

# Blood Transfusion Strategy in Gastrointestinal Tract Bleeding: Liberal or Restrictive

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## ABSTRACT

*Gastrointestinal tract bleeding is an emergency problem, which is frequently found. The manifestations of gastrointestinal tract bleeding vary, ranging from massive bleeding which is life threatening until occult bleeding that is not sensed by the patient. One of the main objectives in the management of gastrointestinal tract bleeding is stabilizing patient's hemodynamic, either by using infusion of crystalloid, colloid, or even with the administration of blood transfusion. In massive gastrointestinal tract bleeding, administration of red blood cells transfusion may be life saving. However, in cases where bleeding is not profuse, the safest and most effective blood transfusion strategy is still controversial. Until now, there is no trial that gives information regarding safety and effectiveness of liberal or restrictive transfusion strategy in lower gastrointestinal tract bleeding. However, for most patients with gastrointestinal bleeding, with or without portal hypertension, it is better to postpone blood transfusion until the hemoglobin level decrease to less than 7 g/dL.*

**Keywords:** *gastrointestinal tract bleeding, blood transfusion, liberal, restrictive*

## ABSTRAK

*Perdarahan saluran cerna merupakan kasus emergensi yang sering ditemui. Manifestasi perdarahan saluran cerna beragam, mulai dari perdarahan masif yang dapat mengancam nyawa sampai dengan perdarahan samar yang tidak disadari oleh pasien. Salah satu tujuan utama dalam penanganan perdarahan saluran cerna adalah stabilisasi hemodinamik pasien, baik dengan pemberian infus cairan kristaloid, koloid, atau bahkan transfusi darah. Pada perdarahan saluran cerna yang berat, transfusi sel darah merah dapat menyelamatkan nyawa. Namun, pada kasus di mana perdarahan tersebut tidak berat, strategi tranfusi darah yang paling aman dan efektif masih kontroversial. Sampai dengan saat ini, tidak ada uji yang memberikan informasi mengenai keamanan dan efektifitas dari strategi tranfusi liberal atau restriktif pada perdarahan saluran cerna bagian bawah. Namun, pada pasien dengan perdarahan saluran cerna, dengan atau tanpa hipertensi porta, sebaiknya tranfusi darah ditunda hingga kadar hemoglobin turun sampai dengan kurang dari 7g/dL.*

**Kata kunci:** *perdarahan saluran cerna, transfusi darah, liberal, restriktif*

## INTRODUCTION

Gastrointestinal tract bleeding is an emergency problem, which is frequently found. In United States, approximately 300,000 patients require hospitalization every year due to gastrointestinal tract bleeding.

Around 36 to 102 patients per 100,000 populations need hospitalization due to upper gastrointestinal bleeding. Lower gastrointestinal bleeding causes approximately 20 patients per 100,000 populations to be hospitalized.<sup>1</sup>

Manifestations of gastrointestinal bleeding vary, starting from massive bleeding which is life threatening until occult bleeding that is not sensed by the patient. Mortality due to upper gastrointestinal tract ranges from 3.5-7%, while mortality due to lower digestive tract was 3.6%.<sup>2</sup>

One of the main objectives in the management of gastrointestinal bleeding is stabilizing patient's hemodynamic, either by using infusion of crystalloid, colloid, or even administration of blood transfusion. Blood transfusion is often performed in patients with gastrointestinal bleeding who require hospitalization, however the threshold of optimal hemoglobin level for administration of blood products is still unclear.<sup>3</sup>

### GASTROINTESTINAL CIRCULATION SYSTEM

Main arteries that supply stomach and intestine are celiac artery, superior mesenteric artery, and inferior mesenteric artery. Celiac artery supplies stomach, part of duodenum, part of pancreas, and liver. Superior mesenteric artery supplies the other part of duodenum and pancreas, jejunum, ileum, and colon up to two third of the transverse segment. Inferior mesenteric artery supplies other part of the colon and rectum, except distal rectum which is supplied by rectal artery which arises from internal iliac artery.<sup>4,5</sup> Blood from the stomach, small intestine, and colon will flow to the portal vein, except blood which comes from the distal rectum that will pass through internal iliac vein. Veins arising from the intestine are located in the mesentery, except those which arises from retroperitoneal part.<sup>4,5</sup>

Submucosal arterioles in the stomach will ramify into capillaries in the base of gastric glands. Blood from the capillaries will flow to the mucosal venules in lamina propria, which will unify in the collecting venules. This collecting venule is directly connected to the submucosal venules.<sup>4,5</sup> Main intramural artery in the small intestine is located in the submucosal plexus. In this plexus, wide anastomosis from arteries and veins occur. Capillary blood vessels in the muscular, submucosal, and mucosal layers are supplied from the branches of this plexus. Intramural arterioles in the colon emerge to the epithelial surface between crypts and create capillary plexus around the crypt. Colon capillaries are located closer to the epithelial compared to the villi capillaries in the small intestine.<sup>4,5</sup>

### GASTROINTESTINAL TRACT BLEEDING

The aetiology of upper gastrointestinal tract bleeding is bleeding which happens in the proximal side of

Treitz ligament. Clinically, upper gastrointestinal tract bleeding can be categorized into two groups, which are variceal bleeding and non-variceal bleeding.<sup>3,6</sup>

Differential diagnoses of upper gastrointestinal tract bleeding include: 1) In peptic ulcer the risk factor include *Helicobacter pylori* (*H. pylori*) infection, use of non-steroidal anti-inflammatory drugs, smoking, and alcoholism; 2) Mallory-Weiss bleeding usually occur in the gastroesophageal junction, ceased spontaneously in 80-90% cases and recur in 0-7%; 3) In esophageal varices, patient with variceal bleeding generally has poorer prognosis compared to those with other source of gastrointestinal bleeding; 4) In hemorrhaging gastritis and erosive gastropathy through endoscopy appear as subepithelial bleeding and erosion, thus usually did not cause profuse bleeding. The risk factors include the use of non-steroidal anti-inflammatory drugs, alcoholism, and stress; 5) Small intestine bleeding is rare, however the most frequent causes are ectasis and tumour. Crohn's disease, infection, ischemia, vasculitis, small intestinal varices and diverticles are the other etiologies; 6) Rare causes of upper gastrointestinal tract bleeding are erosive duodenitis, aortoenteric fistula, vascular lesion, hereditary telangiectasis bleeding, and *gastric antral vascular ectasia* (*watermelon stomach*), Dieulafoy lesion, gastropathy; prolapse and hemobilia, *hemosuccus pancreaticus*.

Generally, lower gastrointestinal tract bleeding is defined as bleeding which originates from the distal side of Treitz ligament. Profuse bleeding usually originates from the proximal and terminal ileum. Eleven percent of patients with haematochezia actually suffer from upper gastrointestinal bleeding.<sup>2,6</sup>

Differential diagnoses in the lower gastrointestinal tract bleeding are as follows. 1) Diverticle bleeding which prevalence increases in line with the increase of age, usually in the eighth decade and contribute as much as 20% to the lower gastrointestinal tract bleeding; 2) Angiodysplasia. known as vascular ectasis or angioectasis. Approximately 30% of lower gastrointestinal tract bleeding caused by angiodysplasia and is the main cause of chronic bleeding and rarely leads to hemodynamic disturbance; 3) Ischemic colitis, the prevalence increases as the cardiovascular disease risks increase. There is decrease on the mesenteric flow due to decrease in blood pressure or vasospasm. Bleeding usually stops by itself; 4) Inflammatory bowel disease, ulcerative colitis, causes massive lower gastrointestinal tract bleeding in 0.1% cases, while Crohn's disease in approximately 0.2%; 5) Neoplasm 2-9% of lower gastrointestinal tract bleeding is caused

by carcinoma due to the presence of erosion and ulceration on the tumour surface. 5-11% is caused by polyps, usually polyp that bleed is more than 1 cm in size; 6) Bleeding post polypectomy usually occur late, approximately 14 days after polypectomy and is the complication of colonoscopy polypectomy, which is 0.2-1.8%; 7) Anorectal disease. Hemorrhoid contributes to 2-9% from lower gastrointestinal tract bleeding. Bleeding due to rectum varices occur in patients with portal hypertension and is usually profuse bleeding.<sup>7</sup>

**MANAGEMENT OF GASTROINTESTINAL TRACT BLEEDING**

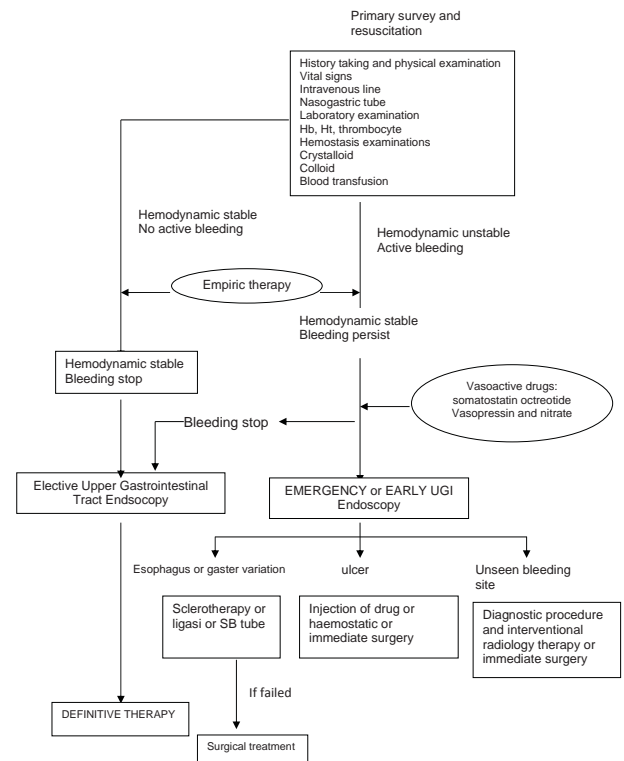
Determining patient’s hemodynamic status is an initial step in the management of gastrointestinal tract, to further identify the severity of occurring bleeding. Massive acute bleeding exceeding 20% intravascular volume will cause unstable hemodynamic condition, with several signs including: 1) Hypotension (blood pressure less than 90/60 mmHg or mean atrial pressure (MAP) less than 70 mmHg); 2) Orthostatic diastolic pressure decreases more than 10 mmHg or systolic decreases more than 20 mmHg; 3) Orthostatic heart rate frequency increases more than 15 bpm; 4) Cold extremities; 5) Decreased consciousness; 6) Anuria or oliguria (urine production less than 30 ml per hour).<sup>3</sup>

Besides in the presence of unstable hemodynamic signs, massive bleeding is suspected if there is hematemesis, hematochezia, fresh blood in nasogastric tube aspiration and with lavage not clearing soon, persistent hypotension, and if in 24 hours consumed blood transfusion more than 800-1,000 mL.

Stabilizing hemodynamic is essential in the management of gastrointestinal tract bleeding and need to be achieved rapidly by administration of crystalloid, colloid, or even blood transfusion. Simultaneous with hemodynamic stabilization efforts, empiric therapy either non-endoscopic or per endoscopy is performed as summarized in figure 1 and figure 2.<sup>2,3</sup>

**Blood Transfusion Strategy In Gastrointestinal Tract Bleeding**

Principle of resuscitation in acute lower gastrointestinal tract bleeding is also recommended in upper gastrointestinal tract bleeding, which is by stabilizing hemodynamic as an initial step. Administration of blood transfusion is very individual, depending on the amount of blood loss, on-going or stopped active bleeding and clinical effect of the bleeding.<sup>2</sup>



Hb: hemoglobin; Ht: hematocryt; UGI: upper gastrointestinal bleeding; SB tube: sengstaken-blakemore tube

Figure 1. Management of upper gastrointestinal bleeding <sup>3</sup>

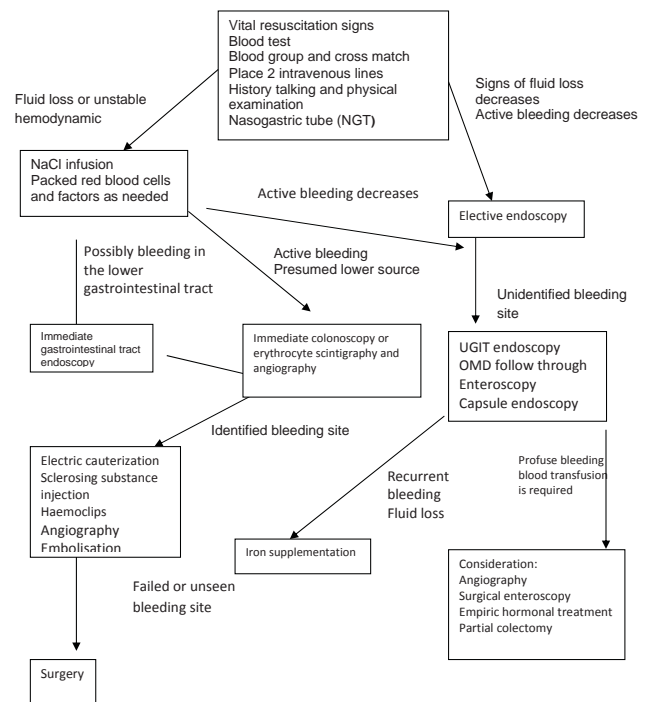


Figure 2. Management of lower gastrointestinal tract bleeding <sup>2</sup>

Administration of blood transfusion is considered in several conditions: 1) bleeding in unstable hemodynamic condition; 2) New or on-going bleeding and the amount is estimated to be one litre or more; 3) New or on-going bleeding with hemoglobin level less

than 10 g/dL or hematocrit less than 30%; 4) Presence of decreased tissue oxygenation.<sup>3</sup>

In these cases, administration of red blood cells transfusion may be life saving. However, in cases where bleeding is not profuse, the safest and most effective blood transfusion strategy is still controversial.<sup>8</sup>

### **Liberal Transfusion Strategy versus Restrictive Transfusion Strategy**

Despite of its advantage in increasing oxygen distribution and preventing increase of mortality in critically ill patients, safety in the administration of red blood transfusion need to be re-evaluated. This is because critically ill patients are riskier towards immunosuppressive and microcellular complications of red blood cells transfusion. With this background, a study was performed to compare liberal transfusion (maintaining the hemoglobin level 10 g/dL or more) to restrictive transfusion (maintaining hemoglobin level more between 7-9 g/dL) in normovolemic patients in the ICU. The study stated that restrictive strategy was as effective as or even more superior than liberal transfusion strategy in critically ill patients with exception for patients with acute myocardial infarct and unstable angina. However, to extrapolate it to gastrointestinal bleeding cases became difficult due to the different patient's criteria being used.<sup>9</sup>

American Association of Blood Banks (AABB) in the most current guidelines for red blood cells transfusion recommends few things including: 1) Recommending the use of restrictive transfusion strategy (hemoglobin 7-8 g/dL) in hospitalised patients and stable; 2) Suggesting restrictive strategy in hospitalised patients with accompanying disease such as cardiovascular disturbance and consider transfusion for patients with symptoms or haemoglobin level less than 8 g/dL; 3) Cannot recommend or prohibit liberal or restrictive transfusion in hospitalised patients and stable hemodynamic with acute coronary syndrome; 5) Suggesting that decision of transfusion is based on symptoms and hemoglobin level.

Meta-analysis from randomized trial which compared restrictive strategy to liberal strategy showed difference in mortality was 30 days, length of hospitalisation or number of unwanted happenings and many excluding the possibility of clinical benefits from liberal transfusion strategy. Nevertheless, only 0-1% patients who were involved in the trial experienced acute gastrointestinal bleeding, thus it is difficult to implement it in patients with gastrointestinal bleeding.<sup>10,11</sup>

Villanueva et al provided the required information regarding recommendation of upper gastrointestinal tract bleeding. With the cut-off hemoglobin level of 7 g/dL if compared to the cut-off hemoglobin level of 9 g/dL, there was significant decrease of relative risk (45%) for 45 days mortality. It was also stated that continuous decrease of bleeding, transfusion reaction, incidence of cardiac disturbances and length of hospitalisation. Overall, these results showed that restrictive transfusion strategy is more superior compared to liberal transfusion strategy. This benefit is particularly obvious in patients with portal hypertension. However, in subgroup analysis, there was no difference between patients with portal hypertension or those without portal hypertension. One of the things need to be considered in the study performed by Villanueva was that in patients with hypotension there was rationalization of transfusion in patients who experienced hypotension although their hemoglobin levels have not reached 7 g/dL. This is because in the early phase of acute bleeding, the hemoglobin level decreases slightly as patient experience intravascular volume depletion. The actual hemoglobin level would appear after fluid resuscitation and have reached equilibration condition. Until now, there is no trial that give information regarding safety and effectiveness of liberal or restrictive transfusion in lower gastrointestinal tract bleeding.

### **CONCLUSION**

One of the main objectives in the management of gastrointestinal bleeding is stabilising patient's hemodynamic, either by using infusion of crystalloid, colloid, or even blood transfusion. However, most patients with gastrointestinal bleeding, with or without portal hypertension, it is better to postpone blood transfusion until the hemoglobin level decrease to less than 7 g/dL.

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