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Gastrointestinal bleeding in athletes

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Abstract

Gastrointestinal (GI) bleeding (GIB) in athletes has previously been reported in several studies, as an important factor of underperformance in competitive sports events. Yet it is still underreported, partly because it is usually occult and self-limited soon after the effort. It can originate in either the upper or the lower GI tract and can be proportionally related to the amount and duration of effort. Key pathophysiological factors seem to include splanchnic hypoperfusion, mechanical trauma of the GI wall, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). Appropriate nutrition, hydration and regulation of exercise, along with substances such as arginine and citrulline can relieve upper and lower GI symptoms, including nausea, vomiting, cramping, diarrhea, and possibly hemorrhage. Cessation of NSAIDs, use of proton pump inhibitors and H_2-receptor-antagonists, as well as "training" the gut, also seem to be effective in reducing the incidence of GIB in athletes. Maintenance of hemodynamic stability and identification of the source of bleeding are key elements in the management of this condition. Endoscopy might be necessary for both. GIB should not be immediately attributed to endurance exercise, and endoscopy should always be performed to rule out other existing pathology.

Keywords Gastrointestinal, bleeding, athletes, sports

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Introduction

The positive impact of exercise on the gastrointestinal (GI) system has been well documented, with several studies indicating an inverse relationship between physical activity and the risk of GI-related diseases such as diverticulosis, constipation and cholelithiasis [1-3]. However, GI symptoms are very common in athletes and perhaps the most common cause of underperformance in endurance events, with studies suggesting that up to 70% of athletes experience such problems [4-6]. Upper GI symptoms include reflux, chest pain, heartburn, belching, nausea, and vomiting. Lower GI symptoms include abdominal pain, flatulence, urge to defecate, and diarrhea [2-6]. Runners seem to be more frequently affected than other athletes, such as cyclists [2-4].

GI bleeding (GIB), in both the upper and lower GI tract, is another common and potentially serious manifestation of GI distress in athletes. In this review, we aim to analyze the incidence of GIB in athletes of different sports, along with its different ways of manifestation (upper and lower GI tract, occult and overt bleeding). We also try to provide an overview of the current understanding of the pathophysiology of GIB in athletes. Finally, we will talk about possible measures for prevention, along with possible treatments of this condition.

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Incidence of GIB in athletes

Despite the evidence of a high incidence of GIB among athletes, especially long-distance runners, there are only some case reports and a few small-scale studies based on samples collected during specific events. As regards upper GIB, there were 4 case reports referring to esophageal or gastric hemorrhage after excessive effort, one related to power lifting and 3 among long-distance runners [7-10,12]. Regarding lower GIB, rectal bleeding can occur in long-distance runners as a result of colon hemorrhage [11,12]. From our literature search, we found only 3 studies that performed endoscopy on long-

distance runners after practice or a demanding race. Gaudin C *et al* performed gastroscopy and took biopsies from 7 athletes. Three of the 7 had pathological gastric antrum mucosa before the race but all of them had petechiae, hemorrhage, congestion or extravasation after, combined with worsened histological findings [13]. Choi *et al* examined 16 athletes for anemia and fecal occult blood (FOB). Two of the 16 were FOB (+) before and after the race. Of the remaining 14, all negative before, 2 switched to positive after the race. In those 2, the researchers performed upper and lower GI endoscopy. One had positive gastroscopy, showing gastritis with a blood clot and esophagitis, but colonoscopy was negative and no anemia was found. The other athlete had positive findings from both the gastroscopy, with esophagitis and pangastric erythema, and colonoscopy, with erosion at the splenic flexure plus anemia [14]. Schwartz *et al* demonstrated that 9 athletes of 41 had FOB (+) after a race: 56% of the FOB (+) had cramping and diarrhea vs. 15.6% of the FOB (-). The investigators performed full GI endoscopies on 3 of them: 2 had gastric erosions and 1 had erosion of the splenic flexure mucosa [15].

Among the studies that we found with our literature search, some included athletes who had FOB (+) before and after the examined event. Herein we adduce their findings in relation to athletes who had bloody stool after the event, extracting those who were FOB (+) before, when possible, because it has been proven to happen for other reasons than the sport event *per se* [16]. We divided the studies on the basis of the physical activity performed, as shown in Table 1. Concerning long-distance runners, 7 studies performed FOB testing. Overall, 74 of 404 athletes switched from a negative test before to positive after the race (19.6%). Two studies examined 60 cyclists combined and 4 of them exhibited FOB (+) after the race (6.7%) [17,18]. One study examined a rugby team and found 1 of 11 FOB (+) after the game (9%) [19]. Three studies included triathletes [20] and ultra-marathoners (races longer than 100 km) [21,22] and found a significantly higher incidence of FOB (+), with a total of 58 of 75 (77%).

One study related fecal blood loss with exercise intensity [20], some studies found anemia in some of the tested athletes [14,21,27], and there were also studies that associated FOB (+) with lower GI symptoms, especially cramping and diarrhea [15,22,23]. Ter Steege *et al* constructed a protocol that tested symptomatic long-distance runners, triathletes and cyclists using tonometry and found that 50% of them had GI ischemia during submaximal effort, while 100% were ischemic during maximal effort [28].

Pathophysiology of GIB in athletes

The pathophysiology of GIB in both the upper and lower GI tract in athletes is not yet fully understood. Based on the current literature, causes of GIB in athletes seem to include splanchnic hypoperfusion, mechanical injury of the gut, and use of nonsteroidal anti-inflammatory drugs (NSAIDs). An overview of factors that may cause GIB in athletes is given in Fig. 1.

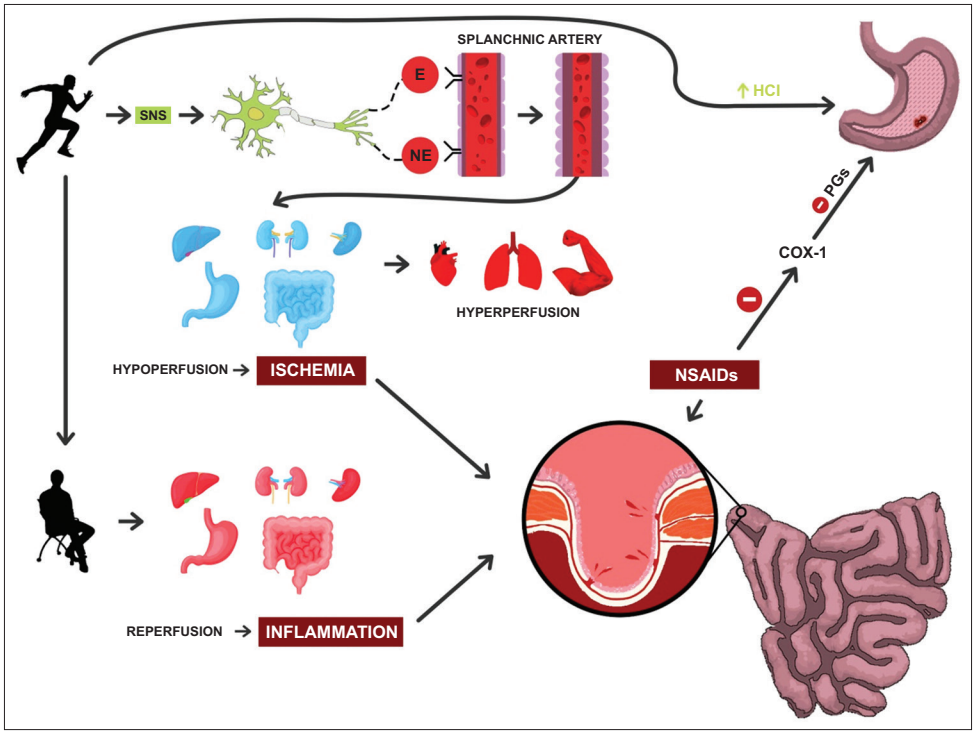

Figure 1 Pathophysiology of gastrointestinal hemorrhage in athletes
SNS, sympathetic nervous system; NSAIDs, nonsteroidal anti-inflammatory drugs; E, epinephrine; NE, norepinephrine; PG, prostaglandin; COX, cyclo-oxygenase

Table 1 Incidence of fecal occult bleeding (FOB) in athletes of different sports

Runners			
Title	Author [ref.], year	Number of FOB (-/+) (before/after)/FOB (-) before	Percentage (%)
Runners' diarrhea. Different patterns and associated factors	Sullivan *et al* [23], 1992	17/109	16
Occult gastrointestinal blood loss in marathon runners	McMahon *et al* [24], 1984	7/31	19
Gastrointestinal bleeding in marathon runners	Halvorsen *et al* [16], 1986	8/58	13.7
Gastrointestinal blood loss associated with running a marathon	McCabe *et al* [25], 1986	28/112	25
The role of gastrointestinal endoscopy in long-distance runners with gastrointestinal symptoms	Choi *et al* [14], 2001	2/14	14.3
Endoscopy to evaluate gastrointestinal bleeding in marathon runners	Schwartz *et al* [15], 1990	9/41	22
Do some marathon runners bleed into the gut?	Porter [26], 1983	3/39	8
Total		74/404	19.6
Super-Athletes			
Title	Author [ref.], year	Number of FOB(-/+) (before/after)/FOB (-) before	Percentage (%)
Gastrointestinal blood loss in triathletes: it's etiology and relationship to sports anaemia	Rudzki *et al* [20], 1995	16/20	80
Early changes of the anemia phenomenon in male 100-km ultramarathoners	Chiu *et al* [21], 2015	13/20	65
Gastrointestinal bleeding during an ultramarathon	Baska *et al* [22], 1990	29/35	83
Total		58/75	77
Cyclists			
Title	Author [ref.], year	Number of FOB (-/+) (before/after)/FOB (-) before	Percentage (%)
Occult gastrointestinal bleeding in endurance cyclists	Wilhite *et al* [17], 1990	2/35	5.7
Gastrointestinal bleeding following a 161-km cycling race in the heat: a pilot study	Adams *et al* [18], 2018	2/25	8
Total		4/60	6.7
Rugby players Title	Author [ref.], year	Number of FOB (-/+) (before/after)/FOB (-) before	Percentage (%)
Occult gastrointestinal bleeding in rugby player	Babić *et al* [19], 2001	1/11	9

Splanchnic hypoperfusion

Alterations in splanchnic blood flow appear to be a major cause of GIB in athletes. At rest, 25% of cardiac output is delivered to the splanchnic organs through the celiac, superior and inferior mesenteric arteries [29]. During exercise, the increased activity of the sympathetic nervous system leads to an excessive release of norepinephrine from post-ganglionic

sympathetic neurons and epinephrine from the adrenal medulla, which act predominantly on α-adrenergic receptors on the smooth muscle of arterioles [29,30]. This results in vasoconstriction, increased splanchnic vascular resistance and subsequent decrease of splanchnic blood flow, which can range up to 80%, especially during maximum intensity exercise [29-32]. Blood is rapidly redistributed from the splanchnic area to tissues with increased activity, such as the heart, lungs, muscle, and skin [33]. The ensuing ischemia causes tissue hypoxia and local depletion of adenosine triphosphate. After exercise, restoration of blood flow is necessary to maintain cell function and viability; however, when splanchnic circulation is restored, reperfusion injury may develop, characterized by local inflammation and the formation of reactive oxygen species [34-36]. Ischemia-reperfusion injury (IRI) can lead to mucosal damage and gut wall integrity loss, which is accompanied by increased permeability of capillaries and arterioles, bacterial translocation and intestinal inflammation [37,38].

IRI seems to affect both the small and large intestines. More specifically, in the small intestine, a counter-current exchange mechanism of oxygen in the villus microvasculature keeps enterocytes at the tips of the villi in a lower oxygenation state compared to enterocytes at the crypts [39]. This makes enterocytes at the tips of the villi very susceptible to low-flow states and ischemic events, such as the ones that take place during intense exercise [40].

The colon has less blood supply per gram compared to the small bowel and is more sensitive to autonomic nerve stimulation, which makes it more vulnerable to ischemia [41]. The splenic flexure (Griffith's point) and the recto-sigmoid (Sudeck's point) appear to be the most frequently affected parts, probably because of the inadequate vessel anastomosis in these areas [42]. Massive and even life threatening GIB due to ischemic colitis in athletes has been described in the literature, with proximal, distal or pancolitis due to ischemia reported, and surgery required in one case [11,12,43,44].

Mechanical trauma

Mechanical trauma related to impact or posture appears to be another mechanism that can cause GIB during intense physical exercise [45]. The mechanical impact of exercise is considered to be greater in running compared with other activities, such as cycling, where the body remains in a more stable position [46]. This theory is supported by studies showing that GI disturbances are experienced mainly during the running part of triathlon events, the running stages of a study of alternate running and cycling, and an absence of occult bleeding in walkers compared to marathon runners [47-49].

Acceleration and deceleration forces in combination with ischemia during running might result in hemorrhagic gastritis [50] and mechanical trauma to the colon, known as "cecal slap syndrome" [51]. It is thought to be due to slapping of the posterior wall of the cecum against the anterior wall, resulting in bleeding and bruising [51,52].

NSAIDs

NSAIDs are a broad class of non-glucocorticoid drugs that are extensively used as anti-inflammatory, analgesic and antipyretic therapies [53]. They are frequently used by athletes, mostly as pain relieving medication, or even for pain prevention before a sports event [54]. However, NSAIDs cause many adverse effects. Their use has been associated with a 3-fold higher risk for developing serious adverse GI events compared to non-users, including GIB [55]. While NSAID-induced GI toxicity is usually associated with the upper GI tract, evidence suggests that NSAIDs increase the risk of lower GIB and perforation to a similar extent [56]. In a study by Van Wijck *et al*, it was demonstrated that ibuprofen aggravates exercise-induced small intestinal injury and induces gut barrier dysfunction [57].

GI damage from NSAIDs is based on the inhibition of cyclooxygenase (COX)-1 and COX-2 enzymes [53]. COX-1 inhibition lowers the production of prostaglandins, which act protectively along the intestinal mucosa, and makes the stomach wall vulnerable to the luminal gastric acid, leading to ulcerations, increased permeability and trauma [53]. As regards COX-2, while it has been suggested that selective COX-2 inhibitors may reduce GI toxicity compared to non-selective NSAIDs [58], it seems that COX-2 plays an important part in the defense of the GI mucosa by maintaining mucosal integrity and participating in ulcer healing [59]. It has been suggested that NSAID-induced epithelial damage may result from mechanisms other than (or in addition to) COX-1 and COX-2 inhibition [58]. Other mechanisms of NSAID GI toxicity are under investigation [60-62].

Prevention of GIB in athletes

To our knowledge, there are currently no specific guidelines that apply to the prevention of GIB in athletes. Most preventative measures currently suggested in the literature aim at one or more of the pathophysiologic mechanisms that seem to cause GIB in this part of the population. A summary of such measures and the ways in which they might help prevent GIB in athletes is given in Table 2.

Several symptoms, such as cramping pain, diarrhea and nausea, might appear even weeks before severe gut ischemia develops [43,63]. Paying attention to warning signs and lowering the intensity of exercise may be the simplest way for athletes to avoid GIB [63]. High intensity training in extreme conditions, such as excessive heat, should also be avoided, as it seems to lower splanchnic blood flow [5].

As mucosal damages caused by gastric acid secretion are a possible mechanism for the development of upper GIB, medications such as H_2-receptor antagonists and proton pump inhibitors (PPIs) have been tested as protection, with some of them showing promising results [10,64-67]. A short-course treatment with such agents seems reasonable prior to a prolonged period of exercise, especially for athletes with regular episodes of gastritis or GIB [68,69]. However, they are

Table 2 Possible ways of prevention of GI hemorrhage in athletes and suggested mechanisms

Preventative measure	Suggested mechanism of prevention
Lower exercise intensity when GI symptoms develop (e.g., diarrhea, cramping pain)	Less GI stress, timely restoration of perfusion
Avoiding training in extreme conditions (e.g., excessive heat)	Prevention of low GI perfusion
Short course treatment with PPIs/H_2-receptor antagonists	Protection of GI mucosa
Cessation of NSAIDs	Lower GI toxicity, no inhibition of prostaglandins
Consumption of agents that increase the availability of NO (e.g., citrulline, nitrite, nitrate)	Improved GI perfusion
Euhydration before training or events	Prevention of lower GI perfusion due to hypovolemia
Stopping the use of high osmolality solutions before sports events	No shift of fluids into the intestinal lumen- prevention of dehydration
"Training the gut" (e.g., gradual increase of exercise intensity, nutrition strategies)	Reduction of GI distress during maximum intensity exercise

GI, gastrointestinal; PPIs, proton pump inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; NO, nitric oxide

not yet recommended for general use before sports events, and further research is required.

As mentioned above, GI toxicity is a very common side-effect of NSAIDs. Based on current research, regular use of NSAIDs by athletes is discouraged, especially in the pre-race period [45,54,57]. It has been argued that, since reduced perfusion of the GI tract is a major pathophysiological factor of GI distress in athletes, its reversion could be of great importance in the effort to reduce GI symptoms during endurance events [6]. The use of agents that increase the availability of nitric oxide, such as arginine, glutamine, citrulline, nitrite and nitrate, has been associated with improved splanchnic perfusion and reduction of GI symptoms during exercise [70,71]. Despite being used for the relief of such symptoms, consumption of substances such as arginine and citrulline has also been associated with adverse effects, such as nausea and diarrhea [72].

Dehydration, usually due to inadequate fluid intake and exercising in the heat, can aggravate splanchnic hypoperfusion by reducing cardiac output and enhancing systemic hypovolemia [73]. Fluid replacement programs tailored to each individual are recommended to maintain euhydration before, during and after exercise [74]. Athletes are advised to start training and competitive events well hydrated, and avoid the intake of high osmolality solutions, such as highly concentrated carbohydrate solutions, since they may cause a shift of fluids into the intestinal lumen and thus aggravate dehydration [75].

For many years, it has been suggested that the gut can be "conditioned" or "trained" in order to reduce GI distress [76]. Reducing GI stress can prevent the frequent occurrence of GI symptoms in athletes, including GIB. By gradually increasing exercise intensity during training, it may be possible to precondition the gut to withstand prolonged episodes of physical exercise [77]. It has also been shown that athletes not accustomed to fluid and food ingestion during exercise are at higher risk of developing GI symptoms during a competitive event [78]. Athletes should try different training nutrition strategies. Experimenting with the pre-event and event-day nutrition plans many times before a sporting event will allow athletes to work out what suits them better individually, and help them determine the most effective strategy to use during competition in order to avoid GI distress [4].

Management of GIB in athletes

GIB in athletes is usually self-limited, with rare reported cases of significant blood loss. An approach to the treatment of GIB in athletes is suggested in Fig. 2.

It is important to point out that GIB should not be attributed to endurance athleticism before other potentially serious causes of GIB that also apply to the general population have been excluded [45,68]. Athletes who present with GIB should always be advised to undergo endoscopy of both the upper and lower GI tract to rule out other causes of hemorrhage, such as inflammatory bowel disease, intestinal neoplasia, esophageal varices, Mallory-Weiss tears, peptic ulcers, coagulopathies, hemorrhoids, anal fissures, diverticulosis, vascular ectasias, and systemic vasculitis [45,77].

In cases of overt bleeding in endurance training or events, athletes should immediately cease every activity and seek medical care [77]. Treatment for overt GIB in athletes is similar to that in the general population. Hemodynamic stability should be assessed immediately. Patients with severe bleeding may be in need of resuscitation with intravenous crystalloids and transfusions [79]. PPIs are useful for ulcers, erosions or gastritis, while vasoactive drugs such as somatostatin or octreotide should be used when varices are suspected as the cause of upper GIB [80]. Some patients require emergency endoscopy or radiographic interventions in order to achieve hemostasis. In rare cases, surgery might be required to stop the bleeding [79-81].

Occult bleeding occurs more frequently, especially in endurance athletes. Endoscopy should be recommended in all athletes with occult GIB, especially those who present

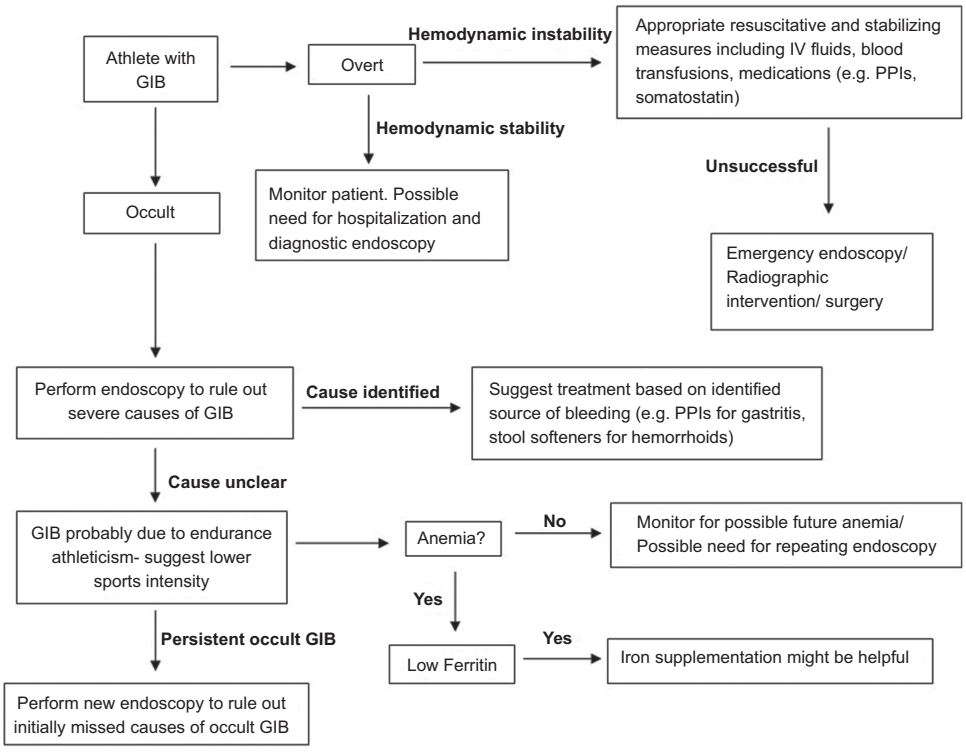

Figure 2 An approach to the treatment of gastrointestinal bleeding (GIB) in athletes

with anemia [14]. In the case of sports anemia with decreased ferritin, iron supplementation might be helpful [77]. Iron can be supplied through nutrition, oral supplements or intravenous infusion. Athletes with repeatedly low ferritin values seem to benefit from intermittent oral iron substitution [82]. Medications that reduce gastric acid secretion, such as H_2-receptor antagonists and PPIs, have been shown to be effective in treating gastritis caused by endurance training [65,69]. Stool softeners might be useful for athletes with fissures or hemorrhoids [45,77]. As in the general population, athletes who have persistent GIB not responding to therapy or lower sports intensity, and had negative initial endoscopy, should be advised to repeat the endoscopy to rule out GIB causes that were not identified the first time [83].

Concluding remarks

GIB is a serious manifestation of GI distress in athletes. Further and larger-scale studies are required for the better understanding of its frequency, pathophysiology and possible new preventive measures. Its incidence could also be studied in other sports, and comparison of such data with those of endurance athletes could provide information on whether those athletes are also in danger of GIB, especially occult. Specific guidelines for the treatment of GIB in this part of the population can help provide faster and more effective care, especially in cases of overt GIB.

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