The Gastrointestinal Tract

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Young Kim and Timothy A. Pritts

Abbreviations

AAST	American Association for the Surgery of Trauma
ATLS	Advanced Trauma Life Support
CCK	Cholecystokinin
CDI	*Clostridium difficile* infection
CT scan	Computed tomography scan
DNA	Deoxyribonucleic acid
EAST	Eastern Association for the Surgery of Trauma
ENS	Enteric nervous system
FAST	Focused assessment with sonography for trauma
GI	Gastrointestinal
HSC	Hematopoietic stem cells
ICU	Intensive care unit
IDSA	Infectious Diseases Society of America
LOS	Length of stay
NK cell	Natural killer cell
NSAID	Nonsteroidal anti-inflammatory drug
OIS	Organ injury scale
SHEA	Society for Healthcare Epidemiology of America
TLR	Toll-like receptor
VTE	Venous thromboembolic event

Introduction

The average life expectancy in the United States is 80 years [1]. With advances in healthcare extending the length and quality of our lives, injuries in the geriatric population continue to be increasingly common. This population harbors multiple medical comorbidities and a decreased physiologic reserve, resulting in higher morbidity and mortality rates following acute trauma [2]. Gastrointestinal injury and illness can be especially devastating among the elderly. The following discussion highlights age-related changes in gastrointestinal physiology, the management of gastrointestinal injury, and other common gastrointestinal diseases affecting the elderly.

Age-Related Changes in Gastrointestinal Physiology

The gastrointestinal system spans multiple organs and is intricately involved with all other systems. While its chief function is digestion and absorption of nutrients, these organs also play vital roles in immunity, fluid and electrolyte balance, detoxification, expulsion of waste, and the neuroendocrine axis. Advanced age confers a natural decline in each of these functions. Reviewed in this section are the effects of aging on gastrointestinal motility, the enteric nervous system, gut mucosa, enteral absorption, and mucosal immunity.

Gastrointestinal Motility

Gastrointestinal motility refers to the transit of ingested food throughout the alimentary tract. After the ingestion of food and other nutrients, coordinated muscle contractions propagate caudal movement of digested material. These involuntary contractions are termed peristalsis. Aging diminishes motility in each of the luminal organs to varying degrees. In the esophagus, advanced age is associated with a decrease in functional peristalsis, and an increase in nonfunctional propagations [3].

Y. Kim, MD, MS
Clinical Instructor in Surgery, University of Cincinnati, Department of Surgery, 231 Albert Sabin Way, ML 0558, Cincinnati, OH 45267-0558, USA
e-mail: kim2yg@ucmail.uc.edu

T.A. Pritts, MD, PhD, FACS (✉)
Divisions of General Surgery and Trauma, Critical Care, and Acute Care Surgery, University of Cincinnati, Department of Surgery, 231 Albert Sabin Way, ML 0558, Cincinnati, OH 45267-0558, USA
e-mail: prittsta@ucmail.uc.edu

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Esophageal resistance is also heightened with age [3]. The lower esophageal sphincter, located between the esophagus and stomach, serves to protect the esophagus from gastric secretions. In healthy adults, this sphincter naturally relaxes with swallowing to allow for the passage of food. Swallow-induced relaxation becomes increasingly impaired with advanced age [4]. Each of these changes is implicated in the development of dysphagia among elderly patients, which may contribute to an overall malnourished state [5].

The stomach is similarly affected by age in several ways. The primary change is hypochlorhydria, or diminished secretion of gastric acid [6]. Because the acidity of digested chyme allows for absorption of iron and certain vitamins, hypochlorhydria may result in iron-deficiency anemia or other hypovitaminoses. Gastric motor function is mostly preserved with aging, with minimal changes in gastric emptying [3]. Fundal compliance is reduced, however, limiting food capacity and further affecting overall nutrition [6].

Once digested food has left the stomach, it enters into the small intestine. The small intestine is subdivided into the duodenum, jejunum, and ileum and is the primary organ responsible for nutrient absorption. Like the esophagus, coordinated smooth muscle contractions mediate the passage of chyme through the lumen. With advanced age, these migrating motor complexes become less frequent in nature [3]. Furthermore, animal models have demonstrated an increase in intestinal length and circumference [7], in addition to increased levels of intramuscular collagen [8], which may affect the strength of intestinal peristalsis. Despite these changes, transit time through the small intestine remains unaffected with healthy aging [3].

The colon is primarily responsible for the reabsorption of water, and delayed colonic motility often results in constipation. Unlike stomach and small intestine, colonic transit time is significantly prolonged with advanced age [9]. Human studies have found a decreased number of myenteric neurons in the colon with aging [10], as well as a proportional increase in abnormally appearing myenteric ganglia [11]. These changes contribute to a decreased number of high-amplitude contractions [12], which may explain the reduced propulsive capacity of the aging colon [13]. Not surprisingly, constipation affects half of community-dwelling elderly and the majority of nursing home population [14].

Enteric Nervous System

The enteric nervous system (ENS) is one of three major subdivisions of the peripheral nervous system. It plays a central role in the coordination of gastrointestinal motility and secretions [15]. Anatomically, the ENS consists of a network of interconnected neurons, arranged into two major plexuses – Auerbach's myenteric plexus and Meissner's submucosal plexus. These plexuses exist within the wall of the alimentary organs themselves. The ENS develops from neural crest cells [16] and continues to develop postnatally over the course of the host life [17]. Like the autonomic nervous system, the ENS functions involuntarily and is affected by a variety of external factors. These factors include the host environment, endocrine system, autonomic nervous system, and specialized gastrointestinal pacemaker cells known as the interstitial cells of Cajal [18].

The principal age-related change in the enteric nervous system is neurodegeneration [8, 19]. As compared with the rest of the nervous system, neurons of the ENS are more susceptible to age-related degeneration and death [20]. Some studies have suggested that age-related neuronal loss does not occur in other parts of the nervous system [21]. Neuronal loss in the ENS is most pronounced in cholinergic neurons within myenteric plexus [3, 22]. In contrast, the submucosal plexus is not affected by age-related decline [23]. Interstitial cells of Cajal also demonstrate an age-related decline within the stomach and colon [24], as do the autonomic nerves associated with the ENS [3]. Intestinal smooth muscle cells innervated by the ENS are similarly affected with aging [25]. Recent studies have proposed oxidative stress and mitochondrial dysfunction as the mechanisms of age-related neurodegeneration [3].

As mentioned previously, small intestinal transit time is minimally affected with healthy aging, while colonic motility is significantly prolonged. These findings are supported by literature regarding age-related changes in the ENS. In one animal study, the loss of half of small intestine myenteric neurons did not change feeding or defecating habits [7]. In a separate animal study, age-associated enteric neurodegeneration resulted in delayed colonic transit [22]. Clearly, the effects of aging on the ENS and gastrointestinal motility are synergistic.

Gut Mucosa

Mucosal epithelium lines the entire alimentary tract and serves multiple functions. In the stomach, the mucosal lining is responsible for the secretion of gastric acid, digestive enzymes, mucous, intrinsic factor, and various enteric hormones. The small intestinal mucosa also secretes mucus but is also involved in vitamin and nutrient absorption. Within the colon, mucosal epithelium functions primarily in water and electrolyte absorption.

In addition, the gut mucosa serves as a barrier to enteric organisms throughout the entire gastrointestinal tract. The stomach itself encompasses numerous defense mechanisms by which it maintains its mucosal integrity [26]. These defense mechanisms are broadly divided into three categories – pre-epithelial, epithelial, and post-epithelial defenses.

Pre-epithelial defense mechanisms include the mucous lining, secreted phospholipids, and an alkaline pH [27]. The gastric mucosal epithelium itself consists of continuously regenerating gastric cells bound by tight junctions, which are responsible for generating these pre-epithelial defenses [27]. Post-epithelial factors include continuous mucosal blood flow and the generation of nitric oxide and prostaglandins [27, 28].

With aging, each of these defense mechanisms becomes attenuated. Gastric glands are atrophied and replaced with fibrous tissue [26]. Mucous and bicarbonate secretion is impaired [29, 30]. There is a reduction in the capacity for prostaglandin generation [31]. Overall gastric blood flow is also diminished [32, 33]. These sums of age-related changes predispose the elderly to gastric injury. Several clinical studies have found advanced age to be a significant risk factor for NSAID-related gastropathy [34, 35]. Even low-dose aspirin, which has a lower risk of drug-related complications, has been linked to gastrointestinal hemorrhage among the elderly [36].

Mucosal cells throughout the intestine and colon also suffer an age-related decline. Mucosal epithelium has a high turnover rate within the intestine, regenerating itself every 4–5 days [37]. Thus, epithelial proliferation and death must be equally balanced. Hematopoietic stem cells (HSC) residing within intestinal crypts are the primary source of mucosal epithelial cells [38]. In animal models, HSC numbers and functional ability are gradually exhausted with advanced age [39].

As with gastric mucosa, aging colonic epithelium is prone to cellular injury [26, 40]. Two cellular mechanisms have been elucidated: increased rates of apoptosis and impaired proliferative potential. Apoptosis, or programmed cell death, is a mechanism by which cells are removed without injuring the surrounding tissue. With old age, colonic epithelial cells alter their protein expression rendering them more prone to apoptosis [40]. These cells also exhibit shortened telomeres [41], which reflect an impaired ability to replicate [42].

Enteral Absorption

Elderly patients are particularly vulnerable to malnourishment, which often goes unrecognized and underdiagnosed [43]. In turn, malnutrition is a significant predictor of morbidity and mortality [44, 45]. Poor nutrition among the elderly can be attributed to two causes: diminished food intake and decreased enteral absorption.

Age-related physiologic decline in food consumption is multifactorial. Sensory dysfunction of taste and smell weakens the appeal of food [46]. Gastric fundal compliance is reduced, which causes pronounced stretching of the stomach with food intake [6]. Aging is associated with elevated cholecystokinin (CCK) levels, which also contribute to early satiety [47]. As the aging stomach becomes hypochlorhydric, the intestine becomes predisposed to malabsorption and bacterial overgrowth [6]. Bacterial overgrowth syndromes, which are more prevalent among the elderly, damage the intestinal brush border and can also contribute a malabsorptive state [48].

Decreased oral intake of food is further compounded by a natural decline in enteral absorption. Cellular senescence within the gut mucosa, as previously described, is the primary mechanism for this decline. Both human and animal models have demonstrated a decreased uptake of macronutrients among the elderly [49]. Impaired carbohydrate absorption has been determined using breath analysis tests [50]. A similar decline in lipid absorption has been linked to a decrease in enterohepatic recycling of bile [51, 52].

Mucosal Immunity

The gut is the largest immune organ, containing the majority of lymphoid cells within the human body [53]. It is also home to an immense number of commensal bacteria. These bacteria, often referred to as the *gut microbiome*, play an important role in host health and disease states [54]. While the interactions between the gut microbiome and its host organism are not completely understood, these bacteria have been linked to obesity [55], diabetes [56], allergies [57], psychiatric disorders [58], and even coronary artery disease [59]. The complex signaling pathways between GI system and its microbiome are still being elucidated [60].

The bacterial composition of the gut microbiome is fluid in nature. Many factors have been linked to changes in the microbiota, including stress, illness, antibiotic exposure, dietary variations, and aging [61]. DNA-based techniques have been used to quantify these population shifts in the elderly, noting a significant reduction in overall microbial load [62].

Like the gut microbiome, mucosal immunity is also attenuated with advanced age. Aging is associated with blunted adaptive immunity and activated innate immunity [63], which lead to a chronic low-grade proinflammatory state [64]. There is an age-dependent variation of lymphocytes within intestinal mucosa, including increased populations of natural killer (NK) cells and double-positive T-cells [65]. Furthermore, immune homeostasis within the alimentary tract becomes imbalanced among the elderly. Intestinal immune homeostasis has been shown to be mediated by negative regulation of toll-like receptors (TLR) [66]. Several studies have shown that the TLR system is dysregulated with advanced age [67, 68]. These age-associated defects in TLR signaling may lead to increased incidence of gastrointestinal infections among the elderly [69].

Gastrointestinal Injury

Gastrointestinal injury refers to traumatic damage to the stomach, small intestine, colon, or rectum. While penetrating trauma is more commonly associated with gastrointestinal injury, blunt abdominal trauma may also harm the alimentary tract [73]. The lesion itself can range from minor hematomas to complete devascularization. The organ injury scale (OIS) was developed by the American Association for the Surgery of Trauma (AAST) as a tool for grading the severity of organ injury and can be found in Table 5.1 [74].

According to the Eastern Association for the Surgery of Trauma (EAST) guidelines, there should be a lower threshold for trauma activation in elderly patients [75]. Once the trauma system has been activated, it is imperative to address life-threatening conditions prior to pursing further diagnostic studies. The Advanced Trauma Life Support (ATLS) primary survey addresses such deficits in ventilation, oxygenation, and circulation and is reviewed elsewhere [76]. It is imperative to note that vital signs are misinterpreted in geriatric trauma victims. For example, normotensive blood pressures may be misleading in a patient with baseline hypertension. Beta blockers, which are commonplace among the elderly, may also blunt the normal adrenergic response to hemorrhage.

Once life-threatening conditions have been addressed, focused assessment with sonography for trauma (FAST) exam is a reliable adjunct for detecting free intraperitoneal fluid. Physical examination is often unreliable due to impaired level of consciousness, neurologic defects, drug or alcohol intoxication, or use of sedatives. Certain physical exam findings, however, should arise suspicion for intra-abdominal injury. These include the seatbelt sign, rebound tenderness, hypotension, abdominal distention or guarding, and concomitant femur fracture [77]. If an intra-abdominal injury is suspected, either by physical finding or mechanism of injury, the hemodynamically normal patient should proceed with computed tomography (CT) imaging of the abdomen.

CT imaging is the gold standard for diagnosis of occult gastrointestinal injury. Findings suggestive of bowel injury include pneumoperitoneum, bowel wall thickening, mesen-

Table 5.1 Organ injury scale

Organ	Grade	Description
Stomach	Grade I	Hematoma <3 cm
		Partial-thickness laceration
	Grade II	Hematoma ≥3 cm
		Full-thickness laceration <3 cm
	Grade III	Full-thickness laceration ≥3 cm
	Grade IV	Full-thickness laceration involving vessels along greater/lesser curvature
	Grade V	Extensive organ rupture
		Devascularization
Small intestine	Grade I	Contusion or hematoma without devascularization
		Partial-thickness laceration
	Grade II	Full-thickness laceration involving <50 % circumference
	Grade III	Full-thickness laceration involving ≥50 % circumference
	Grade IV	Transection without tissue loss
	Grade V	Transection with tissue loss
		Devascularization
Colon	Grade I	Contusion or hematoma
		Partial-thickness laceration
	Grade II	Full-thickness laceration involving <50 % circumference
	Grade III	Full-thickness laceration involving ≥50 % circumference
	Grade IV	Transection without tissue loss
	Grade V	Transection with tissue loss
		Devascularization
Rectum	Grade I	Contusion or hematoma
		Partial-thickness laceration
	Grade II	Full-thickness laceration involving <50 % circumference
	Grade III	Full-thickness laceration involving ≥50 % circumference
	Grade IV	Full-thickness laceration extending into the perineum
	Grade V	Devascularization

teric fat stranding, extravasation of oral contrast, and free intraperitoneal fluid in the absence of solid organ injury. The specificity of CT imaging is greater than 90 % in the presence of these findings, but its sensitivity is only 55 % [78–80]. Because delayed diagnosis is associated with substantial morbidity [80], the patient with suspected bowel injury should be monitored with serial vital signs and abdominal exams regardless of CT findings. Signs of missed bowel injury include abdominal tenderness, peritonitis, abdominal distention, new-onset leukocytosis, hyperamylasemia, and prolonged ileus [81]. Once bowel injuries are detected, treatment is surgical.

Prior to operative intervention, antibiotic prophylaxis and thromboprophylaxis should be considered for all patients. Antibiotics should be directed toward the site of injury for a 24-h duration. Prolonging antimicrobial therapy over 24 h offers no benefit in surgical site or nonsurgical site infection rates [82, 83]. Given that trauma and old age are both predictors of venous thromboembolic events (VTE), mechanical and chemical thromboprophylaxis should both be initiated [84]. Chemoprophylaxis involves either unfractionated or low molecular weight heparin and may be contraindicated with certain patterns of traumatic brain injury.

After prophylactic measures have been addressed, abdominal exploration should proceed in a systematic fashion [85]. Control of intraperitoneal hemorrhage and fecal contamination are of utmost importance and take priority during the initial phase of intraoperative care. Afterward, bowel injury may be assessed and graded according to the aforementioned organ injury scale (OIS). In general, injuries graded OIS I–III may be primarily repaired, while OIS IV and V are resected. A second-look operation may be planned if the viability of a bowel segment is indeterminate. Abdominal closure depends on several factors, including anatomical constraints, the risk of abdominal compartment syndrome, and whether a second-look operation is necessary.

Following surgical exploration, the elderly patient should be monitored in the intensive care unit (ICU) setting. A geriatrician should be consulted for assistance in medical management [86, 87]. Finally, all trauma victims must be reexamined for inventory of any missed injuries.

Gastrointestinal Ileus

Gastrointestinal ileus is defined as a pathologic reduction or absence of intestinal peristalsis. Postoperative ileus is common after surgery in all age groups [88], but elderly patients are particularly sensitive to disturbances in intestinal motility [72]. The pathophysiology of ileus is multifactorial, owing primarily to neurogenic, inflammatory, and enteroendocrine factors [89]. Risk factors for the this condition include advanced age, extensive bowel manipulation, narcotic-type analgesics, and general anesthesia [90]. Furthermore, the intestines are susceptible to age-related neuronal degeneration, placing the geriatric patient at profound risk of prolonged ileus [10, 70, 71].

Signs and symptoms of ileus include lack of flatus, abdominal distention, nausea, and emesis. Postoperative ileus is most pronounced within the large bowel; therefore, flatus is a common sign indicating return of bowel function. Peristalsis within the small intestine and stomach returns to normal within the first postoperative day, but colonic peristalsis may be stunted upward for 72 h [91].

Postoperative ileus is a clinical diagnosis, and its management is largely supportive. Bowel rest and fluid resuscitation are the mainstay of therapy until bowel function returns spontaneously. Nasogastric decompression is theorized to mitigate the risk of aspiration pneumonia in patients with recurrent emesis, though this fact remains debated. Early ambulation is often implemented under the notion that physical motion may stimulate intestinal motility. Minimizing the use of narcotic medications may also accelerate the return of bowel function.

Alvimopan (*Entereg*), a peripherally acting *mu*-receptor antagonist, is the only FDA-approved medication for accelerated return of bowel function [92]. Since opioid medications impede gastrointestinal motility, in theory, peripheral opioid receptor blockade should have the reverse effect. Many studies have analyzed the efficacy of alvimopan on bowel function, with varying results. One multicenter, phase III trial found significantly accelerated return of bowel function and shorter hospital length of stay (LOS) with the use of alvimopan in patients undergoing major abdominal surgery [93]. A separate trial in urologic patients also found significantly decreased hospital LOS, as well as reduced cost per admission [94]. In patients undergoing laparoscopic gastrointestinal surgery, alvimopan reduced the risk of postoperative ileus by 75 %, though there was no significant effect on overall LOS [95]. Colorectal surgical patients benefited highly from alvimopan, with faster return of bowel function, lower incidence of postoperative ileus, shorter hospital LOS, and reduced cost [96]. Further trials may elucidate the optimal use of this promising medication.

Ogilvie Syndrome

Acute intestinal pseudo-obstruction, or Ogilvie syndrome, is an acute-onset, massive colonic dilation in the absence of mechanical obstruction. It is a severe form of gastrointestinal ileus limited to the large bowel. Its pathophysiology is multifactorial and primarily attributed to enteric dysautonomia [97]. Risk factors for Ogilvie syndrome include advanced age (>60 years), trauma, abdominal surgery,

orthopedic surgery, severe medical illness, metabolic derangements, and use of narcotic medications [98]. Thus, like ileus, geriatric trauma victims are at significant risk for developing this condition.

The most feared complication of Ogilvie syndrome is bowel perforation. Once intraluminal pressure exceeds capillary perfusion pressure, the colon is at risk of venous congestion, with resultant tissue ischemia, bowel perforation, intra-abdominal sepsis, and, possibly, death. With timely diagnosis and treatment, mortality rates are less than 20 %. However, this increases to greater than 40 % with delayed recognition and bowel perforation [98]. Therefore, early diagnosis is crucial to patient survival.

Initial evaluation with abdominal X-ray will reveal massive dilation of the colon. Cross-sectional CT imaging can confirm the diagnosis and, more importantly, rule-out secondary causes of obstruction.

Management of Ogilvie syndrome is similar to that of ileus. This includes bowel rest, nasogastric decompression, fluid resuscitation, correction of electrolyte imbalances, and minimizing use of narcotic medications. When cecal diameter reaches 12 cm, the risk of bowel ischemia increases markedly, necessitating chemical or mechanical decompression [99]. Neostigmine, a potent parasympathomimetic drug, stimulates intestinal motility and quickly decompresses the colon [100]. Because geriatric patients are prone to neostigmine-induced arrhythmias, including bradycardia, cardiac telemetry is advised prior to administration [101]. Symptomatic bradycardia is treated with atropine [102]. If neostigmine is ineffective or contraindicated, then endoscopic decompression is warranted [103]. Any evidence of peritonitis or bowel perforation requires surgical exploration.

Summary

Gastrointestinal diseases, such as hemorrhage and motility disorders are much more prevalent among the elderly. Each of these conditions carries significantly higher rates of morbidity and mortality in the older adult. Timely diagnosis and proper management are critical to good outcomes.

Case Vignette

Case 1: An 84-year-old male with a history of hyperlipidemia presents to the trauma bay after suffering a low-velocity motor vehicle collision. His primary survey is intact and his vital signs are normal on arrival. Abdominal ultrasound does not reveal any free intraperitoneal fluid. Physical examination reveals moderate abdominal discomfort and significant ecchymosis across his chest and abdomen, in the pattern of a seat belt. Because of his clinical presentation and mechanism of injury, he undergoes CT imaging of his abdomen, which reveals bowel wall thickening near the terminal ileum along with mesenteric stranding and free fluid in the pelvis. No other injuries are seen. What is the next step in management?

Discussion: The patient should be taken to the operating room for exploratory laparotomy. Gastrointestinal injury should be treated surgically once detected. This may involve primary repair or bowel resection, depending on the grade of injury. Antibiotic and VTE prophylaxis should be considered prior to surgery, as long as no contraindications exist.

Bullet-Point Summary

- Advanced age confers a natural decline in various aspects of gastrointestinal physiology, including gastrointestinal motility, the enteric nervous system, gut mucosa, enteral absorption, and mucosal immunity.
- Gastrointestinal injury is most commonly associated with penetrating abdominal trauma but may also result from severe blunt trauma. Upon recognition of GI injury, surgical intervention is indicated.
- Postoperative ileus can be profound in the geriatric patient.
- Ogilvie syndrome is a severe type of colonic ileus leading to massive colonic distention and may result in cecal perforation with delayed diagnosis.
- In any gastrointestinal condition, peritonitis and bowel ischemia are indications for operative intervention.

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