding in Crohn’s
  - More pain in Crohn’s
  - More perianal disease in Crohn’s

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding per rectum</td>
<td>3+</td>
<td>1+</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3+</td>
<td>3+</td>
</tr>
<tr>
<td>Obstructive symptoms</td>
<td>1+</td>
<td>3+</td>
</tr>
<tr>
<td>Anal or perianal disease</td>
<td>Rare</td>
<td>4+</td>
</tr>
<tr>
<td>Risk for cancer</td>
<td>2+</td>
<td>3+</td>
</tr>
<tr>
<td>Small bowel disease</td>
<td>0</td>
<td>4+</td>
</tr>
</tbody>
</table>
Extra-intestinal manifestations

- Arthritis in 20%
- Ankylosing spondylitis in 3-5%
- Erythema nodosum in 10-15%
- Pyoderma gangrenosum
- Uveitis, episcleritis
- Primary sclerosing cholangitis in 5-8%
- Venous/arterial thromboembolism
- Colectomy typically improves arthritis, ankylosis, erythema nodosum, and pyoderma gangrenosum
- Colectomy does not improve PSC
  - Usually progressive and requiring liver tx

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**Hypercoagulability in inflammatory bowel disease**

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unusual sites</td>
</tr>
<tr>
<td>Associated with active disease and better when disease controlled</td>
</tr>
<tr>
<td>Associated with use of steroids (possibly indicating active disease)</td>
</tr>
<tr>
<td>Recurrent</td>
</tr>
<tr>
<td>Serious</td>
</tr>
<tr>
<td>Younger age</td>
</tr>
</tbody>
</table>

**Abnormalities described**

- Abnormal fibrinolysis
- Abnormal platelet aggregation
- Activated protein C increased
- Circulating immune complexes
- Decreased antithrombin III
- Factor V Leiden mutation
- Increased cytokines (interleukin-6, thrombopoietin)
- Increased factors V and VIII
- Increased plasminogen activator inhibitor
- Increased sedimentation rate, fibrinogen
- Lupus anticoagulant
- Thrombocytosis and leukocytosis (uniformly present in most studies)
### Severity

Montreal classification

<table>
<thead>
<tr>
<th>Severity</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0</td>
<td>Clinical remission</td>
</tr>
<tr>
<td>S1</td>
<td>Mild UC</td>
</tr>
<tr>
<td>S2</td>
<td>Moderate UC</td>
</tr>
<tr>
<td>S3</td>
<td>Severe UC</td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate.
Severity

- At presentation:
  - Most are mild
  - 27% moderate
  - 1% severe

- Acute complications:
  - Severe bleeding
  - Fulminant colitis
  - Toxic megacolon
  - Perforation

Mayo score (0-12)

- Stool pattern
  - Patient reports a normal number of daily stools (0 points)
  - One to two more stools than normal (1 point)
  - Three to four more stools than normal (2 points)
  - Five or more stools than usual (3 points)

- Most severe rectal bleeding of the day
  - None (0 points)
  - Blood streaks seen in the stool less than half the time (1 point)
  - Blood in most stools (2 points)
  - Pure blood passed (3 points)

- Endoscopic findings
  - Normal or inactive colitis seen (0 points)
  - Mild colitis: mild friability, erythema, decrease in vascularity (1 point)
  - Moderate colitis: friability, marked erythema, vascular pattern absent, erosions seen (2 points)
  - Severe colitis: ulcerations and spontaneous bleeding (3 points)

- Global assessment by physician
  - Normal (0 points)
  - Mild colitis (1 point)
  - Moderate colitis (2 points)
  - Severe colitis (3 points)
Investigations

- **Laboratory**
  - Anemia, low albumin
  - ESR, CrP, Electrolyte abnormalities
  - pANCA?
  - Stool cultures to rule out infection

- **Imaging**
  - Radiographs
  - Barium enema
  - CT/MRI
  - Ultrasound

- **Endoscopy**
Barium enema
Endoscopy

- Ileocolonoscopy allows evaluation of TI inflammation (which would suggest Crohn’s disease) and extent and severity of colonic disease
- Should be avoided in severe colitis
- Flexible sigmoidoscopy should be performed instead
- Loss of vascular markings, engorgement of mucosa, erythema
- Granularity, petechiae, exudates, edema, erosions, friability, spontaneous bleeding
- Macroulcerations, profuse bleeding, copious exudates
- Pseudopolyps
Endoscopy

- Rectum – continuous
- 30-50% limited to rectum/sigmoid, 20-30% left sided colitis
- 20% pancolitis
  - Occasional backwash ileitis
### Endoscopic Criteria for Mayo Score

<table>
<thead>
<tr>
<th>ENDOSCOPY</th>
<th>0 Points</th>
<th>1 Points</th>
<th>2 Points</th>
<th>3 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td></td>
<td>Mild Erythema ↓ vascularity</td>
<td>Moderate Marked erythema Lack vascular pattern Friability</td>
<td>Severe Spontaneous bleeding ulceration</td>
</tr>
<tr>
<td>NORMAL</td>
<td></td>
<td>Mild friability</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Endoscopic Images](image)
Biopsy

- Crypt abscesses
- Crypt branching, shortening, disarray, atrophy
- Mucin depletion in epithelial cells, paneth cell metaplasia
- Increased lamina propria cellularity, basal plasmacytosis, basal lymphoid aggregates, lamina propria eosinophils
- None are specific for UC, but two or more is suggestive
- Biopsies also done to rule out CMV – enlarged cytomegalic cells, eosinophilic intranuclear inclusions, immunoperoxidase staining
- Severe urgency and tenesmus – should do Neisseria/HSV cultures also.
Natural history

- Starts with weeks to months attacks of bloody diarrhea
- With treatment, intermittent exacerbations and long periods of asymptomatic remission
- Small percentage ongoing symptoms
- Patients presenting with proctitis are more likely to have a benign course and to respond to topical therapy
- Those with extensive disease are more likely to need systemic therapy or colectomy
Medical management

- Medical therapy is targeted at controlling underlying inflammation to induce remission.
- A careful assessment of disease severity should guide management:
  - Mild to severe severity
  - Proctitis to pancolitis extent
- Surgical management should be reserved for complications or cases unresponsive to medical therapy.
Medical management

- Three broad categories
  - 5-aminosalicylic acid (5-ASA)
    - Pentasa, Asacol
  - Corticosteroids
    - Oral vs. IV
  - Immunomodulators
    - Azathioprine
    - Methotrexate
    - Biologics
    - Cyclosporine
    - Tacrolimus
Mild to Moderate Colitis

- 5-aminosalicylic acid (5-ASA) often used
- Topical 5-ASA or topical steroid for initial treatment of distal colitis
  - 5-ASA may be superior
  - Foams may be better than enemas
- Oral plus topical 5-ASA if extends to splenic flexure
  - Minimum duration: 4 weeks
- For more severe left-sided colitis, can combine oral steroids and 5-ASA
- Pancolitis: initially oral 5-ASA
  - If refractory, oral steroids should be commenced
Severe colitis

- Mainstay of therapy is IV steroids
  - 400mg hydrocortisone daily
  - 40-60mg methylprednisolone daily
- 40% complete response
- 30% will require colectomy during admission
- In those with partial response:
  - 50% will require colectomy within 1 year
  - 70% will require colectomy within 5 years
**Rescue therapy**

- If no response to high dose steroids in 3-5 days **and** no indication for surgery:
  - Single infusion of infliximab (5mg/kg)
  - Daily cyclosporine infusion (4mg/kg)
  - Ongoing RCT to compare the two

- Prolonged response can be achieved to avoid colectomy

- May only be a delay tactic

- Perhaps patients are then in a better condition for surgery?

- Only case series so far on Tacrolimus
Infliximab

- Chimeric monoclonal antibody against tumour necrosis factor alpha (TNFa), a cytokine that:
  - Induces proinflammatory cytokines like IL1, IL6
  - Leukocyte movement into tissues by permeability of endothelial layer of blood vessels
  - Increases release of adhesion molecules
- Used for the treatment of Crohn’s and Ulcerative Colitis, as well as rheumatoid arthritis, psoriasis, ankylosing spondylitis, etc.
- IV infusion typically in 6-8 week intervals
- Binds with high affinity to soluble and transmembrane (TNFa) and neutralizes biological activity
Suggested algorithm

IV Steroids

Response within 2–3 days*

Yes

Commence Maintenance Therapy
Anti-TNF vs AZA/6-MP

No

IV Cyclosporine

OR* IV Infliximab

Response within 5 days*

Yes

No

Colectomy
Optimization

- IV rehydration and electrolytes
- Anemia
- Malnutrition
  - Enteral: less complications
  - NPO + TPN: no benefit
- Thromboembolism prophylaxis
- Identifying and treating superimposed infections
  - C. diff and CMV
- Avoiding precipitants of toxic megacolon
  - Anticolinergics, antidiarrheals, NSAIDs, opiates
Remission

- No diarrhea (<3 BM/day)
- No blood
- No urgency
- Best confirmed by endoscopic mucosal healing
Maintenance

- Oral and topical 5-ASA
  - Response vs. toxicity
- Probiotics
- Azathioprine or 6-mercaptopurine
- Infliximab
- Methotrexate?
- Steroid avoidance
Summary of medical management

Ulcerative Colitis: Mild to Moderate
- Acute flare
  - Exclude enteric pathogen
  - L-sided
  - Extensive
  - Oral 5-ASA
    - Response adequate
    - Maintain oral 5-ASA
    - Response inadequate
    - Consider increased dose
    - Oral steroid
  - Rectal therapy
    - Consider rectal therapy (5-ASA and/or steroid)
    - Response adequate
    - Maintain oral 5-ASA
    - Response inadequate
    - Oral steroid
  - Patient unwilling to take rectal therapy
    - Oral 5-ASA
      - Response adequate
      - Maintain
      - Response inadequate

Ulcerative Colitis: Moderate to Severe
- Moderate
  - Oral steroid
    - Taper
    - Successful
      - Maintain on 5-ASA and observe
    - Response inadequate
      - Consider increased dose
      - Oral steroid
  - Inadequate response
    - IV Steroid
      - Adequate response
      - Successfully tapered
      - Monitor for recurrence
    - Unsuccessful
      - AZA/6-MP
      - Success
      - Maintain AZA/6-MP
      - Colectomy
      - Inadequate response
      - Infliximab
        - Response
        - No response
      - Failure
      - No response
      - Consider CyA

CyA = cyclosporine A.
Surgical management

◦ Surgery for complications of UC
  ◦ Emergent surgery for acute complications
    ◦ Acute severe colitis
    ◦ Toxic megacolon
    ◦ Massive hemorrhage
    ◦ Perforation and peritonitis
  ◦ Elective surgery for chronic complications
    ◦ Dysplasia and cancer
    ◦ Stricture
    ◦ Systemic complications
◦ Elective surgery for failure of medical management
◦ Preoperative evaluation and management
◦ Surgical options (emergent and elective)
Emergent surgery

- Catastrophic complications have been reduced by advances in medical therapy
  - Hemorrhage, perforation, fulminant colitis, obstruction
- 15-50% of patients in emergent setting still require operation during admission
Acute abdomen

- Absolute indication for immediate surgery in patients with acute fulminant colitis
- Results from:
  - Toxic megacolon
  - Perforation
  - Hemorrhage
- Impending perforation – dilatation with thumbprinting
- Free perforation – rare
- Walled off perforation more common
Toxic megacolon

Severe potentially fatal complication of colonic inflammation characterized by:

• Radiographic evidence of colonic distension of > 6cm in the transverse colon
  AND
  • Systemic toxicity
  • Inflammatory or infectious etiology of underlying disease
Epidemiology

Larger studies on toxic megacolon are outdated and focussed only on IBD

- Incidence 6% in patients admitted to hospital with IBD (10% UC, 2.3% Crohn’s) in a study from 1980’s
- Incidence 7.9% in patients admitted with UC in more recent study from 2002
- Toxic megacolon in pseudomembranous colitis 0.4-3%, but this is increasing
  - Annual increase of 23% in rate of C. diff hospitalizations
  - Increase in C. diff mortality from 1.2% in 2000 to 2.2% in 2004
  - Frequent use of broad spectrum antibiotics, emergence of hypervirulent C. difficile strain (BI/NAP1/027), increase in community acquired C. difficile infections
<table>
<thead>
<tr>
<th>Etiological Factors for Toxic Megacolon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflammatory (48%)</strong></td>
</tr>
<tr>
<td>Ulcerative colitis (46%)</td>
</tr>
<tr>
<td>Crohn’s disease (2%)</td>
</tr>
<tr>
<td>Behcet’s disease</td>
</tr>
<tr>
<td><strong>Infectious (34%)</strong></td>
</tr>
<tr>
<td><em>Clostridium difficile</em> pseudomembranous colitis (31%)</td>
</tr>
<tr>
<td><em>Salmonella, Shigella, Yersinia, Campylobacter, E. coli</em></td>
</tr>
<tr>
<td>Entameba (3%)</td>
</tr>
<tr>
<td>CMV, Rotavirus</td>
</tr>
<tr>
<td>Aspergillosis</td>
</tr>
<tr>
<td>Cryptosporidium</td>
</tr>
<tr>
<td><strong>Ischemic (11%)</strong></td>
</tr>
<tr>
<td>Ischemic colitis (11%)</td>
</tr>
<tr>
<td><strong>Other (7%)</strong></td>
</tr>
<tr>
<td>Collagenous colitis</td>
</tr>
<tr>
<td>Colonic lymphoma</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
</tr>
<tr>
<td><strong>Cytotoxic chemotherapy (3%)</strong></td>
</tr>
<tr>
<td>Beta mimetics (4%)</td>
</tr>
</tbody>
</table>

Changing Etiology

Distribution of toxic megacolon etiology during observation period

Pathogenesis

- Not fully understood
- Link between inflammation and decreased smooth muscle contractility
- Mucosal inflammation of UC penetrates into muscularis propria
  - Depth correlates with severity of dilation
  - Neutrophils from mucosa also invade muscle layer, release proteolytic enzymes, cytokines, leukotrienes
- Inflammatory mediators have inhibitory effect on colonic motility
  - Nitric oxide (NO), Inducible nitric oxide synthase (iNOS)
  - Hydrogen peroxide (H₂O₂), IL-1β
  - Changes in neuromuscular signaling but **NOT** decreased neurons in myenteric ganglia (like in Hirschsprung’s)
## Diagnosis

<table>
<thead>
<tr>
<th>Clinical Criteria for Diagnosis of Toxic Megacolon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main criteria:</strong> (3 of 4)</td>
</tr>
<tr>
<td>Fever (&gt;38.6°C)</td>
</tr>
<tr>
<td>Tachycardia (&gt;120bpm)</td>
</tr>
<tr>
<td>Leukocytosis (&gt;10.5x10⁹/l)</td>
</tr>
<tr>
<td>Anemia</td>
</tr>
<tr>
<td><strong>AND at least one of the following:</strong></td>
</tr>
<tr>
<td>Dehydration</td>
</tr>
<tr>
<td>Altered level of consciousness</td>
</tr>
<tr>
<td>Electrolyte imbalances (↓K⁺, ↓Albumin)</td>
</tr>
<tr>
<td>Hypotension</td>
</tr>
</tbody>
</table>

Imaging

Plain abdominal radiographs:

- Colonic dilation >6cm
  - Mean 9.2cm (Fazio et al), ascending and transverse more dilated, disturbance of haustration, air-fluid levels

- Small bowel dilation
  - Persistent small bowel distension on plain films may indicate “impending” megacolon.

CT:

- 4/12 patients were able to pick up missed complications, but did not predict clinical outcome (Balthazar et al)

- Air-filled distension >6cm, abnormal haustral pattern, segmental colonic parietal thinning patognomonic for TM. (Moulin et al)
Endoscopy

- Total colonoscopy has high risk of perforation in acute setting and is generally contraindicated.
- Limited sigmoidoscopy valuable to differentiate etiology (e.g., pseudomembranes in C. diff).
- Contradictory findings in studies regarding usefulness and safety (Johal et al, Hall et al).
- If necessary, should use minimal air insufflation.
Management

- Early medical and surgical involvement
- Treatment of underlying cause and toxemia
- Close monitoring, supportive care with IV fluids
- Stopping opiates, anticholinergics, anti-diarrheals
- NPO, bowel rest
- TPN has no proven benefit
- Some suggest repositioning patients (rolling, prone knee-elbow position) to redistribution of colonic gas to distal colon and rectum
Medical Therapy

- High dose IV steroids started immediately and re-evaluated frequently
  - Not to be delayed by pending microbiology
  - 400mg hydrocortisone daily (100mg q6hrs) OR 60mg methylprednisolone daily for 5 days
  - No data to support higher steroid doses causing perforation BUT can mask signs of it
  - Should be stopped if infectious cause established

- Empiric treatment with antibiotics
  - Metronidazole 500mg TID
  - Many advocate antibiotics even without infectious cause (eg. Ceftriaxone, metronidazole)
  - If PMC cause for megacolon, antibiotics maintaining C. diff should be stopped
Role for biologics or calcineurin inhibitors?

- No studies in toxic megacolon specifically
- Two case reports for Infliximab in toxic megacolon
  - One due to UC, one due to Crohn’s
  - Rapid clinical response and remission
  - Avoided surgery
Surgery

Indications for Surgery

- Progressive colonic dilatation
- Peritonitis +/- free air
- Clinical deterioration

- Timing of surgery in toxic megacolon is still controversial:
  - Goal of medical treatment is to avoid surgery
  - Delay in surgery has risk of complications like perforation, compartment syndrome

Surgery

- First-line surgery for acute toxic megacolon:
  - Subtotal colectomy
  - Ileostomy
  - Hartmann’s pouch OR sigmoidostomy OR rectostomy

- For patients with UC as underlying cause:
  - Elective resection of remaining rectum and ileal pouch once acute phase has resolved

- Studies suggest subtotal colectomy with end ileostomy and Hartmann closure of rectum has lower mortality than total proctocolectomy
Acute fulminant colitis with no acute abdomen

- Joint involvement of gastroenterologists and surgeons at early stage
  - Even if rescue therapy is being trialed
  - Frequent reassessment
  - May help mentally prepare patients
- Treatment choice for steroid-refractory colitis is controversial (infliximab trial of rescue therapy vs colectomy)
Elective surgery

- 20 to 30% of patients with UC will eventually require a colectomy
- Retrospective cohort study – surgery associated with improved survival
- Continence-preserving procedures has made surgery more attractive
Colorectal cancer in UC

- Risk of colorectal cancer increases by 0.5 to 1% per year after first 10 years of disease
- Cumulative risk 5-10% after 20 years, 12-20% after 30 years
- Longstanding and extensive colitis (>10 years and involving >50% of the colon) increased risk of CRC compared to general population
  - Extent to or beyond hepatic flexure increases risk
- Patients with PSC may have increased risk of cancer compared to those without PSC
- Risk of colorectal cancer may be reduced by use of ASA, NSAIDs, 5-ASA and by surveillance colonoscopy
- Most common in rectum and sigmoid and always in areas of chronic inflammation
Dysplasia

- CRC in UC is always preceded by dysplasia
- Dysplasia is a marker for coexisting malignancy → surveillance
- Classification:
  - Negative, indefinite, positive (low vs. high grade)
- Flat, slightly elevated, plaque-like, polyps, masses [DALM]
Patients with DALMs may have underlying invasive carcinomas not detectable on biopsy.

Sporadic adenomas occur at the same rate as in the general population and can be removed endoscopically.

Both are distinct from inflammatory pseudopolyps.
Inflammatory pseudopolyps and adenomas
DALM
DALM

- High grade dysplasia → colectomy
  - High rate of synchronous CRC (42%)
- Low grade dysplasia → rates of CRC highly variable among studies
- Diagnosis difficult; experienced pathologist necessary
- Optimal surveillance controversial
- Unclear if surveillance improves survival
- Patients with Crohn’s likely have similar risk of CRC as those with UC
Screening

- UC extending proximal to splenic flexure or Crohn’s (2B)
  - 8 years of disease
  - Yearly
- Left sided UC (2C)
  - 12 years of disease
  - Yearly
- UC post subtotal colectomy with rectum in situ (2B)
  - Yearly
- UC limited to rectum (2B)
  - No surveillance
- Pouch patients
  - Flex sig 3-5 years (yearly if severe inflammation)
Screening

- 4 biopsies every 10 cm plus irregular areas
- High grade dysplasia $\rightarrow$ proctocolectomy (1B)
- Low grade dysplasia $\rightarrow$ proctocolectomy (controversial) (2B)
  - If not acceptable to patients, biopsies to be repeated 4-6 months
- If endoscopically/pathologically an adenoma $\rightarrow$ extensive biopsies in area and remaining colon
Surgery for intractable disease

- Intractable is difficult to define
- “disease is intractable when it or its treatment is associated with severe or persistent impairment in the quality of life”
  - Persistent despite high dose steroids
  - Dependence upon steroids to maintain remission
  - Progression of disease with worsening of symptoms or new onset of complications while on max. medical therapy
  - Severe side effects or treatment related complications
Pre-operative considerations

- Patients are young but seriously ill, malnourished, immunosuppressed
- Medical optimization
  - Anemia
  - Fluid depletion
  - Electrolyte abnormalities
  - Nutritional deficiencies
  - ?TPN
- Immunosuppressive therapy
  - Steroids to be tapered
  - Other immunomodulators can be stopped
  - May be an association between infliximab and increased complications, but evidence is weak
A Prospective, Randomized, Noninferiority Trial of Steroid Dosing After Major Colorectal Surgery

Karen Zaghigian, MD,* Gil Y. Melmed, MD,† Dror Berel, MS,‡ Gayane Osyayan, BS,* Zuri Murrell, MD,* and Phillip Fleschner, MD*

Objective: To evaluate the safety of perioperative low-dose steroids (LDS) versus high-dose steroids (HDS) in steroid-treated patients with inflammatory bowel disease (IBD) undergoing major colorectal surgery.

Background: Corticosteroid-treated patients undergoing major colorectal surgery are commonly prescribed HDS to prevent perioperative adrenal insufficiency and cardiovascular collapse. There is little evidence to support this practice.

Methods: We performed a single-blinded noninferiority trial to compare perioperative hemodynamic instability in 20 steroid-treated IBD patients undergoing major colorectal surgery. Patients were randomly assigned to receive perioperative high-dose corticosteroids (HDS; hydrocortisone, 100 mg, intravenously 3 times daily, followed by taper) or low-dose corticosteroids (LDS; intravenous hydrocortisone equivalent to presurgical oral dosing, followed by taper). The primary outcome was the absence of postural hypotension on postoperative day 1, defined as a decrease in systolic blood pressure by 20 mm Hg after sitting from a supine position.

Results: The primary outcome, absence of postural hypotension on postoperative day 1, occurred in 95% of those randomized to receive high doses of corticosteroids compared with 96% of those who received low doses (noninferiority 95% confidence interval = −0.08 to 0.09; P = 0.007).

Conclusions: In IBD patients undergoing abdominal surgery, the incidence of postural hypotension or adrenal insufficiency is similar among those receiving high doses or low doses of corticosteroids in the perioperative period. To reduce complications associated with unnecessarily high doses of steroids, steroid-treated IBD patients undergoing major colorectal surgery should be treated with low doses of steroids in the perioperative period. (ClinicalTrials.gov ID NCT01559675)

patients not taking steroids at the time of surgery who have previously been treated with steroids within 12 months before surgery. However, sufficient evidence to support these recommendations is lacking. Furthermore, high-dose steroids (HDS) are not without consequence and have been associated with impaired wound healing, hyperglycemia, hypertension, fluid and electrolyte imbalance, immunosuppression, and psychological effects. Retrospective data suggest that perioperative low-dose steroids (LDS) may be as safe as HDS in steroid-treated patients undergoing major colorectal surgery. We therefore sought to prospectively compare the safety of perioperative LDS against HDS in steroid-treated patients with inflammatory bowel disease (IBD) undergoing major colorectal surgery.

METHODS

Study Design

This was a single-center, patient-blinded, randomized, noninferiority study to assess the safety of LDS compared with HDS in steroid-treated IBD patients undergoing major colorectal surgery. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and local regulations. All research-related activities were approved by the Cedars Sinai Medical Center Institutional Review Board (#22170) and all subjects provided written informed consent. A data safety and monitoring committee reviewed safety data after 50% of subjects were enrolled.

Study Population
Pre-operative considerations

- Patient education
  - Should understand indications, remaining medical options, surgical alternatives, expected outcome and potential complications
- Ostomy site selection
- Mechanical bowel preparation
- Antibiotic prophylaxis
  - Oral and IV antibiotics may decrease SSI
- VTE prophylaxis
  - Increased risk of VTE in UC patients
  - Heparin/low molecular weight heparin and intermittent pneumatic compression devices
  - Extended VTE prophylaxis after discharge?
Preoperative Oral Antibiotics and Intravenous Antimicrobial Prophylaxis Reduce the Incidence of Surgical Site Infections in Patients With Ulcerative Colitis Undergoing IPAA

Tsutomu Oshima, M.D.¹ • Yoshiio Takesue, M.D., Ph.D.² • Hiroki Ikeuchi, M.D., Ph.D.¹ Hiroki Matsuoka, M.D., Ph.D.¹ • Kazuhiko Nakajima, M.D., Ph.D.² Motoi Uchino, M.D., Ph.D.¹ • Naohiro Tomita, M.D., Ph.D.¹ Mitsuru Sasako, M.D., Ph.D.¹

1 Department of Surgery, Hyogo College of Medicine, Mukogawa-cho, Nishinomiya-shi, Hyogo, Japan
2 Department of Infection Control and Prevention, Hyogo College of Medicine, Mukogawa-cho, Nishinomiya-shi, Hyogo, Japan

BACKGROUND: The usefulness of preoperative oral antibiotics for the prevention of surgical site infection in elective colorectal surgery remains controversial.

OBJECTIVE: This study aimed to investigate the effects of oral antimicrobial prophylaxis in addition to intravenous antimicrobial prophylaxis on patients with ulcerative colitis undergoing restorative proctocolectomy.

DESIGN: This study was a randomized, nonblinded, single-center clinical trial.

SETTING: This study was conducted between July 1, 2006, and April 30, 2009, at Hyogo College of Medicine.

PATIENTS: Two hundred patients with ulcerative colitis scheduled to undergo restorative proctocolectomy with IPAA with an open approach were randomly assigned to either group A or B (n = 100). Combined use of preoperative oral antibiotics and intravenous antimicrobial prophylaxis were given to group A and underwent preoperative mechanical bowel preparation, and intravenous antimicrobial prophylaxis with second-generation cephalosporin was given for 24 hours.

MAIN OUTCOME MEASURES: The primary end point of this study was the incidence of overall surgical site infection according to intention-to-treat analysis.

RESULTS: The incidence of overall surgical site infection was significantly lower in group A (6/97 patients, 6.1%) than in group B (22/98 patients, 22.4%) (p = 0.0024). In multivariate analysis, the administration of oral antibiotics (OR, 0.178; 95% CI, 0.057–0.552; p = 0.003) and ASA score ≥3 (OR, 5.343; 95% CI, 1.595–17.891; p = 0.007) were independent risk factors for surgical site infection.

LIMITATIONS: This study is limited because of its open-label nature.

CONCLUSIONS: Combined oral and intravenous...
Ulcerative Colitis Is Associated With an Increased Risk of Venous Thromboembolism in the Postoperative Period

The Results of a Matched Cohort Analysis

Matthew Z. Wilson, MD, MS,* Tara M. Connelly, MB, BCH, MS,† Andrew Tinsley, MD,‡ Christopher S. Hollenbeak, PhD,†§ Walter A. Koltun, MD,† and Evangelos Messaris, MD, PhD†

Objectives: To determine the rates of venous thromboembolism (VTE) during admission and within 30 days of hospital discharge in inflammatory bowel (IBD) patients undergoing colonic resection using the ACS National Surgical Quality Improvement Project (NSQIP) database and to compare these rates to VTE rates in cohorts of patients undergoing colonic resection for several other colonic pathologies.

Background: High rates of VTE have been demonstrated in hospitalized IBD patients. However, rates of postdischarge VTE in IBD patients are understudied.

Methods: Demographic, operative, and outcomes data for 96,999 patients undergoing colonic resection for diverticulitis, colorectal cancer (CRC), benign neoplasms, ulcerative colitis (UC), and Crohn’s disease (CD) between 2005 and 2011 was obtained. Student’s t and χ² tests were used for univariate analysis. A multivariate analysis was performed with all significant variables. Propensity score matching was utilized to compare the VTE incidences between the groups.

Results: Highest VTE risk was seen in obese patients [odds ratio (OR) = 1.41], those older than 73 years (OR = 1.58) and with bleeding disorders (OR = 1.44). American Society of Anesthesiology class III/IV (OR = 1.52/1.86), preoperative systemic inflammatory response syndrome (OR = 1.53), sepsis (OR = 1.48) or steroid use (OR = 1.63), and primary diagnosis of UC (OR = 2.10). The UC group had the highest incidence of VTE (2.74%), followed by CRC patients (1.74%). A 1.2% incidence was seen in the CD population, and 41.5% of the UC-VTEs were diagnosed during discharge.

Conclusions: This study affirms that inpatient UC patients undergoing colonic resection are at high risk for VTE and suggests that this risk persists into the postdischarge period. Thus, these patients should be given appropriate prophylaxis.

In addition, postoperative VTEs are associated with hospital lengths of stay (LOS) up to 3 times longer and costing twice as much when compared with non-VTE admissions. The increased mortality in inflammatory bowel disease (IBD) patients with VTEs has been demonstrated to be up to 4 times greater than that of IBD patients without VTE. VTE rates in colorectal surgery patients, particularly after undergoing resections for colorectal cancer (CRC), are greater than VTE rates in surgical patients from other surgical specialties with reported incidences as high as 40% in those not given VTE prophylaxis. Recommendations for postdischarge thromboprophylactic treatment in patients undergoing CRC resections are clearly defined because of the known high risk in this cohort. IBD is a chronic immune mediated inflammatory condition and, as such, constitutes a hypercoagulable state with relatively high rates of VTE demonstrated in medically and surgically managed patients. Studies comparing the 2 main forms of IBD have suggested higher VTE rates in ulcerative colitis (UC) versus Crohn disease (CD) for reasons not yet known. Despise these high rates of VTE, particularly in UC patients, little data exists on VTE rates postdischarge after colonic resections. Although clear guidelines regarding postoperative anticoagulation to prevent VTE in the CRC population are found, guidelines that specifically address the pharmacoprevention of postoperative VTE in IBD patients have yet to be defined. In addition, no large scale investigation into postdischarge VTE rates in IBD has yet been undertaken.

The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) records postoperative outcomes including incidence of postoperative VTE from more than 450 institutions across the United States and Canada.
The Importance of Extended Postoperative Venous Thromboembolism Prophylaxis in IBD: A National Surgical Quality Improvement Program Analysis

Molly E. Gross, M.D.1 • Sarah A. Vogler, M.D.1 • Mary C. Mone, R.N., B.S.E.1
Xiaoming Sheng, Ph.D.2 • Bradford Sklow, M.D.1

1 Department of Surgery, University of Utah, Salt Lake City, Utah
2 Department of Pediatrics, University of Utah, Salt Lake City, Utah

BACKGROUND: The National Comprehensive Cancer Network recommends that patients who have colorectal cancer receive up to 4 weeks of postoperative out-of-hospital venous thromboembolism prophylaxis. Patients with IBD are at high risk for venous thromboembolism, but there are no recommendations for routine postdischarge prophylaxis.

OBJECTIVE: The purpose of this study was to compare the postoperative venous thromboembolism rate in IBD patients versus patients who have colorectal cancer to determine if IBD patients warrant postdischarge thromboembolism prophylaxis.

DESIGN: This study is a retrospective review of IBD patients and patients who had colorectal cancer who underwent major abdominal and pelvic surgery.

PATIENTS: Data were collected from the American College of Surgeons National Surgical Quality Improvement Program (2005–2010).

MAIN OUTCOME MEASURES: The primary outcome was 30-day postoperative venous thromboembolism in IBD patients and patients who had colorectal cancer. Risk factors for venous thromboembolism were analyzed.

RESULTS: A total of 45,964 patients were identified with IBD (8888) and colorectal cancer (37,076). The 30-day postoperative rate of venous thromboembolism in IBD patients was significantly higher than in patients who had colorectal cancer (2.7% vs 2.1%, p < 0.001). In a model with 15 significant covariates, the OR for venous thromboembolism was 1.26 (95% CI, 1.021–1.56; p = 0.03) for the IBD patients in comparison with the patients who have colorectal cancer.

LIMITATIONS: This study was limited by the retrospective design and the limitations of the data included in the database.

CONCLUSIONS: Patients with IBD had a significantly increased risk for postoperative venous thromboembolism in comparison with patients who had colorectal cancer. Therefore, postdischarge venous thromboembolism prophylaxis recommendations for IBD patients should mirror that for patients who have colorectal cancer. This would suggest a change in clinical practice to extend out-of-hospital prophylaxis for 4 weeks in postoperative IBD patients.
Surgical options - emergent

- Total abdominal colectomy and end ileostomy is the best operation for acute fulminant UC +/- toxic megacolon
  - Rectum is not removed
  - Mucous fistula or Hartmann procedure (plus rectal tube)
  - Rectum is divided at sacral promontory
  - Superior rectal artery preserved
Surgical options - emergent

- Subsequent elective completion proctectomy or ileal pouch-anal anastomosis
  - +/- third operation for reversal of loop ileostomy

- Historical: blowhole colostomy and ileostomy
<table>
<thead>
<tr>
<th>Operation</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal mucosectomy with ileal pouch-anal canal anastomosis</td>
<td>Complete excision of large intestinal disease. Transanal defecation and fecal continence preserved. No ileostomy.</td>
<td>Two operations required. At risk for pouchitis. Nocturnal fecal spotting present.</td>
</tr>
<tr>
<td>Stapled, ileal pouch-distal rectal anastomosis</td>
<td>Transanal defecation and fecal continence preserved. No ileostomy. Easier technically.</td>
<td>At risk for pouchitis and cancer from residual rectal mucosa.</td>
</tr>
<tr>
<td>Ileorectal anastomosis</td>
<td>Transanal defecation and fecal continence preserved. No ileostomy.</td>
<td>Diseased rectum remains to produce symptoms, require treatment and predispose to cancer.</td>
</tr>
</tbody>
</table>
Total proctocolectomy and Brooke ileostomy

- Removal of all rectal mucosa in one operation – curative for UC
- Indications:
  - Elderly patients
  - Poor sphincter function
  - Rectal carcinoma
  - Patient choice
  - Morbidity is associated with perianal wound healing, parastomal hernias, complications of pelvic dissection
- Can be performed laparoscopically
Systematic review and meta-analysis of laparoscopic versus open colectomy with end ileostomy for non-toxic colitis

S. A. L. Bartels¹, T. J. Gardenbroek¹, D. T. Ubbink¹,², C. J. Buskens¹, P. J. Tanis¹ and W. A. Bemelman¹

Departments of ¹Surgery and ²Quality Assurance and Process Innovation, Academic Medical Centre, Amsterdam, The Netherlands
Correspondence to: Professor W. A. Bemelman, Department of Surgery, Academic Medical Centre, PO Box 22660, 1100 DD Amsterdam, The Netherlands (e-mail: w.a.bemelman@amc.uva.nl)

**Background:** This review compared short-term outcomes after laparoscopic versus open subtotal colectomy for acute, colitis medically refractory.

**Methods:** A systematic review of the literature was carried out using MEDLINE, Embase and the Cochrane databases. Overall study quality was assessed by the modified Methodological Index for Non-Randomized Studies (MINORS). Meta-analysis was performed for conversion, reoperation, wound infection, ileus, gastrointestinal bleeding, intra-abdominal abscess, postoperative length of stay and mortality.

**Results:** The search identified nine non-randomized studies: six cohort studies and three case-matched series, comprising 966 patients in total. The pooled conversion rate was 5.5 (95 per cent confidence interval (c.i.) 3.6 to 8.4) per cent in the laparoscopic group. The pooled risk ratio of wound infection was 0.60 (95 per cent c.i. 0.38 to 0.95; \( P = 0.03 \)) and that of intra-abdominal abscess was 0.27 (0.08 to 0.91; \( P = 0.04 \)), both in favour of laparoscopic surgery. Pooled risk ratios for other complications showed no significant differences. Length of stay was significantly shorter after laparoscopic subtotal colectomy, with a pooled mean difference of 3.17 (95 per cent c.i. 2.37 to 3.98) days (\( P < 0.001 \)).

**Conclusion:** Where the procedure can be completed laparoscopically, there may be short-term benefits over open colectomy for colitis. These results cannot be generalized to critically ill patients in need of an emergency subtotal colectomy.

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Total colectomy and ileo-rectal anastamosis

- Patients who are not suitable for IPAA but refuse ileostomy or have relative contraindications to ileostomy (eg. Ascites)
- Women of childbearing age
- Crohns disease
- Residual rectum not excised
  - Persistent symptoms
  - Future malignancy
    - 6% at 20 years, 15% at 30 years
  - Strict rectal surveillance necessary
Total proctocolectomy and continent (Kock) ileostomy

- Continent pouch of 30 cm ileum constructed and 20 cm is intussuscepted to create a valve
- Intubated by patient via wide bore catheter and drained 3-4 times per day
- Many complications:
  - Strictures
  - Volvulus
  - Herniation
  - Fistulisation
  - Valve slippage (30%)
- Up to 50% underwent revision
Total colectomy and stapled ileal pouch-distal rectal anastomosis (IPDRA)

- IPAA sometimes abandoned intraoperatively due to technical reasons, Crohn’s evidence, or cancer (4.1%)
- IPDRA technically easier
- But leaves diseased rectal mucosa behind
- May be considered in older patients or where a tension free anastomosis cannot be achieved
Total proctocolectomy and ileal pouch-anal anastamosis

- A neo-rectum fashioned from ileum and anastamosed to the anus
- Contraindications:
  - Crohn’s
  - Incontinence
  - Rectal cancer
  - Emergent surgery
- J-pouch most common
  - Also S, H, W
- Can also be done laparoscopically
Steps:

1. Modified lithotomy
2. Laparotomy
3. Total colectomy with division of ileum flush with the caecum
4. Dissection of rectum (TME excision to levators)
5. Rectum divided 1-2 cm above dentate line
Steps:

6. Mobilization of small bowel mesentery
Steps:

- 7. Creation of J-pouch
  - 30 cm of ileum and enterotomy at the apex
  - Anti-mesenteric side-to-side anastomosis
Steps:

8. Construction of IPAA
   - Anvil secured to pouch and stapled
Steps:

vs.

8. Mucosectomy and hand-sewn pouch-anal anastomosis
Steps:

8. Anastamosis is tested
9. Loop ileostomy is created
Laparoscopic approach
Perioperative complications

- Small bowel obstruction (11-26%)
- Pelvic abscess or leak (2-15%)
  - Most commonly at pouch-anal anastomosis
  - steroid use
- Pouch fistula formation (2.8-12%)
- Cuffitis (5%-14%)
- Sexual dysfunction (5-20%)
- Pouch failure (5-10%)
- Cancer (rare)
Long-term functional outcomes

- Mean number of stools:
  - 5.7/day at 1 year
  - 6.4/day at 20 years
- Incontinence:
  - 5 to 11% during day
  - 12 to 21% at night
- Pouch success:
  - 5 years – 96%
  - 10 years – 93%
  - 15 years – 92%
  - 20 years – 92%
- Quality of life same
- 92% in same employment

Results at up to 20 years after ileal pouch–anal anastomosis for chronic ulcerative colitis

D. Hahnloser², J. H. Pemberton¹, B. G. Wolff³, D. R. Larson¹, B. S. Crownhart¹ and R. R. Dozois¹

¹Division of Colon and Rectal Surgery, Mayo Clinic, Mayo Clinic College of Medicine, Rochester, Minnesota, USA and ²Department of Visceral and Transplantation Surgery, University Hospital, Zurich, Switzerland

Correspondence to: Dr. J. H. Pemberton, Division of Colon and Rectal Surgery, Mayo Clinic, Gonda 9-S, 200 First Street SW, Rochester, Minnesota 55905, USA (e-mail: pemberton.john@mayo.edu)
Long-term functional outcomes

- 11% anal canal strictures
  - Nonfibrotic – responded to dilatation
  - Fibrotic – required surgery
- Pouch failure – 6.8%
- Pelvic sepsis – 9.5%
- Severe incontinence 3.7%
- Mild incontinence 17%
- Current techniques are still not perfect and require further development
- IPAA can have effects on female reproductive health
  - Dyspareunia
  - Significant decrease in fertility (adhesions?)
  - Pregnancy/delivery is safe
Follow-up

- All patients with IPAA should be followed for complications including dysplasia
- Inflammation in retained rectal cuff associated with dysplasia long term
- Systematic review – 1.13% of dysplasia
- Therefore risk of neoplasia not completely eliminated
  - Surveillance recommended
  - Optimal frequency not well documented
Surgery for indeterminate colitis

- Acute fulminant colitis during first presentation requiring colectomy before definitive diagnosis is available
- Uncertain diagnosis (Crohn’s vs. UC) despite investigations
- Indications for surgery are the same **BUT**:
  - Surgery should be total abdominal colectomy and ileostomy and Hartmann procedure or mucous fistula
  - Subsequent proctectomy and IPAA is an option for those with confirmed UC
Surgery for extraintestinal manifestations of UC

- Role of colectomy for these indications not well defined
- Improvement in extraintestinal manifestations is variable
  - VTE, erythema nodosum, massive hemolytic anemia, arthralgia of joints improve
  - Pyoderma gangrenosum, PSC, and ankylosing spondylitis do not improve
Thank you!