ISSN: 2457-0400

Impact Factor: 7.675

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

www.wjahr.com

Volume: 10, Issue: 2

Page N. 185-190

Year: 2026

Original Article

Coden USA: WJAMA3

UPPER GASTROINTESTINAL BLEEDING: A COMPARATIVE STUDY BETWEEN LIBERAL AND RESTRICTIVE TRANSFUSION STRATEGIES

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Article Received: 05 January 2026 **Article Revised:** 25 January 2026 **Article Published:** 04 February 2026

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DOI: https://doi.org/10.5281/zenodo.18481607

How to cite this Article: *Tahseen Ali Raheemah (MBChB, CABEM), Firas Kahttan Abbas (MBChB, CJBAEM) (2026). Upper Gastrointestinal Bleeding: A Comparative Study Between Liberal And Restrictive Transfusion Strategies. World Journal of Advance Healthcare Research, 10(2), 185–190.

ABSTRACT

Background: Upper gastrointestinal bleeding is a prevalent condition with a mortality rate that is as high as 15%. The optimal red blood cell transfusion strategy in acute gastrointestinal bleeding is debated. **Aim of study:** This study aims to compare between patients with upper GI bleeding receiving restrictive and liberal transfusion strategies regarding in hospital management, complications, overall survival, and adverse outcomes. **Patients and methods:** This is an analytic prospective cohort study that included 227 patients and was conducted in Baghdad Teaching Hospital/ Medical city, Baghdad. The data was collected from the 1st of January 2023 to the 1st of January 2024. All adult patients (>18 years) diagnosed with presenting with upper gastrointestinal bleeding to the emergency department during the study period were included in the study. At admission, patients were assigned to undergo either liberal transfusion protocol or restrictive protocol. In the restrictive-strategy group, the hemoglobin threshold for transfusion was 7 g per deciliter. In the liberal-strategy group, the hemoglobin threshold for transfusion was 9 g per deciliter. The primary outcome measure was the rate of death in the emergency department. Secondary outcomes included the rate of further bleeding and the rate of in-hospital complications. **Results:** Patients of the liberal group were significantly more likely to need variceal banding (P=0.002) and octreotide injection (P=0.008). Overall emergency department mortality was seen in 3 (2.7%) cases of the restrictive group and 12 (10.4%) cases of the liberal group, with the difference being statistically significant (P value = 0.030). A statistically significant difference was detected between both study groups regarding the incidence of transfusion-associated circulatory overload and pulmonary edema. **Conclusion:** According to the results of the current study, patients who underwent transfusion with a restrictive strategy exhibited a notable decrease in the requirement for banding and octreotide therapy. Additionally, there was an enhancement in the overall survival and a decrease in transfusion-related complications.

KEYWORDS: Secondary outcomes included the rate of further bleeding and the rate of in-hospital complications.

INTRODUCTION

A potentially life-threatening clinical event, upper gastrointestinal bleeding (UGB) accounts for over 400 thousand annual hospital admissions in the US and places a heavy financial strain on healthcare systems. If left untreated, UGB can cause significant mortality and morbidity.[1][2] Upper gastrointestinal bleeding is most often caused by peptic ulcer disease (PUD), which accounts for 31–67 percent of cases, while variceal bleeding is the leading cause of death, accounting for 11–50 percent of cases. There is mounting evidence that the causes of UGIB and the deaths caused by it are not static, but have evolved over the last three decades. The mortality rate of UGIB has decreased, in part, due to innovations in endoscopic hemostatic procedures that have occurred during the last 30 years. The broad usage of proton pump inhibitors for PUD has also been suggested to have an impact on the epidemiology of UGIB etiologies and outcomes.[3]

There are three steps to managing UGIB: managing before the endoscopic procedure, doing the endoscopic evaluation and therapy, and managing after the endoscopic procedure. There has been a decrease in mortality from UGIB over the last twenty years, which is attributed to better management practices such as resuscitation, the use of proton pump inhibitors, and endoscopic therapies.[4]

Transfusing patients just when their hemoglobin drops below 7 g/dL seems to cut down on further bleeding and mortality. A transfusion of greater hemoglobin levels may be administered to hypotensive patients in order to facilitate equilibration during fluid resuscitation. A suitable threshold for individuals with pre-existing cardiovascular disease is 8 g/d.[5]

This study aims to compare between patients with upper GI bleeding receiving restrictive and liberal transfusion strategies regarding in hospital management, complications, overall survival, and adverse outcomes.

PATIENTS AND METHODS

Study place and time

The study has been conducted in Baghdad Teaching Hospital/ Medical city, Baghdad. The data was collected from the 1st of January 2023 to the 1st of January 2024.

Study design

An analytic prospective cohort design has been chosen for this study.

Research population

All adult patients (>18 years) diagnosed with presenting with upper gastrointestinal bleeding to the emergency department during the study period were included in the study.

Exclusion criteria

Patients with the following conditions were excluded from the study.

1. Massive exsanguinating bleeding.
2. An acute coronary syndrome.
3. Stroke or transient ischemic attack.
4. Transfusion within the previous 90 days.
5. A recent history of trauma or surgery.
6. Lower gastrointestinal bleeding.
7. Clinical Rockall score of 0.
8. Hemoglobin level >9 g/dl.

Ethical consideration

Verbal consent has been obtained from all participants before data collection. An official letter of approval has been obtained from the scientific committee of the scientific council of Emergency Medicine – Iraqi Board for Medical Specializations.

Data Collection

As the start of study, patients basic characteristics were collected (age, sex, BMI, comorbidities, Rockall score and Hb at admission). At admission, patients were assigned to undergo either liberal transfusion protocol or restrictive protocol according to the decision of the treating emergency physician. In the restrictive-strategy group, the hemoglobin threshold for transfusion was 7 g per deciliter, with a target range for the post-transfusion hemoglobin level of 7 to 9 g per deciliter. In the liberal-strategy group, the hemoglobin threshold for transfusion was 9 g per deciliter, with a target range for the post-transfusion hemoglobin level of 9 to 11 g per deciliter. In both groups, 1 unit of red cells was transfused initially; the hemoglobin level was assessed after the transfusion, and an additional unit was transfused if the hemoglobin level was below the threshold value. The transfusion protocol was applied until the patient's discharge from the hospital or death. The protocol allowed for a transfusion to be administered any time symptoms or signs related to anemia developed, massive bleeding occurred during follow-up, or surgical intervention was required. Hemoglobin levels were measured after admission and again every 8 hours during the first 24 hours and every day thereafter. Hemoglobin levels were also assessed when further bleeding was suspected. All the patients underwent emergency endoscopy within the first 6 hours. When endoscopic examination disclosed a nonvariceal lesion with active arterial bleeding, a nonbleeding visible vessel, or an adherent clot, patients underwent endoscopic therapy with injection of adrenaline plus multipolar electrocoagulation or application of endoscopic clips. Patients with peptic ulcer received a continuous intravenous infusion of omeprazole (80 mg per 10-hour period after an initial bolus of 80 mg) for the first 72 hours, followed by oral administration of omeprazole. When portal hypertension was suspected, a continuous intravenous infusion of somatostatin (250 µg per hour) and prophylactic antibiotic therapy with ceftriaxone were administered at the time of admission and continued for 5 days. Bleeding esophageal varices were also treated with band ligation or with sclerotherapy, and gastric varices with injection of cyanoacrylate.

The outcomes were the rate of death from any cause in the emergency department and transfusion-associated adverse events.

Data entry and analysis

Data entry was done using Microsoft Excel 2019. Data was recorded into different quantitative and qualitative variables for the purpose of analysis.

Analysis was done using statistical package for social sciences (SPSS version 26).

Data was summarized using measures of frequency (mean), dispersion (standard deviation), tables and graphs. A two-tailed p value of less than or equal to 0.05 was assigned as a criterion for declaring statistical significance.

RESULTS

The study sample

A total number of 227 patients were included in the study sample.

Basic characteristics of the studied sample

No significant difference was detected between both study groups regarding age, sex, and BMI as shown in table (1).

Table 1: Basic characteristics of the studied sample.

Basic characteristics	Group		P value
	Restrictive group (N=112)	Liberal group (N=115)	
Age			
Mean ± SD	41.5 ± 18.2	42.3 ± 20.3	0.674
Sex			
Male	74	71	0.489
	66.7%	61.7%	
Female	37	44	
	33.3%	38.3%	
BMI			
Mean ± SD	24.3 ± 2.7	25.1 ± 2.4	0.530

Clinical characteristics of the studied sample

No statistically significant difference was detected between both study groups regarding preexisting comorbidities, Rockall score, and Hb at admission; as shown in table (2).

Table 2: Clinical characteristics of the studied sample.

Clinical History	Group		P value
	Restrictive group (N=112)	Liberal group (N=115)	
Comorbidities			
Hypertension	26	32	0.450
	23.2%	27.8%	
Diabetes Mellitus	41	37	0.489
	36.6%	32.2%	
Cirrhosis	40	41	1.000
	36.4%	35.7%	
Alcoholism	43	48	0.685
	38.4%	41.7%	
Previous upper GI bleeding	11	13	0.830
	9.8%	11.3%	
Rockall score			
Mean ± SD	6.6 ± 1.3	6.8 ± 0.8	0.684
Hb at admission (g/dl)			
Mean ± SD	8.1 ± 2.9	8.2 ± 2.6	0.801

Distribution of upper GI bleeding cases according to the source of bleeding

Regarding the source of bleeding, no significant difference was detected between both study groups; as illustrated in table (3).

Table 3: Distribution of upper GI bleeding cases according to the source of bleeding.

Source of bleeding	Group		P value
	Restrictive group (N=112)	Liberal group (N=115)	
Source of bleeding			
Peptic ulcer	30	31	0.974
	26.8%	27.0%	
Gastroesophageal varices	33	36	
	29.5%	31.3%	
Erosive lesions (gastritis, esophagitis, duodenitis)	19	22	
	17.0%	19.1%	
Portal hypertensive gastropathy	5	5	

	4.5%	4.3%	
Malignancy	16	15	
	14.3%	13.0%	
Mallory-Weiss tear	6	5	
	5.4%	4.3%	
No abnormality detected on endoscopy	3	1	
	2.7%	0.9%	

In-hospital management of both study groups

Regarding in-hospital management, patients of the liberal group were significantly more likely to need variceal banding (P=0.002) and octreotide injection (P=0.008); as shown in table (4).

Table 4: Comparison of in-hospital management between both study groups.

In-hospital management	Group		P value
	Restrictive group (N=112)	Liberal group (N=115)	
Fresh frozen plasma	11	16	0.414
	9.8%	13.9%	
Platelet transfusion	8	9	1.000
	7.1%	7.8%	
Banding	51	76	**0.002**
	45.5%	66.1%	
Sclerosant	7	12	0.339
	6.3%	10.4%	
Octreotide	28	48	**0.008**
	25.0%	41.7%	
Fluid administration (ml): Mean ± SD	5193	5839	0.098

Comparison of overall survival between both study groups

Overall emergency department mortality was seen in 3 (2.7%) cases of the restrictive group and 12 (10.4%) cases of the liberal group, with the difference being statistically significant (P value = 0.030); as shown in table (5).

Table 5: Comparison of overall survival between both study groups.

Survival (within emergency department)	Group	
	Restrictive group (N=112)	Liberal group (N=115)
Survived	109	103
	97.3%	89.6%
Died	3	12
	2.7%	10.4%

Adverse consequences of blood transfusion in both study groups

A statistically significant difference was detected between both study groups regarding the incidence of transfusion-associated circulatory overload and pulmonary edema; as shown in table (6).

Table 6: Adverse consequences of blood transfusion.

Adverse consequences	Group		P value
	Restrictive group (N=112)	Liberal group (N=115)	
Transfusion-**associated circulatory overload**			
Yes	13	26	**0.035**
	11.6%	22.6%	
No	99	89	
	88.4%	77.4%	
Allergic reactions			
Yes	2	3	1.000
	1.8%	2.6%	
No	110	112	
	98.2%	97.4%	

Pulmonary edema			
Yes	4	14	**0.025**
	3.6%	12.2%	
No	108	101	
	96.4%	87.8%	
Acute kidney injury			
Yes	18	33	**0.026**
	16.1%	28.7%	
No	94	82	
	83.9%	71.3%	

DISCUSSION

Upper gastrointestinal bleeding is a common problem that is estimated to occur in 80 to 150 out of 100,000 people each year. Estimated mortality rates are between 2 and 15 percent.[6]

The current research has discovered that in patients experiencing severe acute upper gastrointestinal bleeding, the results were notably enhanced with a restrictive transfusion approach, where the hemoglobin threshold was set at 7 g per deciliter, in comparison to a liberal transfusion approach, where the hemoglobin threshold was set at 9 g per deciliter, as patients belonging to the restrictive group had improved survival. These findings are in concordance with Villanueva et al. who included 921 patients and reported that a restrictive strategy for transfusion significantly improved outcomes in patients with acute upper gastrointestinal bleeding, when compared to a liberal strategy, as patients who underwent the restrictive strategy had better control of factors contributing to death, such as further bleeding, the need for rescue therapy, and serious adverse events.[7] In the study conducted by Hébert et al., it was discovered that out of 838 critically-ill patients, the mortality rate during hospitalization was notably lower in the group that followed a restrictive-strategy for red-cell transfusion (22.3 percent vs. 28.1 percent). The study concluded that a restrictive strategy for red-cell transfusion is at least equally effective and potentially better than a liberal transfusion strategy for critically ill patients.[8] The systematic review by Marik et al. suggested that RBC transfusions are associated with increased morbidity and mortality and demonstrated evidence that routine RBC transfusion in the nonbleeding patient with a hemoglobin concentration greater than 7.0 g/dL leads to improved outcome.[9] The systematic review and meta-analysis by Odutayo et al. reported that the number of RBC units transfused was lower in the restrictive transfusion group than in the liberal transfusion group and that restrictive transfusion was associated with lower risk of all-cause mortality and rebleeding overall.[10] Galal et al. observed that, among the Egyptian patients experiencing variceal bleeding, the approach of using a restrictive strategy for blood transfusion yielded superior outcomes in terms of complications, length of hospital stay, and mortality.[11] In their study, Chen et al. examined a substantial cohort of patients with upper gastrointestinal bleeding (UGIB) and observed that the group of patients who received a liberal blood transfusion had a greater incidence of mortality and rebleeding.[12]

Other studies have reported no difference between the two transfusion strategies, as the liberal strategy was not associated with better outcomes.[13][14]

The reason for increased rebleeding and mortality in the liberal group may be attributed to the reason that transfusions may be harmful in hypovolemic anemia and there is a high chance of re bleeding in portal hypertensive patients, as the redistribution of blood after transfusion may cause a rebound increase in the portal pressure.[15]

The present study has also found significantly reduced circulatory overload and pulmonary edema in the restrictive group, which is in concordance with Hebert et al. and Kola et al. who reported that Cardiac complications, particularly pulmonary edema, occurred more frequently with the liberal transfusion strategy.[8,16] The elevated incidence of cardiac complications suggests an increased likelihood of circulatory overload linked to a permissive transfusion approach.

Teutsch et al.'s meta-analysis found that initiating transfusion at a lower threshold resulted in a decreased incidence of transfusion reactions and the need for post-transfusion intervention.[17]

CONCLUSION

According to the results of the current study, patients who underwent transfusion with a restrictive strategy exhibited a notable decrease in the requirement for banding and octreotide therapy. Additionally, there was an enhancement in the overall survival and a decrease in transfusion-related complications.

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