Managing Inflammatory Bowel Diseases in the Elderly Population (Those After the Age of 60)

The incidence of Inflammatory Bowel Diseases (IBD) is increasing worldwide and as our population ages, we will be caring for a growing number of IBD patients who are transitioning into advanced age. Although the peak incidence of IBD is between ages 20-39 years, a second peak is recognized between ages 50-70. (Molodecky, Soon, Rabi, et al. 2012; Katz, Pardi, 2011)

The debilitating effects of IBD compounded with age-related decrements in health and functional capacity, make medical management of older patients distinctly challenging to clinicians.

**TIP #1: Compare the important clinically different presentations in the elderly to the younger patient.** (Nimmons, Limdi, 2016. Gisbert, Chaparro, 2014)

**Crohn’s Disease**
- Diagnosis is delayed in older individuals with a mean time delay of 6 years compared to 2 years in younger individuals
- More colonic involvement and inflammatory disease with lower frequency of fistulas and strictures
- Presents with less bleeding and abdominal pain
- First episode is more severe compared to the younger individual
- Change in disease behavior is less progressive in the elderly

**Ulcerative Colitis**
- Left-sided or extensive disease more common than isolated proctitis
- Presents with less diarrhea, abdominal pain, and weight loss
- Disease behavior more likely to remain stable

**Both**
- Extraintestinal manifestations are less
- Less likely to have family history of IBD
- Higher risk of non-Hodgkin’s lymphoma with thiopurines
- Higher risk of non-melanomatous skin cancer with anti-TNF therapy

**TIP #2: Recognize barriers for the delay in diagnosis in the elderly.** (Harper, McAuliffe,Beeken, 1986)

- Disinclination to seek medical advice
- Lack of access to specialist healthcare
- An initial misdiagnosis compared to younger patients
- Higher prevalence of conditions mimicking and confused with IBD in the elderly. This prevalence may affect the true incidence of IBD assessed.
  - Complicated diverticular disease (diverticulitis and diverticular bleeding)
  - Radiation colitis
  - Non-steroidal anti-inflammatory intestinal injury
  - Ischemic colitis
  - Infective colitis
**TIP #3:** Identify complex management challenges in the elderly. (Roman, Munoz, 2011. Charpentier, Salleron, Savoye, et al. 2014.)

- Clinical co-morbidities
- Polypharmacy
- Social issues
- Mismatch between chronological and biological age (functional status)
- Currently no consensus guidelines to manage the elderly
- Patients’ over the age of 65 frequently excluded from clinical studies may limit evidence-based decision making


- More ill
- More malnourished
- Anemic/higher transfusion requirements
- Hypovolemic
- Longer post-op hospital stay especially after surgery


- Immune function declines with age
  - Malnutrition also accentuates decline in immune function
- Treatment with immunosuppressive medications increases risk of opportunistic infection and possibly even malignancy
- Polypharmacy is common and may impact adherence and thus, clinical outcomes
- Age-related conditions
- Home circumstances
- Impaired mobility
- Impaired memory
- Consequent need for practical support


- Aminosalicylates
  - Lead to decreased GFR
  - Unable to retain/maneuver topical therapy (fecal incontinence common in the elderly)
  - Leukopenia can occur when used in combination with thiopurine due to increased 6-thioguanin levels, the active metabolite of azathioprine and 6-mercaptopurine
  - Non-adherence due to: pill burden, polypharmacy, financial issues, and perceived risk of side effects
  - Paradoxical worsening of colitis
- **Adverse effects that are infrequent: nausea, dyspepsia, headache, and rash**

  - **Antibiotics**
    - **Metronidazole**
      - Neuropathy with prolonged use
      - Nausea, metal taste in the mouth
      - Inhibition of cytochrome P450, may lead to increased levels of HMG-CoA reductase inhibitors such as simvastatin, sildenafil, and calcium channel blockers.
      - May affect warfarin, prolonging the INR
      - Patients need to be advised to avoid alcohol, may cause Antabuse affect
      - Metabolism of Metronidazole increased with phenytoin use
      - May increase risk of lithium toxicity
    - **Ciprofloxacin**
      - Risk of ruptured Achilles tendon
      - Decreases theophylline clearance
      - Can cause CNS adverse effects including lowering of seizure threshold
      - Risk of prolonged QT interval
      - Risk of clostridium difficile
      - May increase INR

  - **Corticosteroids**
    - Studies have identified that there is frequent long-term use of steroids in the elderly, even as maintenance therapy, over choosing biologics or immunosuppressants (Juneja 2012)
    - Risk for osteoporosis and hip fracture (osteonecrosis)
    - Worsening psychiatric diagnosis
    - Increased risk of infection
    - Risk of glaucoma/cataracts
    - Fluid retention
    - Adrenal suppression
    - Hypertension

- **Immune modulator therapy/thiopurines**
  - Increased risk for non-Hodgkin’s lymphoma
  - Increased risk nonmelanoma skin cancer
  - Drug interactions: warfarin, ACE inhibitors, NSAIDS
  - Pancreatitis
  - Bone marrow suppression

- **Methotrexate**
  - Low dose appears safe
  - Patients with impaired renal function are at risk for toxicity
  - Liver enzyme elevations, resolve with discontinuation of medication
  - Liver fibrosis
  - Leucopenia
  - Gastrointestinal symptoms to cause discontinuation of medication
  - Folic acid depleted by methotrexate must be replenished through supplementation, which will add to pill burden
- Cyclosporine
  - Elderly most likely to experience side effects
  - Interacts:
    - with certain antibiotics (e.g. gentamicin and vancomycin) and leads to nephrotoxicity
    - NSAIDs
    - H2 receptor antagonists
    - Cyclosporine oral will increase level or effect of verapamil and allopurinol oral by alternating drug metabolism
    - Phenytoin, rifampin, carbamazepine and phenobarbital reduce cyclosporine blood levels via increased hepatic metabolism

- Biologic therapies
  - Increased infection risk
  - Heart failure
  - Decreased clearance
  - Unable to receive live vaccines

**TIP #7**: Recognize that nonadherence to medications is common among the elderly and consequences are profound. Adherence to medications remains vital to achieving optimal outcomes with most medication regimens. (van Eijken, Tsang, et al 2003. MacLaughlin, Raehl, et al 2005. Balkrishnan, 1996)

- True rate of adherence to medication regimens is only about 50% in the general population and ranges from 26-59% in persons aged ≥60 years
- More problematic for older patients who experience a higher number of medical conditions and use more medications
- Leads to higher physician visits, hospitalizations, and nursing home admissions
- May result from forgetfulness, avoidance of troublesome adverse effects, physical inability to self-administer medications, economic limitations, and intentional underdosage.
- High incidence of marginal or inadequate functional health literacy (inability to read, understand, and act on health information)
- Increased nonadherence from medical-related factors, e.g., decreased visual acuity, hearing, and manual dexterity
- Other medical conditions predict nonadherence, e.g., cognitive impairment, increased psychological stress, and depression
- Over the counter (OTC) and herbal medications are often overlooked
  - Supplements may indicate enthusiasm for alternative medications and disappointment with traditional prescribed medications with intentional nonadherence to prescription drug regimens
  - Extensive cost of OTCs, herbal supplements, and alternative medications further prompt the elderly to intentionally underdose prescription medications
- Several socio-behavioral characteristics and patient beliefs predict medication adherence, such as
  - Provider-patient interactions
  - Patients’ knowledge, understanding, and beliefs about their disease
  - Adherence differs whether treatment targeted towards prophylaxis and symptomatic treatment versus symptomatic treatment
  - Maintenance therapy important treatment for IBD
  - Medication adherence demands a relationship between a patient and his/her caregiver
Medication adherence demands a working relationship between patient, caregiver, and prescriber that values open and honest discussion about medications, i.e., the administration schedule, intended benefits, adverse effects, and costs.

Routine assessment of medication adherence in the elderly is rarely performed in everyday clinical practice.

**TIP #8: Identify incidence of surgery in the elderly and the risks associated before, during and after surgery.** (Tremaine, Timmons, et al. 2007)

In Crohn’s disease (CD):
- Necessity for surgery is lower in CD patients with a higher age of onset of disease
- Surgery for obstruction, fistula, and bleeding is associated with increased risk of postoperative complications in the elderly compared to young patients
- Recurrence of Crohn’s disease after bowel resection is reportedly less in elderly than in younger patients, but when it did occur, time to recurrence was significantly shorter
- Corticosteroid or immunosuppressive treatment increases postoperative complication rate
- High-dose corticosteroid use is worse in CD than in UC
- Need to take into account cognitive function or other conditions that would interfere with ability to comply with treatment associated with surgery

In ulcerative colitis (UC):
- Dysplasia is a more common indication for colectomy
- Because of the lower life expectancy, the functional outcome might be more important than the long-term risk of malignancy.
- Ileal J pouch anal anastomosis (IPAA) is a surgical technique of choice in UC if patient has good anal sphincter function and no history of fecal incontinence
- Ileal J pouch anal anastomosis (IPAA) still has a place in elderly UC patients with report of high patient satisfaction
- Incidence of anastomotic leak, pouch-related septic complications, and ileal anal pouch failure rates do not differ between younger and older patients undergoing surgery for UC.


- Acknowledge that colitis associated colorectal cancer is one of the most feared complications of long-standing UC and Crohn’s colitis.

- Risk factors associated with the development of colorectal neoplasia in this patient group:
  - Disease extent and duration
    - Patients with subtotal colitis and pancolitis have the highest risk
    - Patients with proctitis or distal proctosigmoiditis have lower risk, same as the general population
    - Patients with left-sided disease to the splenic flexure carry intermediate risk but their risk increases as disease duration increases
    - Relative risk (RR) increases after 8-10 years of disease, this is the rationale for initiation of surveillance colonoscopy, then every 1-3 years thereafter
  - Severity of histologic and endoscopic inflammation
  - Colitis associated dysplasia
Family history

Primary sclerosing cholangitis

Guidelines are not different than a younger IBD population but need a considered approach.

Refer to Table 1 under Guidelines in Tips for Colorectal Cancer already established (adapted from Guagnozzi and Lucendo, 2012)

Elderly patients with IBD must be considered in two groups: those diagnosed at a younger age, i.e., before the age of 60 (longstanding IBD) and those with onset of IBD at a later age (late-onset IBD)

Those with long standing IBD have a higher risk of CRC

With advances in therapy for UC, patients are keeping their colons longer, thereby increasing risk of dysplasia as well as sporadic (not related to UC) polyps

The risk of sporadic colon polyps increases with age

The overriding principle governing colorectal cancer screening is that it should only be done in patients deemed fit to undergo colectomy should dysplasia be found and in patients with a life expectancy such that they would benefit

Increasing age is an independent risk factor for developing complications at colonoscopy such as colonic perforation.

Careful patient selection and counseling are key determinants to good outcomes.

TIP #10: Learn the different reasons for why the elderly have both increased risk of infection and increased severity of infection. (Werner, Kuntsche 2000, Castle 2000)

- Different epidemiology, age related-alteration in immune function
- Increased co-morbidities
- Elderly present with non-specific symptoms of infection that may lead to life-threatening delay in diagnosis and therapy
- Infections are the leading cause of hospital admissions and death in this population
- Immunosuppressive therapy is a leading risk factor for infectious complications
- Incidence of TB increases with age

TIP #11: Develop preventive infection measures fundamental to these patients, based on risk identification, vaccination, and prophylactic treatment. (Viget, Vernier-Massouille 2008. Melmed, Agarwal, et al 2010)

- Before initiating therapy:
  
  Evaluate for latent TB infection
  
  • Chest X-Ray (CXR)
  
  • Interferon gamma release assay (TB Quanterferon)
  
  • Contact with infectious patients
  
  • Travel history
  
  Hepatitis B virus
  
  HIV in high risk populations
  
  History VZV, HSV and CMV infection
  
  Serum and urine screening for endemic mycoses recommended
  
  Verify vaccine status
  
  • Vaccine response is diminished in the elderly
  
  Prophylaxis with sulfamethoxazole/trimethoprim for patients on cyclosporine A or tacrolimus or a combination therapy of three immunosuppressant agents
References


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