Initial management and timing of endoscopy in nonvariceal upper GI bleeding

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Upper GI bleeding (UGIB) from a nonvariceal source is a common cause of hospital admission, accounting for nearly 300,000 hospitalizations per year in the United States alone.[1] The costs to manage patients with UGIB are rising, with in-hospital nationwide expenditures increasing from $3.3 billion in 1989 to $7.6 billion in 2009.[2] Although the estimated mortality rate has been widely reported to be 5% to 14%, recent evidence suggests that in-hospital mortality has decreased to approximately 2%, most likely because of advances in both medical and endoscopic therapies.[2-4]

The initial management of patients with nonvariceal UGIB includes resuscitation, close hemodynamic monitoring, treatment with a proton pump inhibitor, management of antithrombotics, and, in some patients, blood transfusion. The next step in management is typically endoscopy. Current guidelines recommend that endoscopy be performed within 24 hours of presentation in patients with nonvariceal UGIB.[5-9] However, the role of more urgent endoscopy, especially with regard to patients presenting with higher-risk bleeding episodes, remains controversial. In this article we review the existing literature on initial management of nonvariceal UGIB and on the timing of endoscopy.

INITIAL MANAGEMENT

Resuscitation, monitoring, and triage

The first step in the management of UGIB is fluid resuscitation. For adequate venous access, 2 large-bore peripheral venous lines (16 or 18 gauge) should be placed immediately. Isotonic intravenous fluids (eg, normal saline solution) are then administered to restore a normal circulating blood volume. For patients with evidence of hemodynamic instability (heart rate > 100 bpm, systolic blood pressure < 100 mm Hg, or orthostatic hypotension), a bolus of 500 mL of intravenous isotonic fluid should be given and repeated as necessary to achieve hemodynamic stability. Patients typically are also given supplemental oxygen.

Vasopressor therapy may be required to maintain adequate end-organ perfusion if a patient remains hypotensive despite aggressive fluid resuscitation. Endotracheal intubation should be considered for patients who develop signs of volume overload, have persistent hemodynamic instability, or are at increased risk of aspiration (eg, those with altered mental status or massive hematemesis).

All patients with UGIB require close monitoring of their vital signs for ongoing assessment of their hemodynamic and respiratory status, including monitoring with telemetry. Patients who are hemodynamically stable after initial attempts at resuscitation can often be managed on a telemetry ward. However, patients who remain hemodynamically unstable or who have signs of respiratory compromise are best managed in an intensive care unit.

Proton pump inhibitors

A key element in the initial management of UGIB is initiation of a proton pump inhibitor. By elevating the gastric pH, proton pump inhibitors facilitate clot stabilization within the stomach and have been shown to improve outcomes such as rebleeding and the need for surgery.[10-15]

Although proton pump inhibitors are often given as high-dose continuous infusions (eg, omeprazole 80 mg IV bolus followed by an 8-mg/hr continuous infusion), continuous infusions have not been shown to be more effective than high-dose intermittent dosing (eg, omeprazole 40 mg IV every 12 hours). This was illustrated in a meta-analysis of 13 randomized controlled trials in which intermittent dosing was not inferior to continuous infusion with regard to rebleeding, need for surgery/repeat intervention, or need for urgent intervention.[16]

Abbreviations: AUC, area under curve; GBS, Glasgow Blatchford score; INR, international normalized ratio; UGIB, upper GI bleeding.

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Blood transfusion

For patients with UGIB, transfusion of blood products can help replace ongoing blood loss and increase delivery of oxygen to tissues. In cases of exsanguinating bleeding, blood transfusion is necessary regardless of the patient's hemoglobin level (because initially there has not been enough time for equilibration, so the hemoglobin value may not reflect the degree of blood loss). However, for patients with less-severe bleeding, the decision to give a blood transfusion should balance the benefit of increasing the oxygen-carrying capacity of the blood with the risks of blood transfusion. Risks associated with blood transfusion include allergic reactions, transfusion-related acute lung injury, and volume overload.

Traditionally, a hemoglobin threshold of 9 to 10 g/dL was used to identify patients who should receive a blood transfusion. However, studies have found that patient outcomes are improved when a *lower* hemoglobin value is chosen as the transfusion threshold.[17-20] This was directly evaluated in a randomized controlled trial conducted by Villanueva et al[18] that included 921 patients with acute UGIB. Patients were assigned to a restrictive (transfusion for hemoglobin < 7 g/dL) or a liberal (transfusion for hemoglobin < 9 g/dL) strategy. Patients were excluded if they had massive exsanguinating bleeding, a blood transfusion within the past 90 days, or a recent acute coronary syndrome or stroke/transient ischemic attack. Patients with portal hypertension were not excluded. All patients received an endoscopy within 6 hours of presentation, which is more rapid than standard clinical practice. Mortality, rebleeding, and adverse event rates were all lower with the restrictive transfusion strategy compared with the liberal transfusion strategy (Table 1).

These results are consistent with prior observational studies that found worse outcomes with increased rates of blood transfusion in acute UGIB.[19,20] Possible reasons for increased mortality and rebleeding rates with a liberal transfusion strategy include impairment of coagulation and an increase in portal pressure from excessive blood volume.[21-23] Although the decision to transfuse should be individualized for each patient, the existing literature supports a restrictive transfusion strategy in UGIB, with a hemoglobin threshold of 7 g/dL except in cases of massive exsanguinating bleeding or if the patient has significant cardiovascular comorbidities (eg, unstable coronary artery disease).

TABLE 1. Restrictive vs liberal packed red blood cell transfusion strategy in upper GI bleeding[18]

Outcomes	Restrictive strategy (transfuse for hemoglobin < 7 g/dL)	Liberal strategy (transfuse for hemoglobin < 9 g/dL)	*P* value
No. of patients	444	445	
Probability of survival at 6 weeks	95%	91%	.02
Rebleeding rate	10%	16%	.01
Need for rescue therapy*	2%	6%	.04
Adverse event rate	40%	48%	.02

*Rescue therapy defined as interventional radiology or surgery.

Management of patients receiving antiplatelets

The most common antiplatelet agents in patients presenting with UGIB are aspirin and thienopyridines ($P2Y_{12}$ receptor blockers). These medications should generally be held at the time of presentation, and platelet transfusion can be considered for severe bleeding. In a randomized controlled trial of patients presenting with acute peptic ulcer bleeding on daily aspirin for secondary prophylaxis of established cardiovascular or cerebrovascular diseases that required regular antiplatelet therapy, patients who resumed aspirin after successful hemostasis had a nonsignificant trend toward recurrent bleeding but a lower 30-day mortality compared with patients whose aspirin was held.[24] Although additional data (particularly on thienopyridines) are generally lacking, current guidelines recommend restarting antiplatelet agents once patients are deemed stable after the UGIB.[25]

Management of patients receiving anticoagulants

Warfarin. For patients presenting with UGIB, an elevated international normalized ratio (INR) > 1.5 has been associated with an increase in mortality.[26,27] Warfarin should generally be stopped at the time of presentation. However, for patients at high risk of thromboembolic events, the benefits of stopping anticoagulation need to be weighed against the risks.

Endoscopy does not need to be delayed for patients with mildly to moderately elevated INRs. Retrospective studies have shown that therapeutic upper endoscopy can be safely and effectively performed in such patients.[28-30] Choudari et al[28] evaluated 52 patients on warfarin who were seen with acute UGIB. If necessary, anticoagulated patients received fresh frozen plasma before endoscopy to lower the INR to 1.5 to 2.5. Of the anticoagulated patients, 23 received endoscopic therapy for bleeding peptic ulcers, and there was no significant difference in sustained hemostasis (91% vs 92%) or mortality (0% vs 4%) compared with 50 closely matched control subjects with similar risk factors for rebleeding.

Consistent with these results, a retrospective analysis of a large cohort of patients with acute UGIB found that admission INR was not predictive of rebleeding.[29] A subsequent retrospective study of 233 patients with UGIB evaluated the effect of an elevated INR on 30-day

rebleeding rates.[30] There were 102 patients (44%) who had an INR $\geq$ 1.3 at the time of endoscopy, 95% of whom had an INR between 1.3 and 2.7. When compared with patients without a coagulopathy, there was no difference in rebleeding rate (23% vs 21%). As with prior studies, INR was not predictive of rebleeding or other secondary outcomes (mortality, surgery, length of stay, transfusion requirement) on multivariable analyses.

Given the available evidence, upper endoscopy appears to be both safe and effective for patients with acute UGIB with a mild to moderate INR elevation. Current consensus guidelines advise that correction of a moderate coagulopathy (INR up to 2.5) should not delay endoscopy.[31]

Direct-acting oral anticoagulants. Because of a fixed oral dosing schedule without the need for drug monitoring, direct-acting oral anticoagulants have become a popular anticoagulation alternative to warfarin therapy. This group of drugs currently includes the direct thrombin inhibitor dabigatran etexilate (Pradaxa, Boehringer Ingelheim, Ingelheim am Rhein, Germany) and the direct oral factor Xa inhibitors rivaroxaban (Xarelto, Jaussen Pharmaceutica, Beerse, Belgium), apixaban (Eliquis, Bristol-Meyers Squibb, New York, NY, USA), and edoxaban (Lixiana, Daiichi-Sankyo, Tokyo, Japan).[32] A recent meta-analysis found that direct-acting oral anticoagulants as a class significantly reduced the risk of stroke or systemic embolic effects compared with warfarin but increased the risk of GI bleeding.[33] These drugs have short half-lives (5-15 hours) and are primarily cleared by the kidneys, so withholding the drug and providing adequate fluid resuscitation is a critical step in the management of most patients with UGIB who are receiving direct-acting oral anticoagulants (as with warfarin, in patients at very high thromboembolic risk the benefits of discontinuing the drug need to weighed against the potential harms).

If bleeding is severe and persistent, there is a potential role for transfusion of clotting factors such as fresh frozen plasma, activated factor VII, or prothrombin complex concentrate (which contains factors II, VII, IX, and X). Activated prothrombin complex concentrate is particularly effective for patients on dabigatran, although it may be replaced by the newly U.S. Food and Drug Administration–approved reversal agent, idarucizumab (see next paragraph). For patients on factor Xa inhibitors who have persistent, severe bleeding, nonactivated prothrombin complex concentrate is the most effective product currently available.[34]

In 2015 the U.S. Food and Drug Administration approved the use of idarucizumab (Praxbind), a monoclonal antibody against dabigatran that reverses the anticoagulant effect within minutes.[35] Andexanet alfa, a decoy protein that binds the active site of factor Xa inhibitors, effectively reverses the effects of the direct oral factor Xa inhibitors but is not currently approved by the U.S. Food and Drug Administration.[36] There will be more options for managing patients who are taking direct-acting oral anticoagulants and present with acute UGIB with the arrival of these reversal agents.

Risk stratification

Prognostic scores have been developed to stratify patients with UGIB into high- and low-risk categories. Patients at low risk may be appropriate for outpatient management, whereas very high-risk patients may benefit from admission to an intensive care unit. The Rockall score[37] accurately predicts mortality but requires endoscopic data to fully calculate, whereas the Glasgow Blatchford score[38] (GBS) and the AIMS65 score[27] are 2 extensively studied scores that do not require endoscopic data and thus can be calculated at initial presentation (Table 2).

The GBS was developed to predict which patients with UGIB would require an intervention, as defined by need for blood transfusion, endoscopic therapy, or surgery.[38] The score uses only clinical data available at presentation and ranges from 0 to 23. In the original validation study the score accurately identified patients at low risk (GBS $\leq$ 2) and high risk (GBS $\geq$ 10) of needing a clinical intervention. A subsequent study showed that patients who were seen with UGIB and a GBS score of 0 could be safely managed as outpatients, with no readmissions for UGIB or deaths within a 6-month follow-up period.[39] A meta-analysis found that a GBS threshold > 2 is 98% sensitive for determining the need for urgent evaluation of UGIB.[40]

The AIMS65 score was shown to predict inpatient mortality as well as length of stay and cost of admission in patients with acute UGIB.[27] The score contains 5 components that are readily available at presentation. Because each factor contributes 1 point to the total score, the AIMS65 score can easily be calculated at the bedside. In a validation study patients with an AIMS65 score of 0 or 1 had a lower risk of mortality (.3% and 1%, respectively) compared with those with a score of 4 or 5 (22% and 32%, respectively).

Recent studies have compared the AIMS65 score with the GBS. In a retrospective study with 278 patients with UGIB, the AIMS65 score was superior for predicting inpatient mortality compared with the GBS (area under the curve [AUC], .93 vs .68; $P < .001$), similar for predicting a composite clinical endpoint that included rebleeding (AUC, .62 vs .68; $P = .13$) and inferior for predicting blood transfusions (AUC, .65 vs .85; $P < .01$).[41] In a subsequent study of 298 patients with UGIB, the AIMS65 score again was superior to the GBS for predicting inpatient mortality (AUC, .85 vs .66; $P < .01$) but similar for predicting in-hospital rebleeding (AUC, .69 vs .62; $P = .19$) and a composite clinical endpoint (AUC, .57 vs .59; $P = .49$).[42]

Erythromycin

In patients with acute UGIB, retained blood and clots within the stomach can impair endoscopic visualization. Erythromycin, a macrolide antibiotic with motilin-like

TABLE 2. Components of the AIMS65, Glasgow-Blatchford, and Rockall scores

AIMS65 score		Glasgow-Blatchford score		Rockall score	
Risk factor	**Points**	**Risk factor**	**Points**	**Risk factor**	**Points**
Albumin < 3.0 g/dL	1	*BUN, mg/dL*		*Age, y*	
INR > 1.5	1	≥18.2 to <22.4	2	<60	0
Altered **m**ental status	1	≥22.4 to <28.0	3	60-79	1
SBP ≤ 90 mm Hg	1	≥28.0 to <70.0	4	>80	2
Age > **65** y	1	≥70.0	6	*Shock*	
		Hemoglobin, men, g/dL		No shock	0
		≥12.0 to <13.0	1	Pulse > 100 bpm, SBP > 100 mm Hg	1
		≥10.0 to <12.0	3	SBP < 100 mm Hg	2
		<10.0	6	*Comorbidity*	
		Hemoglobin, women, g/dL		No major	0
		≥10.0 to <12.0	1	CHF, IHD, or major comorbidity	2
		<10.0	6	Renal failure, liver failure, or metastatic cancer	3
		SBP, mm Hg		*Diagnosis*	
		100-109	1	Mallory-Weiss tear or no lesion and no stigmata	0
		90-99	2	All other diagnoses	1
		<90	3	GI malignancy	2
		Other clinical parameters		*Evidence of bleeding*	
		Heart rate ≥ 100 bpm	1	No stigmata or dark spot on ulcer	0
		Melena	1	Blood in upper GI tract, adherent clot, visible or spurting vessel	2
		Syncope	2		
		Liver disease	2		
		CHF	2		
Maximum score	5	Maximum score	23	Maximum score	11

SBP, Systolic blood pressure; *CHF*, congestive heart failure; *IHD*, ischemic heart disease; *INR*, international normalized ratio; *BUN*, blood urea nitrogen.

properties, increases gastric emptying and thereby allows for improved views of the gastric mucosa. Intravenous erythromycin (250 mg or 3 mg/kg as a single dose over 30-120 minutes) improves endoscopic visualization while also shortening length of stay and reducing the need for repeat endoscopy and amount of blood transfusion.[9] However, it has not been shown to alter patient-related outcomes, including rebleeding or mortality.

TIMING OF ENDOSCOPY

An important component of the management of patients with acute UGIB is upper endoscopy, and many studies have been performed to try to determine the optimal timing of endoscopy. Performing endoscopy too early may not allow for adequate resuscitation and could result in worse patient outcomes. In addition, early endoscopy may be performed at off-hours, when fewer resources may be available to the endoscopist. However, delaying endoscopy could result in worse patient outcomes because of ongoing bleeding. Overall, studies suggest that performing endoscopy within 24 hours decreases length of stay and possibly the need for surgery while reducing rebleeding and mortality rates in patients at higher risk.

Nine studies of patients with acute UGIB have evaluated the effect of endoscopy timing on clinical outcomes and/or healthcare resource use, although the studies differed significantly in their designs, which complicates the interpretation of the results as a whole (Table 3).[43-51] Three studies were randomized controlled trials, 5 were retrospective cohort trials, and 1 was a prospective cohort trial. Six studies included both hemodynamically unstable and stable patients, 2 studies focused only on hemodynamically stable patients, and 1 study only included hemodynamically unstable patients. Finally, 1 study included patients with variceal bleeding sources.[46] The major findings of the studies are summarized in Table 4.

Immediate endoscopy

Two studies have looked at the value of performing an immediate endoscopy and failed to show improvements in clinically important outcomes.[43,44] In a randomized trial, 110 patients were randomly assigned at admission to receive early endoscopy in the emergency department

TABLE 3. Study design and characteristics of selected articles on timing of endoscopy for nonvariceal UGIB

Study	Study period	Follow-up period	Notable inclusion criteria	Notable exclusion criteria	Hemodynamic status	Multicenter
Randomized controlled trials						
Lin[48]	1993-1994	60 days	–	Coagulopathy	Both	No
Lee[43]	12 months	30 days	HD stable	Comorbidity requiring ICU Coagulopathy Recent UGIB	Stable	No
Bjorkman[45]	N/A (early termination)	30 days	HD stable	Severe comorbidity	Stable	Yes (3)
Prospective cohort trial						
Lim[51]	18 months	Variable (length of stay)	Any patient with UGIB (from ED or hospital ward)	–	Both	No
Retrospective cohort trials						
Cooper[49]	1994	Variable (length of stay)	Included variceal source	–	Both	Yes (13)
Schacher[44]	1997-1998	14 days	Bleeding ulcer on EGD	Transfer and > 12 hr from initial presentation	Both	No
Targownik[46]	1999-2004	30 days	HD unstable	Transfer and > 6 hr from initial presentation	Unstable	Yes (2)
Tai[47]	7/2004-12/2004	Variable (length of stay)	Age > 60 y Severe comorbidity Active bleeding >6 units PRBCs Coagulopathy	Only minor lesions on EGD	Both	No
Cooper[50]	2004	30 days	Age ≥ 66 years Diagnosis of peptic ulcer bleed (inpatients and outpatients)	–	Both	Yes (5% of nationwide sample)

HD, Hemodynamically; *ICU*, intensive care unit; *ED*, emergency department; *PRBCs*, packed RBCs.

(treatment group) or endoscopy within 2 days (control group).[43] There were no significant differences in key clinical outcomes between the 2 groups, including mortality, recurrent bleeding, surgery, transfusion requirement, or repeat endoscopy. However, the early group did have a significantly lower length of stay (1 vs 2 days; $P = .001$) and hospitalization costs ($2068 vs $3662; $P < .001$).

In a retrospective study of 81 patients with UGIB from a peptic ulcer, patients were divided into 2 groups: those who underwent endoscopy within 3 hours (n = 43) and those who underwent endoscopy within 48 hours (n = 38).[44] Although the median time to endoscopy was significantly shorter in the early endoscopy group (2.1 vs 12.0 hours; $P < .001$), there was no significant reduction in mortality, recurrent bleeding, surgery, or length of stay compared with later endoscopy. However, there was a significantly increased rate of endoscopic therapy in the early group (77% vs 47%; $P = .006$) and a higher rate of detecting actively spurting peptic ulcers (19% vs 3%; $P = .022$).

Early endoscopy

Four studies have examined outcomes when early endoscopy (within 6-12 hours) is performed.[45-48] Overall, the studies found that early endoscopy did not improve healthcare resource use or clinical outcomes and was largely ineffective in influencing endoscopic triage for early discharge. However, the studies did find increases in endoscopic therapy rates in those who underwent early endoscopy.

In a randomized controlled trial performed at 3 academic medical centers, 93 patients with hemodynamically stable nonvariceal UGIB were randomly assigned to either undergo early endoscopy (within 6 hours) or elective endoscopy (within 48 hours).[45] For patients in the early endoscopy group, the results of the endoscopy and recommendations for discharge were conveyed to the emergency department physician, who then made the final decision on the patient's disposition (rather than the endoscopist). The timing of endoscopy made no difference in either healthcare resource use or clinical outcomes. However, the early endoscopy group did have more high-risk endoscopic lesions (32% vs 20%; $P = .017$). Despite gastroenterology recommendations for 19 patients to be discharged home based on the findings of early endoscopy, only 4 patients (21%) were discharged.

A retrospective study investigated the role of early endoscopy within 6 hours in 169 patients with acute nonvariceal UGIB who were hemodynamically unstable.[46]

TABLE 4. Summary of results of selected articles on timing of endoscopy for nonvariceal UGIB

Study	Sample size (early vs standard timing)	Definition of early endoscopy	Early vs standard timing outcomes			
			Death (%)	Rebleeding (%)	Surgery (%)	LOS (days)
Immediate endoscopy						
Lee[43]	110 (56 vs 54)	≤2 *h*	0 vs 3.7	3.6 vs 5.6	3.6 vs 1.9	1 vs 2*
Schacher[44]	81 (43 vs 38)	≤3 *h*	0 vs 0	14.0 vs 15.8	9.3 vs 7.9	5.1 vs 5.9
Endoscopy within 12 h						
Bjorkman[45]	93 (47 vs 46)	≤6 *h*	0 vs 0	–	2.1 vs 2.2	3 vs 3
Targownik[46]	169 (77 vs 92)	≤6 *h*	8 vs 6	9 vs 8	8 vs 2	4 vs 4
Tai[47]	189 (88 vs 101)	≤8 *h*	1.1 vs 5.9	–	.0 vs .0	5.1 vs 6.0
Lin[48],†	107 (53 vs 54)	≤12 *h*	1.9 vs 1.9	5.7 vs 9.3	5.7 vs 7.4	–
Endoscopy within 24 h						
Lim[51],‡	97 (47 vs 50)	≤13 *h*	0 vs 44*	12.0 vs 14.9	0.0 vs 2.1	5.6 vs 19.5*
Cooper[49]	909 (583 vs 326)	≤24 *h*	3.8 vs 3.4	–	–	5.0 vs 6.4*
Cooper[50]	2592 (1854 vs 738)	≤24 *h*	6.2 vs 7.3	–	1.2 vs 3.4*	4 vs 6*

LOS, Length of stay; *UGIB*, upper GI bleeding.
*Statistically significant.
†Subgroup analysis of patients with coffee-ground or bloody aspirate on nasogastric lavage.
‡Subgroup analysis of high-risk patients.

Seventy-seven patients (46%) underwent endoscopy within 6 hours and 92 patients (54%) underwent endoscopy between 6 and 24 hours from the time of admission. As in the randomized controlled trial, the early endoscopy group had a significantly increased rate of high-risk endoscopic lesions (57% vs 37%; $P = .01$) and use of therapeutic endoscopy (53% vs 37%; $P = .04$). However, there were no differences in mortality, recurrent bleeding, or surgery between the 2 groups. Healthcare use measures were similar as well. However, it is important to note that despite the fact that patients were hemodynamically unstable, patients in the early endoscopy and standard endoscopy timing groups both had relatively low pre-endoscopic Rockall scores (3.2 and 3.3, respectively).

In another retrospective study of nonvariceal UGIB with 189 patients, clinical outcomes were compared between those receiving endoscopy within 8 hours (88 patients; 47%) and those who received endoscopy between 8 and 24 hours from the time of admission (101 patients; 53%).[47] There were no significant differences in mortality, recurrent bleeding, total amount of blood transfusion, or length of stay between the 2 groups. However, high-risk ulcers, including active bleeding (19% vs 8%; $P = .03$) or visible vessels (34% vs 12%; $P < .01$), were more commonly identified in the early endoscopy group, and there was a corresponding increased rate of combination endoscopic therapy in the early endoscopy group (40% vs 15%; $P < .001$). Increased blood retention was noted in the stomach in the early endoscopy group (40% vs 15%; $P < .001$).

In a second randomized controlled trial of 325 patients with peptic ulcer bleeding, patients were assigned to endoscopy within 12 hours or endoscopy after 12 hours.[48] Unique to this study, each patient received a nasogastric lavage in the emergency department and was then classified into 1 of 3 groups (clear, coffee grounds, or bloody) based on the aspirate. In the analysis of patients with clear (67.1%) or coffee-ground (23.7%) aspirates, there was no difference in mortality, recurrent bleeding, surgery, total blood transfusion, or length of stay between those who underwent early endoscopy and those who underwent more delayed endoscopy. However, there was a significantly decreased volume of blood transfused (mean, 450 ± 465 mL vs 666 ± 548 mL; $P < .001$) and length of stay (mean, 4 ± 6 days vs 14.5 ± 10 days; $P < .001$) in the patients with bloody aspirate who received early endoscopy. Although nasogastric lavage is not currently recommended in the routine evaluation of UGIB, this study did identify a potential benefit for endoscopy within 12 hours in patients with higher-risk bleeding.

Endoscopy within 24 hours

Two studies looked at the performance of endoscopy within 24 hours of presentation. Performing endoscopy within 24 hours appears to decrease length of stay as well as the need for surgery and the rebleeding rates, at least among those who require endoscopic therapy. In addition, endoscopy within 13 hours may decrease mortality rates among those with a GBS ≥ 12.

In a retrospective study of 909 patients with UGIB from 13 different hospitals, healthcare use and patient outcomes were compared between those who underwent endoscopy within 24 hours and those who underwent endoscopy after 24 hours.[49] Endoscopy within 24 hours was performed in 583 patients (64%). There was no significant difference in the rate of recurrent bleeding or need for surgical

intervention in the early versus late endoscopy group (adjusted odds ratio [OR], .70; $P = .15$). However, length of stay was significantly shorter in the early endoscopy group (5.0 vs 6.4 days; $P < .001$). In addition, lower rebleeding and surgery rates were seen in the subgroup of patients who underwent early endoscopy and who required endoscopic intervention.

A retrospective, nationwide study used a random sample of inpatient and outpatient Medicare claims from 2004 in patients aged 66 years and older with a principal ICD-9 code for peptic ulcer hemorrhage to examine the importance of the timing of endoscopy.[50] In total, 2592 patients were included in the analysis, and 1854 patients (71.5%) underwent endoscopy within 1 day of presentation. When comparing this group with those who received endoscopy after 1 day, there was a significant decrease in length of stay (–1.95 days; 95% confidence interval [CI], –1.29 to –2.60) and need for surgery (adjusted OR, .37; 95% CI, .21-.66) in the early endoscopy group. However, patients with delayed endoscopy were more likely to be inpatients and to have more comorbidities compared with the early endoscopy group. As with other studies, there was no significant difference in mortality with early endoscopy (6.2% vs 7.3%; $P = .28$).

In a novel approach, Lim et al[51] assessed the timing of endoscopy in nonvariceal UGIB based on a bleeding prognostic score. This study was performed in a university hospital with 24-hour endoscopy service and included patients who developed bleeding while hospitalized for other reasons (19.4% of patients). The timing of endoscopy was determined by the on-call gastroenterologist (without the aid of a formal risk score calculation) and the time of presentation. GBS was calculated retrospectively for each patient. A total of 934 patients was included in the study, and 77.6% of the patients underwent endoscopy within 24 hours. The authors then stratified the study sample into lower-risk (GBS < 12) and high-risk (GBS ≥ 12) groups and compared the timing of endoscopy with inpatient mortality within each group. In the lower-risk group ($n = 837$), which comprised most of the study sample, timing of endoscopy was not associated with inpatient mortality. However, in the high-risk group ($n = 97$), time to endoscopy was the only significant predictor of mortality after adjusting for multiple confounders (adjusted OR, 1.09; 95% CI, 1.02-1.17). The authors found that all deaths in the high-risk group occurred when endoscopy was delayed for more than 13 hours (44% vs 0%; $P < .001$). Of note, there was no difference in other clinical outcomes such as rebleeding rate, surgery, or transfusion requirement. The authors concluded that patients with high-risk bleeding prognostic scores benefit from earlier endoscopy, although it is also possible that clinical judgment underestimated the severity of bleeding or that high-risk patients with delayed endoscopy required more prolonged resuscitative efforts and thus were more likely to die.

CONCLUSIONS

With advances in medical and endoscopic therapy, the in-hospital mortality rate for nonvariceal UGIB has decreased in recent years.[2] Initial management includes resuscitation, close hemodynamic monitoring, treatment with a proton pump inhibitor, management of antithrombotics, and, in some patients, blood transfusion. The next step in management is typically endoscopy. In most patients with nonvariceal UGIB, endoscopy should be performed within 24 hours of presentation. One notable exception is patients with very low risk of adverse outcomes from UGIB (ie, GBS score of 0), who may be managed safely as outpatients.[39] Immediate and early endoscopy (within 12 hours of presentation) are associated with an increased use of endoscopic therapy without an overall improvement in clinical outcomes, including mortality, recurrent bleeding, or need for surgical intervention, when compared with endoscopy performed within 24 hours. However, there may be a benefit of early endoscopy for select patients at higher risk of bleeding.[49,51]

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