Lower GI Bleeding: An Update on Incidences and Causes

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Abstract

Keywords

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- diverticulosis
- vascular malformations
- cancer
- inflammatory bowel disease
- hemorrhoids

Bleeding from the lower gastrointestinal tract represents a significant source of morbidity and mortality. The colon represents the vast majority of the location of bleeding with only a much smaller incidence occurring in the small intestine. The major causes of lower gastrointestinal bleeding (LGIB) are from diverticulosis, vascular malformations, and cancer. We discuss the incidence and causes of LGIB.

Lower gastrointestinal bleeding (LGIB) is defined as any bleeding distal to the ligament of Treitz. LGIB constitutes about 20% of all GIBs and, therefore, it is important to rule out an upper GIB as a source. The annual incidence of LGIB ranges from 20.5 to 27 cases per 100,000 adults with hospital admissions ranging from 21 to 40 cases per 100,000 adults.^{1,2} The overall mortality is 2 to 4%. It occurs more frequently in elderly patients with an average age of 63 to 77 years.³ Of all LGIB, the vast majority is from the colon and anus with only about 5 to 10% originating from the small intestine.³ The nature of the GIB may be chronic and as such the presentation more insidious. Patients with chronic blood loss often present with anemia or hematochezia at a level which may not raise much concern for patient or practitioner. On the contrary, acute LGIB usually presents with melena, frank blood per rectum, and hemodynamic instability which often results in hospitalizations and may require resuscitation and/or transfusion to maintain normal vital signs. Fortunately, most LGIB resolve spontaneously. A comprehensive understanding of the common causes of LGIB is important for prompt diagnosis, localization, and treatment of bleeding. There is a wide variation in the reported causes of LGIB (► **Table 1**). The heterogeneity in the population studies, mode of diagnosis, nature of LGIB (chronic vs. acute), and

characterization of LGIB may explain the wide variation in the epidemiology across studies.

Diverticular Hemorrhage

Diverticular bleeding is the leading cause of LGIB with most studies reporting rates between 20 and 50%¹ but as high as 66%.⁴ However, the actual incidence of diverticular hemorrhage is often difficult to characterize as there are many instances of presumed diverticular hemorrhage when no clear source of bleeding is identified but diverticulosis is noted. Because of this discrepancy, the Centre for Ulcer Research and Education (CURE) hemostasis research group proposed a classification system of presumptive diverticular hemorrhage (diverticulosis identified on workup but no other evidence of bleeding on complete endoscopy), incidental diverticulosis (diverticulosis identified but another clear source of bleeding found), and definite diverticular hemorrhage. Based on this classification, definite diverticular hemorrhage was only found in 20% of patients with presumptive diverticular hemorrhage noted in 46%.⁵ Diverticular bleeding occurs in about 10 to 15% of patients with diverticular disease with severe hemorrhage occurring in an even smaller subset, approximately 3 to 5%.⁴ Diverticula form the point of weakness where the blood vessels,

Table 1 Causes of lower gastrointestinal bleeds

Author	Year	Diverticular bleeding	Ischemic colitis	Colon cancer	Polyps	Infectious colitis	Hemorrhoids	IBD	Rectal ulcer	Angiodysplasia	Non-specific colitis	Postpolypectomy bleeding	Radiation proctitis	Small intestine	Unknown	Miscellaneous/ other	Chronic colitis	Anorectal disease
Aoki et al ⁶⁸	2015	49.7	12.9	8.8	-	5	4.4	3.8	2.9	2.3	2.1	1.7	1.2	0.6	4.3	-	-	-
Bai et al ⁵⁸	2011	-	-	24.4	24.1	-	-	9.5	-	-	-	-	-	-	7.2	8.1	16.8	9.8
Ghassemi and Jensen ³⁵	2013	30	12	6	-	-	14	9	6	6	-	8	3	-	6	-	-	-
Gayer ¹⁹	2009	33.5	-	12.7	-	-	22.5	5.8	-	3.4	8	-	-	1.3	7.5	5.5	-	-
Richter et al	1995	48	-	11	-	-	-	-	-	12	6	-	-	-	-	6	-	3
Jensen and Machado ³⁹	1997	23	-	15	-	-	-	-	-	40	12	-	-	-	-	4	-	5
Longstreth ³⁶	1997	41	-	9	-	-	-	-	-	3	16	-	-	-	-	14	-	5
Strate and Syngal ³⁸	2003	30	-	6	-	-	-	-	-	3	21	-	-	-	-	28	-	14
Vernava et al ⁴²	1997	40	-	14	-	-	-	21	-	2	-	-	-	-	-	-	-	11
Venkatesh et al ⁶⁹	2014	26	6	8	14.2	-	19	4	1.3	4.5	-	-	-	-	-	-	-	1
Sengupta et al ⁷⁰	2015	18	7	-	-	3	8	18	3	-	-	8	3	1	30	-	-	-
Heinsson et al ⁷¹	2013	23.3	16	7.4	3.1	-	10.4	11.7	-	3.1	-	-	-	3.1	9.2	11	-	1.8

Abbreviation: IBD, inflammatory bowel disease.

Note: Values listed are % of the patients in each study with corresponding cause of LGIB.

which usually run outside the circular muscle layer, penetrates the colonic wall obliquely to run below the mucosa layer. As the diverticulum forms, the vessel is often displaced over the fundus and is in close proximity to the mucosa. Bleeding occurs from erosion or rupture of the vasa recti. Bleeding is usually not associated with inflammation and such not a hallmark of diverticulitis.⁶

Diverticular hemorrhage occurs mostly in the elderly and rarely seen in patients under the age of 40 years. This is likely based on the epidemiology of diverticulosis which is present in approximately 5% of population at 40 years of age but increases to about 65% of the population age 85 years in the United States and countries in Western Europe.⁷ Other risk factors for diverticula bleeding include hypertension, diabetes mellitus, coronary artery disease, and use of anticoagulation and non-steroidal anti-inflammatory drugs.⁸⁻¹⁰

Although diverticulosis is concentrated on the left side of the colon, bleeding frequently occurs from the proximal colon. This makes localization of the bleeding diverticulum a priority in management of these patients, especially if surgical intervention is deemed necessary.

The location of the diverticula bleed is often cited as more prevalent on the right side of the colon.⁷ However, this finding is based on the mode of localization. On colonoscopy, 60% of diverticula bleeds are noted on the left side. Conversely, when angiography is utilized and positive, 50 to 90% of the bleeding is found in the right colon.¹¹ The increased frequency of right sided diverticular bleed in relation to the prevalence of right sided diverticulosis may be based on the wider necks and domes of diverticula in this region; therefore, exposing a longer length of the vasa recta to injury.⁷

Most diverticular bleeds are self-limited with 75 to 90% resolving spontaneously.^{8,11-14} In a review article by Cirocchi et al, only 16% of patients with diverticula bleeding required any form of intervention (114 patients out of 700). Of the 114 patients that required intervention, endoscopic approach was used in 66% while transcatheter arterial embolization was performed 10.5% of the time. When conservative approach was employed, the overall failure rate was 2.6%. Surgical intervention was required in 28 patients, accounting for 25% of patients that required intervention for diverticular bleed.¹⁴ The likelihood of needing surgical intervention increases with more increasing amounts of blood products. When four or more units of blood were required in a day, approximately 60% of patients required emergency surgery.¹³

When diverticula bleed resolves spontaneously, it is important for providers and patients to be counseled about the risk of recurrent bleeding. Of the 123 patients with diverticular bleed managed conservatively, 13.8% presented with a recurrent diverticular bleed over an average follow-up period of 47.5 months. The estimated bleeding recurrence increased over time; 3.8% at 1 year, 6.9% at 5 years and 9.8% at 10 years.¹⁵ In a different study by McGuire, 38% of patients discharged without surgery had recurrent diverticular bleed.¹³ In a study by Aytac et al, 82% of patients with proven diverticular bleed were managed nonoperatively and 47% had a recurrent diverticular bleed after a median of 8.1 months. When recurrent diverticular bleeding occurs, there is a high likelihood of

surgical intervention required to stop bleeding. Of the 37 patients that had recurrent diverticular bleeding, all but one patient required surgical intervention.⁸ Rebleeding after surgical resection of the bleeding diverticulum is rare; however, can be as high as 42% when a blind resection is performed with morbidity and mortality rates as high as 83 and 57% respectively.¹¹

Hemorrhoids

Hemorrhoids are one of the most common problems encountered by colorectal surgeons with a prevalence ranging from 10 million people (4.4%) of the population to 23 million people (12.8%) of adult population in the United States.^{16,17} A diagnosis of hemorrhoids was associated with 3.2 million ambulatory care visits and 306,000 hospitalizations in the 2004 National Institutes of Health report.¹⁸

Bleeding from hemorrhoids is a major contributor to LGIB, although there is a large variation in proportion of LGIB that is due to hemorrhoids (► **Table 1**). In a series of 608 patients hospitalized for LGIB from 1998 to 2006 by Gayer et al, 128 patients (21.05%) was from hemorrhoids.¹⁹

Bleeding is usually from internal hemorrhoids and most patients present with painless hematochezia.

Bleeding is often in small amounts but a small subset of patients can present with significant bleeding to result in hemodynamic instability or severe anemia with associated consequences from chronic blood loss. A retrospective chart review of patients from the Mayo Clinic over a 15-year period showed that the incidence of hemorrhoidal bleeding that caused anemia was 0.5 patients per 100,000 population per year and definitive treatment with hemorrhoidectomy resulted in resolution of anemia.²⁰ Ibrahim et al reported five patients with obscure GIB requiring multiple transfusions that was ultimately from hemorrhoids.²¹

Neoplasia

Bleeding is a common symptom of neoplasms. Patients may present with hematochezia, melena, and more often with anemia as the blood loss is frequently occult. Bleeding from neoplasia is often reported to account for 10 to 15% of LGIB.²² Nonetheless, the incidence can be as high as 33%, as was reported by Rossini et al, out of over 400 patients.²³ Bleeding neoplastic lesions are often adenomatous polyps or adenocarcinoma of the colon. However, there have been a variety of reports of other forms of neoplasms causing bleeding including lipoma, multiple myeloma, metastatic tumors to colon, as well as angiosarcomas of the colon.^{24–27}

Inflammatory Bowel Disease

Bleeding is a common symptom in patients with inflammatory bowel disease (IBD). Bleeding may be occult or present as hematochezia. Acute LGIB is a rare but life-threatening complication of IBD. The prevalence ranges from 0.6 to 6% in patients with Crohn's disease (CD) to 1.4 to 4.2% in patients with ulcerative colitis (UC).^{28,29} In a series of 1,374 patients with

Crohn's disease, Li et al found 5.3% incidence of acute LGIB with an overall mortality of 8.2%.³⁰ Risk factors for acute LGIB include duration of CD, perianal disease, left colon involvement, and steroid use. The probability of bleeding increases with duration of Crohn's disease from 1.7% after 1 year, to 3.6% after 5 years, 6.5% after 10 years, and 10.3% after 20 years.³¹ Papi et al reported a series of 101 patients in which 40% (37 patients) underwent surgery during their first bleed with a mortality of 7%. Recurrent bleeding was higher among those who did not undergo surgery initially, 38.5% compared to 5.7%.³²

Acute LGIB in ulcerative colitis is often in the setting of severe disease refractory to medical therapy. Most UC patients with severe hemorrhage have extensive colitis and almost all have pancolitis.³³ The degree of hemorrhage often correlates with the severity of disease.³⁴

In an overview of emergencies in inflammatory bowel disease patients, up to 10% of all the urgent colectomies performed were due to hemorrhage in ulcerative colitis.³⁴

Vascular Malformations

A variety of vascular lesions are implicated in GIB. The major categories include arteriovenous malformations (AVMs), hemangiomas, and colonic varices with AVMs being the most common cause.⁶ The proportion of LGIB attributed to vascular malformations varies significantly in the literature. More recent studies report a range of 3 to 6%^{35–38}; however, there have been series that reported incidence as high as 40%.³⁹ AVMs are characterized by areas of ectasia in existing vessels which are tortuous and thin walled. AVMs are often used interchangeably with angiodysplasia in the literature; however Moore et al developed a classifications system of three categories in 1976.⁴⁰ Type I lesions are referred to as angiodysplasia which is the most common lesions and also the most common cause of bleeding.⁶ It occurs throughout the GI tract but most commonly on the right side of the colon. Meyer et al reviewed 218 cases of AVMs and found 78% in the cecum and right colon, 10.5% in the jejunum, 8.5% in the ileum, and 2.3% in the duodenum.⁴¹ It is acquired and, therefore, incidence increases with age. The exact etiology is unknown but chronic venous obstruction is thought to play a role. This theory explains the high prevalence of these lesions in the right colon based on Laplace's law.⁴² In a review of screening colonoscopies in 964 asymptomatic patients over the age of 50, Foutch et al noted the prevalence of angiodysplasia to be 0.83%.⁴³ Types II and III AVMs are congenital and, therefore, present in younger patients. They usually occur in the small bowel and are multiple.⁶

Hemangiomas are another form of vascular lesion present in the GI tract that can result in bleeding. It is further subclassified into capillary hemangiomas which consist of proliferation of capillaries with thin-walled spaces lined by endothelial cells; and cavernous hemangiomas which contain large endothelial lined blood filled sinuses. Cavernous hemangiomas are more common and usually involve the distal colon and rectum. They are implicated in a variety of syndromes including blue rubber bleb nevus and Klippel-Trenaunay syndromes.⁶

Colonic varices are a very rare cause of LGIB. They constitute permanently dilated veins in the submucosa and majority is due to portal hypertension. The incidence of colonic varices is 0.07% but it may account for 1 to 8% of LGIB in patients with cirrhosis.⁴⁴ Bleeding from varices carries a poor prognosis often due to the underlying cause of portal hypertension. There have been reports of familial varices which presented with LGIB in young patients.⁴⁵

Parastomal varices can present as LGIB. They are a result of anastomoses between the high-pressure portal venous system and the low-pressure systemic venous system around the stoma.⁴⁶ Bleeding results from trauma or erosion of a submucosal varix. In a review of 71 cases of bleeding from stomal varices, by Conte et al, 49 involved ileostomy varices, 15 involved colostomy varices, and eight involved ileal conduit varices. The average time from creation of the stoma to presentation with bleeding was 48, 38, and 23 months for ileostomy patients, ileal conduit patients, and colostomy patients, respectively.⁴⁶

Ischemic Colitis

Ischemic colitis was first described by Bailey in 1963. It has an estimated incidence of 4.5 to 44 cases per 100,000 person-years and accounts for about 1 in 2,000 hospital admissions. Hemorrhage is a common symptom occurring in 50 to 60% of patients.⁴⁷ Incidence increases with advancing age and is often cited among the leading causes of LGIB in elderly after diverticular bleed. The two common areas of ischemia in the colon are the splenic flexure (Griffith's point) and the rectosigmoid junction (Sudek's point) due to decreased collateral blood flow.⁷ Endoscopic evaluation of 57 patients with ischemic colitis showed left sided colitis in 88% of patient.⁴⁸ When compared to 313 patient hospitalized for LGIB, patients hospitalized with ischemic colitis had further bleeding, shorter hospital stay, and a lower transfusion requirement. In addition, the rebleeding rate was significantly lower in patients with ischemic colitis at 5.3% compared to other LGIB cases (19.3%) over a mean follow-up period of 22 months.⁴⁸

Radiation Enteritis/Colitis

Radiation is frequently utilized in the treatment of many malignancies. The rectum is the portion of the bowel most frequently affected with the late effects of radiation. Radiation causes changes in the mucosa characterized by telangiectasias, pallor, and friability caused by a chronic ischemic process due to obliterative endarteritis.⁴⁹ Studies report radiation proctopathy in 5 to 30% of irradiated patients but may be higher especially in patients treated for cervical cancer.^{47,49,50} Radiation related bowel complications are both dose and time dependent. Acute radiation symptoms develop within the first 6 weeks after treatment completion, while chronic radiation symptoms refer to those that develop or persist beyond 6 to 12 months after completion of radiation. Hematochezia is the most common symptom. It affects approximately 20 to 51% of patients. Approximately, 4 to 10% of patients who undergo radiation therapy are developed

significant bowel issues in the 5 to 10 years following treatment. This increases to 15 to 20% at 20 years.⁴⁷

Infectious Colitis

Diarrheal illnesses remain a leading cause of mortality worldwide and accounts for almost 2.5 million deaths annually. It accounts for 6,000 deaths and 900,000 hospitalizations in the U.S. annually.

Most cases of infectious gastroenteritis are viral but bacterial infections remain a significant contributor to morbidity and mortality from infectious colitis. The common bacterial causes include *Clostridium difficile*, *Escherichia coli*, O157:H7, *Salmonella*, *Campylobacter*, *Shigella*, and *Yersinia*. These mostly present with diarrhea; however, hematochezia can be a symptom.⁴⁷ It is important to rule out infectious causes when evaluating patients who present with LGIB, especially if presentation is acute and associated with diarrhea.

Anorectal Bleeding

Rectal bleeding is a common complaint from patients and is to be the sixth most common symptom prompting an outpatient clinic visit. Although the true incidence and prevalence of rectal bleeding is unknown, community based surveys suggest a 13 to 20% prevalence.⁵¹ Hemorrhoids constitute a significant portion of anorectal bleeding that present as LGIB and have been discussed earlier. However, there are a variety of other common anorectal diseases that can present with bleeding, such as anal fissures, fistula, solitary rectal ulcers, rectal prolapse, dieulafoy lesion, and anal cancer. Some of these have been implicated in massive LGIB. The presence of these diseases can be easily diagnosed with a thorough history and physical exam including anoscopy.

Small Intestinal Bleeding

Bleeding from the small intestine constitutes about 5 to 10% of all LGIB. A variety of lesions are responsible for bleeding from the small intestine with the most common being vascular lesions. Zhang et al found that in patients above 65 years, vascular anomalies accounted for 54.4% of the obscure GIB with small intestinal ulcers and tumors accounting for 13 and 12%, respectively. In patients aged 41 to 64 years, vascular abnormalities still accounted for a majority at 35%. Small bowel tumors followed closely at 31% and nonspecific enteritis accounted for 10%. In patients younger than 40 years, Crohn's disease was the leading cause at 35% and small bowel tumors and nonspecific enteritis accounted for 23.6 and 11%, respectively.⁵²

Small bowel tumors, although uncommon, include adenocarcinoma, carcinoid, GI stromal tumors, lymphoma, and sarcomas. They comprise about 5% of all GI tumors. Adenocarcinoma is the most common primary malignancy of the small bowel accounting for 35 to 55% of small bowel tumors. The other most common small bowel malignancies are carcinoids, lymphomas and sarcomas accounting for 20 to 40, 14, and 11 to 13%, respectively.⁵³

In a review of 49 patients with primary small bowel tumors, Ciresi and Scholten noted that benign tumors were more likely to present with acute hemorrhage (29 vs. 6%), and were more often asymptomatic (47 vs. 6%) when compared with malignant small bowel tumors.⁵⁴

The small intestine is the second most common site of GI stromal tumors (GIST) with GI bleeding being the most common clinical presentation in 70% of patients. Among the 121 GIST, reported by Vij et al, the jejunum was the most common site in the small intestine at 17.4%, followed by the ileum at 6.6%, and duodenum at 3.3%.⁵⁵

Meckel's diverticulum which results from incomplete closure of the vitelline duct can present with bleeding. In a review of 1,476 patients with Meckel's diverticulum from the Mayo clinic from 1950 to 2002, 16% of patients were symptomatic, with GI bleeding being the most common presentation in adults at 38%.⁵⁶

Other rare sources of small bowel bleeding that should be included in differential include small bowel ulcers, dieulafoy lesions, hemobilia, hemosuccus pancreaticus, and bleeding from small bowel diverticula.⁵³

Special Populations

The differential diagnosis for LGIB is not static across various demographics. In children, the most common causes of LGIB are Meckel's diverticulum, juvenile polyps, intussusception, infectious colitis, and vascular lesions. In a study of 363 pediatric patients with LGIB, by Zahmatkeshan et al, the most common pathological findings was juvenile polyp in 84 patients (23.1%), followed by lymphoid nodular hyperplasia in 55 patients (15.2%), and solitary rectal ulcers in 25 (6.9%) patients.⁵⁷ In neonates, it is important to consider necrotizing enterocolitis and malrotation with volvulus as a cause for acute onset of bleeding.

Since diverticulosis and colorectal cancer are more common with advancing age, young adults with LGIB are more likely to have other factors as a cause, such as IBD. It is important to consider rare causes like endometriosis in women, especially if bleeding is cyclical in nature. It is also important to note that the incidence of various diseases, such as diverticulitis and colon cancer, varies significantly across the world. Diverticulosis is more common in western society, likely due to dietary intake and as such is not among the most common cause of LGIB in areas with a low incidence. For instance, in a review of almost 54,000 Chinese patients, by Bai et al, the most common causes of LGIB were colorectal cancer (24.4%), colorectal polyps (24.1%), chronic colitis (16.8%), anorectal disease (9.8%), and IBD (9.5%). Approximately 7% of patients in this series had no obvious source of bleeding from the colon or rectum. Diverticulosis, however, was accounted for only 1.1% of LGIB in this series.⁵⁸

Iatrogenic Causes

In evaluation of patients with LGIB, it is important to consider iatrogenic causes which a good history can decipher. The common causes in this category include post

polypectomy bleed, anastomotic bleed, post hemorrhoidectomy bleeding, and aortoenteric fistulas.

Post polypectomy bleed is among the common complications of colonoscopy and can occur immediately or in a delayed fashion with rate of 2.8% and 0.3 to 0.6%, respectively.⁵⁹ Immediate postpolypectomy bleeding is usually recognized and treated at the time of colonoscopy. Conversely, delayed bleeding can occur 2 to 14 days following procedure. In a review of endoscopic data of 5,600 patients with 15,553 polyps removed from 2005 to 2013, by Zhang et al, delayed postpolypectomy bleeding occurred in 99 polyps (0.6%). Bleeding rates varied by polypectomy method with the highest being endoscopy piecemeal mucosal resection at 6.9%, followed by snare polypectomy at 1%, endoscopic mucosal resection at 0.9%, and hot biopsy forcep at 0.1%. Risk factors for delayed postpolypectomy bleeding include size of polyp over 10 mm, immediate postpolypectomy bleeding, and the pathology of the polyp. The risk of delayed postpolypectomy bleed was higher for juvenile polyps (odds ratio [OR] = 4.3), Peutz-Jegher syndrome (OR = 3.3), serrated polyps (OR = 1.5), and adenomatous polyps (OR = 1.4) compared to inflammatory/hyperplastic polyps.⁵⁹ In a systematic review of 1,074 studies for colonoscopy complications, by Reumkens et al, the bleeding rate in colonoscopy without polypectomy was 0.6 per 1,000 colonoscopies and increased to 9.8 per 1,000 colonoscopies when polypectomy was performed.⁶⁰

Bleeding can occur at the site of GI anastomosis. It is often minor and self-limited. The incidence ranges from 0.3 to 4.9% and in some cases endoscopic, surgical, or radiologic intervention is required to stop bleeding.⁶¹⁻⁶⁴ In a review of 350 patients undergoing right colectomy with ileocolic anastomosis, by Golda et al, 17 patients (4.9%) had LGIB following surgery, although only five patients (1.4%) were classified as severe hemorrhage and required intervention.⁶⁴

Bleeding is frequently reported following hemorrhoidectomy but is occurs in small amounts and is self-limited. Nonetheless, a small portion of patients require intervention due to significant bleeding after hemorrhoidectomy. In a prospective multicenter study of 633 patients undergoing hemorrhoidectomy, by Bouchard et al, the bleeding requiring intervention occurred in 11 patients (1.8%) and was the most common immediate complication.⁶⁵ In another review of 666 patients undergoing LigaSure hemorrhoidectomy with a minimum of 2 year follow-up, by Chen et al, 21 patients had delayed bleeding corresponding to 3.2% of the overall cohort. Of the 21 patients, 3 required reoperation (0.4%).⁶⁶ The placement of tamponade dressing following hemorrhoidectomy does not decrease the risk of severe anal bleeding as indicated in a randomized control trial of 100 patients by Langenbach et al.⁶⁷

In addition, numerous medications have been implicated in GIB including NSAIDs, proton pump inhibitors, selective serotonin reuptake inhibitors (SSRIs), and various anticoagulation medications.

In summary, LGIB represents a common problem with an extensive differential diagnosis. Diverticular disease, colon cancer/polyps, hemorrhoids, inflammatory bowel disease, and colitis are among the leading causes of LGIB. A thorough history, physical exam, and utilization of endoscopic and

radiographic adjunct are crucial in identification of the etiology of the bleeding.

Conflict of Interest

None declared.

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