What’s New in Colon Ischemia (CI)?

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Conflicts of Interest

- None
- But... I am Chair of ACG Guidelines Committee on Colon Ischemia (CI)
**Spectrum of CI**

**Reversible**
- Colopathy: intramural hemorrhage, edema
- Transient segmental colitis
- Stricture

**Irreversible**
- Gangrenous infarction
- Stricture
- Persistent segmental colitis
- Fulminating universal colitis

**Of Note and Other**
- Colitis simulating carcinoma
- Colitis associated with distal obstruction
- Protein-losing colopathy
- Recurrent sepsis

**Clinical Presentations of CI**

**Usual:** sudden cramping, mild, abdominal pain; urgent desire to defecate; passage within 24 h of RBBPR or bloody diarrhea. Symptoms usually resolve within 10 -14 days
  
  - bleeding > pain
  - pain > bleeding with IRCI

**Unusual:** stricture, gangrene and fulminant, universal colitis
CI is a Segmental Disease

- The left-colon is most commonly affected, but any colonic segment can be affected.
- CI isolated to the right colon is associated with poorer outcome than other patterns of CI except for pan-colonic disease.
- CI may be a recurrent or (even) a chronic disease.
Causes of CI

**Nosologic**
- emboli, thrombi
- vasculitis, arteriopathy
- thrombophilia
- arrhythmias, shock, CHF
- volvulus, hernia
- trauma
- rupt. ectopic pregnancy
- infection (E. coli O157:H7, CMV, HBV)

**Iatrogenic**
- aortic surgery
- colectomy, colon bypass
- lumbar aortography
- colonoscopy, BE

**Miscellaneous**
- long-distance running
- long-distance flying

**Medications and drugs:**
- digoxin, estrogens, vasopressin, sumatriptan, pseudoephedrine, amphetamines, alosetron, cocaine

**What’s New in CI?**

1. Increasing incidence of CI in relatively young people; female predominance is maintained
CI
(740 cases/5.4x10^6 people)

<table>
<thead>
<tr>
<th>Age</th>
<th># (%)</th>
<th>IR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>14 (1.9)</td>
<td>0.5</td>
<td>0.03</td>
</tr>
<tr>
<td>20-29</td>
<td>23 (3.1)</td>
<td>2.1</td>
<td>0.10</td>
</tr>
<tr>
<td>30-39</td>
<td>68 (9.2)</td>
<td>4.0</td>
<td>0.18</td>
</tr>
<tr>
<td>40-49</td>
<td>178 (24.0)</td>
<td>10.8</td>
<td>0.46</td>
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<tr>
<td>50-59</td>
<td>258 (34.9)</td>
<td>24.2</td>
<td>1.00</td>
</tr>
<tr>
<td>60-69</td>
<td>148 (20.0)</td>
<td>40.6</td>
<td>1.64</td>
</tr>
<tr>
<td>70-79</td>
<td>43 (5.8)</td>
<td>96.9</td>
<td>3.69</td>
</tr>
<tr>
<td>≥80</td>
<td>8 (1.1)</td>
<td>64.8</td>
<td>2.49</td>
</tr>
</tbody>
</table>

Cole et al. Am J Gastroenterol, 2004

CI
(740 cases/5.4x10^6 people)

<table>
<thead>
<tr>
<th>Sex</th>
<th># (%)</th>
<th>IR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>284 (38.3)</td>
<td>6.7</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>456 (61.6)</td>
<td>10.7</td>
<td>1.48</td>
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<tr>
<td>No IBS</td>
<td>594 (91.5)</td>
<td>7.2</td>
<td>1.00</td>
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<tr>
<td>IBS</td>
<td>55 (8.5)</td>
<td>42.8</td>
<td>3.39</td>
</tr>
</tbody>
</table>

CI is 3-4X more common in IBS patients than in controls

Cole et al. Am J Gastroenterol, 2004
What’s New in CI?

2. CI is increased in patients with IBS, COPD, constipation and with a wide variety of medications

3. In *young patients*, CI is seen with IBS, vasculitis/vasculopathy, thrombophilia, and medications

Medications/Drugs Associated with CI

- **Antibiotics**: penicillins and derivatives (amoxicillin, ampicillin); also macrolides, cephalosporins, chloramphenicol, fluoroquinolones, tetracyclines
- **Chemotherapeutic agents**: alkaloids (e.g., vinorelbine) and taxanes (e.g., paclitaxel, docetaxel)
- **Constipation-inducing agents** (>250 medications)
- **Decongestants** (e.g., pseudoephedrine)
- **Diuretics** (e.g., HCTZ)
- **Hormonal agents** (e.g., OCP, HRT)- r/o Factor V Leyden
- **Controlled or illicit pharmacologic agents** (e.g., amphetamines, cocaine)
- **Interferon** – HCV is a risk factor for poor outcome of CI
- **Laxatives** (e.g., SPS/kayexelate, bisacodyl, Mg citrate, Na phosphate, glycerin enemas)
- **NSAIDs**
- **Psychotropic agents** (1st and 2nd generation neuroleptics)
- **Serotonin agonists** (sumatriptan) and **antagonists** (alosetron)
Mechanisms of Drug-Induced CI

**Direct Effects**
- vasoconstriction/vasodilation
- endothelial damage
- coagulopathy
- release of vasoactive neuromodulators

**Indirect Effects**
- allergic vasculitis
- constipation

Thrombophilia & CI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CI (%)</th>
<th>Healthy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APCR</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>APL antibody</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Protein S defic.</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Anti-thrombin defic.</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Protein C defic.</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Prothrombin 20210A</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>C677T (MTHFR)</td>
<td>23</td>
<td>1</td>
</tr>
</tbody>
</table>

Greek study: ≥1 thrombophilic abnl in 72% of pts
U. S. study: 28% CI vs 8.4% controls

Koutoubakis et al, Gastroenterology, 2001; Midian-Singh, 2004;
Post-colonoscopy CI

What’s New in CI?

4. Evolving roles of colonoscopy and imaging modalities
Colonoscopy and CI*

- Colonoscopy with biopsy is the best test to dx CI
- In suspected CI, the colon should be insufflated minimally with CO₂ rather than with RA, if possible

**Expert Opinion**

- *In severe CI, CT should be used to evaluate disease distribution and a limited colonoscopy to confirm the nature of CT abnormality*
- *No need to reach the cecum and passage should be halted at the distal most extent of disease*
- *Biopsies should be taken in most cases, except in cases of gangrene*
What is the Role of CT in CI?

- **Diagnosis**
  - segment of colon involved
  - non-specific vs. more specific findings
  - tissue for histology

- **Prognosis**
  - IRCI
  - pneumatosis linearis, portal vein gas

*Common findings (good prognosis) are non-specific and specific findings (bad prognosis) are uncommon*
CT in CI*

- CT with IV and oral contrast is the imaging modality of choice to assess the distribution and phase of colitis.
- Findings on CT or MRI (e.g., bowel wall thickening, edema, thumbprinting) are suggestive of CI, but not specific for diagnosis.
- CT or MRI findings of colonic pneumatosis and porto-mesenteric venous gas are highly suggestive of transmural colonic infarction, but not diagnostic.

**Expert Opinion**

- Multi-phasic CTA should be performed for any pt with suspected IRCI or when AMI cannot be excluded.

Is There a Role for Angiography in The Management of CI?

- By the time of presentation, colon blood flow has already returned to normal.
- Angiography will show age-related changes in the vasculature, but not reveal a causative lesion.
- Angiography plays no role in CI except perhaps a) patients with isolated right colon ischemia b) combined colon and acute mesenteric ischemia c) recurrent disease?
At presentation: 1) blood flow has returned to normal  
2) angiography is usually normal

What’s New in CI?

5. IRCl has a worse prognosis than CI involving any other segment of colon
Anatomic Patterns of CI: 313 Biopsy-Proven Cases

Right Colon
- 25.2%

Transverse Colon
- 10.2%

Distal Colon
- 24.6%

Left Colon
- 32.6%

Pan Colon
- 7.3%


Lesser representation of women
Higher incidence of CAD, AF, and stage V CKD
Cause established in 22.8%, most likely sepsis
Longer length of stay
Greater need for surgery
Higher mortality rate

Outcomes of Anatomic Patterns of CI

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Pan Colon</th>
<th>Right Colon</th>
<th>Trans Colon</th>
<th>Left Colon</th>
<th>Distal Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS</td>
<td>7 (1-115)</td>
<td>9 (1-54)</td>
<td>10 (1-89)</td>
<td>6 (1-113)</td>
<td>5 (1-75)</td>
<td>6 (1-55)</td>
</tr>
<tr>
<td>Surgery</td>
<td>19.8%</td>
<td>30.4%</td>
<td>44.3%</td>
<td>18.8%</td>
<td>5.9%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Mortality</td>
<td>11.8%</td>
<td>21.7%</td>
<td>20.3%</td>
<td>12.5%</td>
<td>6.9%</td>
<td>6.5%</td>
</tr>
</tbody>
</table>

*Brandt, et al. Am J Gastro, 2010*
Serologic testing in CI*

- There are no serologic tests to diagnose (early) CI
- Serologic testing can be used to predict CI severity
- The most useful serologic test results to predict severity are:
  - ↑ WBC, BUN, LDH
  - ↓ Hgb, albumin, Na⁺, HCO₃

What’s New in CI?

6. Colon ischemia may have an auto-immune component to explain why some patients develop recurrent or chronic disease
IBD Markers in CI

<table>
<thead>
<tr>
<th></th>
<th>Recurrent CI</th>
<th>Chronic CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td># patients</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>≥ 1(+)marker</td>
<td>56%</td>
<td>88%</td>
<td>0.173</td>
</tr>
<tr>
<td>≥ 2(+)markers</td>
<td>11%</td>
<td>62%</td>
<td>0.030</td>
</tr>
<tr>
<td>p-ANCA</td>
<td>0%</td>
<td>88%</td>
<td>0.001</td>
</tr>
<tr>
<td>ASCA IgG</td>
<td>0%</td>
<td>25%</td>
<td>0.125</td>
</tr>
<tr>
<td>ASCA IgA</td>
<td>11%</td>
<td>0%</td>
<td>0.362</td>
</tr>
<tr>
<td>Any ASCA</td>
<td>11%</td>
<td>25%</td>
<td>0.485</td>
</tr>
<tr>
<td>Anti-OmpC</td>
<td>22%</td>
<td>38%</td>
<td>0.521</td>
</tr>
<tr>
<td>Anti-C-Bir1</td>
<td>40%</td>
<td>42%</td>
<td>0.590</td>
</tr>
</tbody>
</table>

Aroniadis, Feuerstadt, Brandt. ACG, 2008

IBD Markers in CI

- IBD markers are not specific for IBD and are seen in 71% of patients with recurrent or chronic CI.
- 56% of patients with *recurrent CI* had ≥ one marker, most common of which was anti-CBir1.
- 88% of patients with *chronic CI* had ≥ one marker, most common of which was pANCA.
- “IBD” marker seropositivity in patients with recurrent /chronic CI suggests an etiologic role for *autoimmunity*.
**Treatment of CI**

- Most cases of CI do not require specific therapy and resolve spontaneously
- Total/sub-total colectomy, right hemicolectomy and segmental colectomy are the most common surgical procedures for the treatment of acute CI, removing only the area of ischemic bowel

**Expert Opinion**

- Antimicrobial therapy should be considered for patients with moderate or severe disease

**Axioms of CI**

- CI is common and increasingly diagnosed in younger patients
- Etiology usually is not apparent in elderly, but more commonly discovered in younger patients (IBS, vasculitis/opathy, thrombophilia, medication/drugs)
- Site of involvement influences presentation and course
  - Non-IRCI: BRBPR or bloody diarrhea > abdominal pain; Good outcome
  - IRCI: Abdominal pain > BRBPR or bloody diarrhea; More severe course
- Patients usually are not ill, but may develop recurrent disease
- Evaluation is by colonoscopy not angiography (except possibly IRCI); CT scan may help in determining prognosis
- Serologic tests may be prognostic
- Treatment is supportive and antibiotics
- Excellent prognosis (except IRCI)