

# CLINICAL UPDATE

## Myths and Misconceptions in the Management of Elderly Patients With Inflammatory Bowel Disease



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The diagnosis and management of elderly patients with inflammatory bowel disease (IBD) can be very challenging, even to experienced clinicians. These tasks can be further complicated by a series of misconceptions that can impact appropriate use of therapies. This column attempts to correct such misconceptions by reviewing the published literature.

### **G&H** Do elderly patients with IBD have milder disease?

**SK** Elderly patients often have more severe disease and higher hospitalization, infection, and surgical rates. Comorbidities limit the use of immunomodulators, as elderly patients have more frequent complications from these agents.<sup>1</sup> The cumulative median 1-, 5-, and 10-year risk of surgery in elderly-onset Crohn's disease (CD) is 13.5%, 24.0%, and 31.5%, respectively, with a higher surgical risk in the first year of diagnosis compared with younger adult-onset CD.<sup>2-6</sup> In ulcerative colitis (UC), the median risk of colectomy at 1, 5, and 10 years is 4.0%, 7.5%, and 8.0%, respectively. IBD-related mortality is higher in elderly-onset CD than in younger adult-onset CD (33.1 vs 5.6 per 10,000 person-years;  $P<.01$ ) and in elderly-onset UC vs younger adult-onset UC (2.89 vs 1.33 per 10,000 person-years;  $P=.25$ ).<sup>7</sup>

### **G&H** Do elderly patients represent a small percentage of the IBD population?

**SK** Elderly patients will represent one-third of the IBD population by 2030.<sup>8-10</sup> Currently, 26% of patients with IBD are older than 65 years. The highest age-specific prevalence for IBD occurs between ages 60 to 64 years for women and ages 70 to 74 years for men.<sup>11</sup> The incidence of elderly CD (>60 years) is 4.5 per 100,000 person-years, whereas the incidence of elderly UC is 11.6 per 100,000 person-years.<sup>12,13</sup>

### **G&H** Are symptom presentation and phenotype the same in elderly patients as in younger patients?

**SK** Colonic disease is more frequent in elderly patients, as are paradoxical constipation and more severe first attacks

of UC.<sup>14</sup> There is less progression of Crohn's ileocolonic/colonic disease to fistula/stricture.<sup>5</sup>

### G&H Is the differential diagnosis the same in elderly and younger patients with IBD?

**SK** Elderly patients have a more complicated differential diagnosis given other comorbidities (ie, segmental colitis associated with diverticular disease, ischemic colitis,

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medication-associated diarrhea, immune checkpoint inhibitor colitis, microscopic colitis, radiation colitis, and infectious diarrhea),<sup>15</sup> often delaying diagnosis by as long as 6.4 years compared with 2.4 years in younger patients with IBD.

### G&H Is surgery too risky in elderly patients with IBD?

**SK** Careful selection of elderly patients (eg, with retained anal sphincter function) and avoidance of corticosteroids and narcotics allow for ileoanal pouch surgery with essentially the same outcomes as in younger patients and no greater incidence of anastomotic leaks.<sup>3,16,17</sup> Frail elderly patients have more postoperative complications, longer hospital stays,<sup>18</sup> and greater fecal incontinence after colonic resections, giving pause to the use of ileal pouch-anal anastomosis in unselected patients.<sup>19</sup>

### G&H Is medical therapy the same in elderly and younger patients with IBD?

**SVK** Drug-drug interactions (eg, warfarin and IBD drugs) are more prevalent in elderly patients who have IBD. In addition, altered pharmacokinetics merit dose

reduction or alternative therapy.<sup>20-22</sup> The greatest risks occur with corticosteroids,<sup>23-27</sup> with a greater than 2-fold increased risk for serious infection. In addition, there is a higher incidence of corticosteroid-related insomnia and delirium,<sup>27</sup> as well as long-term worsened osteoporosis, fractures, hyperglycemia, cataracts, and cardiovascular disease, and even an increased risk of death with chronic corticosteroid use<sup>28</sup> vs anti-tumor necrosis factor (TNF) treatments.

### G&H Does the immune system function the same in elderly vs younger patients?

**SVK** The aging immune system is associated with an increased risk of infection, mortality, and malignancy. In addition, immunosenescence<sup>29-31</sup> creates an altered microbiome.<sup>32-36</sup> Infection susceptibility is markedly increased with thiopurines, with a higher risk of serious and opportunistic infections as well as lymphoma. The risk of infection in elderly patients older than 65 years was 15 times higher than in younger adults, corresponding to incidence rates of 5.41 vs 0.37 per 1000 patient-years, respectively.<sup>37,38</sup> Elderly patients exposed to thiopurines had a 4.8-times greater lymphoma risk than younger adults. The absolute risk is 1 lymphoma per 354 thiopurine-treated patients per year.<sup>39</sup> Aging confers immunodeficiency of innate and adaptive immunity, giving rise to increased vulnerability to immune-mediated disease.<sup>29,40</sup> These alterations are accompanied by an increase in mortality and changes in mucosal activity, permeability, and the gut microbiome (eg, more facultative and obligate anaerobes and *Bacteroides* and fewer Firmicutes and Bifidobacteria).<sup>41</sup>

### G&H Should biologics be avoided in elderly patients with IBD?

**SVK** If managed with care and pharmacologic vigilance, biologics can be used to control active disease in elderly patients. However, there can be an increase in infections, and combination therapy is less well tolerated.<sup>42-47</sup> Older French IBD patients given anti-TNF monotherapy had a higher risk of lymphoma,<sup>48</sup> yet no significant increased risk of serious infection compared with older IBD patients who received combination anti-TNF therapy and vedolizumab (Entyvio, Takeda).<sup>49</sup>

### G&H Should the approach to IBD treatment change after a certain age?

**SVK** Aging itself is not a risk factor for worsening disease activity. Fit patients are chosen for more aggressive therapies and are distinct from frail IBD patients.<sup>50</sup>

Frailty is a decline in the brain, immune, and endocrine systems, as well as in skeletal muscle, that is more rapid and supersedes the expected gradual decline in normal aging.<sup>51</sup> Frailty assessment supersedes chronologic age.<sup>52</sup> Sarcopenia, the loss of muscle mass, quality, and strength especially common in elderly patients, plays a key role in

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frailty, as does malnutrition.<sup>53,54</sup> Frailty is an independent predictor or risk factor for surgery and postoperative complications in IBD.<sup>55</sup> The Geriatric Nutritional Risk Index, which is calculated from serum albumin, body weight, and height, negatively correlates with disease activity, is predictive of hospitalization and surgery, and is of greater value than age or albumin alone.<sup>5,56,57</sup>

### G&H Does COVID-19 carry excessive risk in elderly patients with IBD?

**SVK** Indeed, the literature on COVID-19 noted excess mortality approaching 80% in patients with IBD who are older than age 65 years.<sup>46</sup> The Chinese experience recorded an overall fatality rate of 8% in patients ages 70 to 78 years and 14.5% in patients older than age 85 years.<sup>58</sup>

Of 2257 IBD patients in 4 clinical trials, 231 were age 60 years or older. Although these older patients had an increased risk of serious adverse events at baseline, there was no increased risk attributed to anti-TNF therapy—that is, no significant differences from placebo for severe or nonsevere infections with anti-TNF therapy (serious adverse events were reduced by 5.4% in elderly patients vs 2.4% in younger patients). Hospitalizations were reduced by 6.7% in elderly IBD patients vs 2.5%

in younger IBD patients, and there was no decrease in efficacy of anti-TNF–induced remission (odds ratio [OR], 1.05; 95% CI, 0.33–3.39) or in maintaining remission (OR, 0.49; 95% CI, 0.18–1.33).<sup>59</sup> The experience to date does not indicate an increased risk of COVID-19 with IBD or with biologic therapy. Increased age in a Veterans Affairs study of 37,857 patients was not a risk on its own, but was linked to an increase in severe outcomes when combined with comorbidities.<sup>60</sup> Glucocorticoids are a known risk factor for worse outcomes,<sup>61</sup> yet a meta-analysis of 249,095 patients revealed a lower COVID-19 incidence in IBD patients on anti-TNF therapy. Conceivably, anti-TNF agents may be protective against COVID-19.<sup>61–63</sup>

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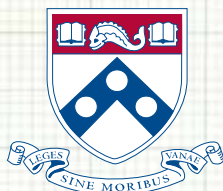
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