



## Timing of Emergency Endoscopy for Acute Upper Gastrointestinal Bleeding: A Literature Review

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### ABSTRACT

Upper gastrointestinal (GI) bleeding is a common cause for Emergency Department and hospital admissions and has significant mortality and morbidity if it remains untreated. Upper endoscopy is the key procedure for both diagnosis and treatment of acute upper GI bleeding. The aim of this article is to review the optimal timing of endoscopy in patients with acute upper GI bleeding. The cost-effectiveness and the influence of urgent or emergent endoscopy on patients' outcomes are discussed. Also, we compare and contrast the available evidence and guidelines regarding the recommended time points for performing endoscopy in different clinical settings.

### KEYWORDS:

Gastrointestinal bleeding, Endoscopy timing, Diagnosis, Emergency medical care

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### INTRODUCTION

Upper gastrointestinal (GI) bleeding is a common cause of Emergency Department referrals and hospital admissions, which has significant morbidity and mortality if it remains untreated.<sup>1-4</sup> Acute massive GI bleeding incidence is about 40-150 episodes per 100,000 persons per year<sup>5-7</sup> with 5-11% mortality rate<sup>8-11</sup> and higher incidence and mortality rate among the elderly patients.<sup>12,13</sup> The cost of overall upper GI bleeding is estimated to be more than 2 billion dollars in the United States annually.<sup>14,15</sup> Upper endoscopy is the procedure of choice for both diagnosis and treatment of acute upper GI bleeding and has a well known and established role in decreased mortality and re-bleeding.<sup>16-19</sup> Although there have been many advances in the endoscopy techniques and development of modern devices, the mortality rate has not decreased significantly in recent decades.<sup>20,21</sup> Most of the current guidelines and recommendations emphasize the role of early endoscopy (i.e. in the first 24 hours) and even during the first 16 hours as recommended by the Guidelines of the Romanian Society of Gastroenterology.<sup>22-25</sup> Also, urgent endoscopy, as defined by the phrase "as soon as possible", is recommended for most of the severe, ongoing bleeding, hemodynamic instability, or in the patients with cirrhosis.<sup>24</sup> However, in this setting, the optimal timing of endoscopy is necessary, and the cost-effectiveness and the influence of urgent or emergency endoscopy on patients' outcomes must be evaluated.

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**Table 1: Pre and post endoscopy Rockall scoring system**

Variable	Score 0	Score 1	Score 2	Score 3
Age	< 60	60 - 79	> 80	
Shock	No shock	Pulse > 100 BP > 100 Systolic	SBP < 100	Renal failure, liver failure, disseminated malignancy
Comorbidity	No major comorbidity		CHF, IHD any major comorbidity	
Endoscopy diagnosis	Mallory-Weiss tear, no lesion identified, and no stigmata of recent bleeding	All other diagnoses	Malignancy of upper GI tract	
Evidence of recent bleeding	None or dark spot only		Blood in upper GI tract, adherent clot, visible or spurting vessel	

Maximum additive score prior to diagnosis = 7. Maximum additive score following diagnosis = 11, Adapted from reference <sup>29</sup>  
Abbreviations: CHF, congestive heart failure; IHD, ischemic heart disease;

Also, local issues such as the availability of the resorts, equipment, intensive care unit (ICU) beds, active emergency operation rooms, and experienced gastroenterologist and nurses are among other concerns.<sup>10,26,27</sup>

The aim of this study was to review the literature for performing endoscopy in the setting of acute upper GI bleeding and patient preparation that could be lifesaving, applicable, and cost-effective without imposing extra risk either to the patient or the equipment and the staff.

### Risk assessment

Patients with upper GI bleeding may present with different symptoms such as coffee ground vomiting, hematochezia, melena, and fresh rectal bleeding.<sup>23</sup> The source and cause of bleeding and clinical signs and symptoms are important predictors of mortality, morbidity, and chance of re-bleeding.<sup>28</sup> In order to perform quantitative evaluation and risk assessment of the patients with GI bleeding, risk scoring systems have evolved and become more popular in recent years and are more often used to identify patients with increased risk of re-bleeding (> 5%) and mortality (>1%).<sup>29-31</sup>

The two most accepted and sensitive numerical scoring systems for GI bleeding risk assessment are the Glasgow-Blatchford Scoring system<sup>29</sup> and the Rockall scoring system.<sup>31</sup> Rockall scoring system, which was first introduced in 1996, is a mortality predictor scoring system that estimates the risk of

re-bleeding too.<sup>32,33</sup> The test can be applied both prior to endoscopy (Clinical Rockall score) and after endoscopy (Full Rockall scoring) (Table 1). Rockall scoring system with a pre-endoscopy score of “0” identifies patients at very low risk of re-bleeding or death. With this score, it may even be possible to discharge the patients to perform outpatient (OPD) endoscopy as soon as possible. Patients with a full (including the endoscopic findings) Rockall score of < 3 have a low risk of re-bleeding or death and can be considered for early discharge.<sup>33, 34</sup>

The Glasgow-Blatchford Scoring system predicts poor outcomes and the need for endoscopy in patients with non-variceal GI bleeding based on the clinical and laboratory parameters without the need for endoscopy<sup>32, 35</sup> (Table 2). The score includes pulse, systolic blood pressure, hemoglobin, and blood urea level, presence of syncope or melena, and evidence or history of heart failure or liver disease.<sup>29, 36-38</sup> Patients with a score of “0” are considered as low risk and have the least need for endoscopy, surgery, or transfusion. However, any other patients with scores of more than “0” are considered high-risk patients. Patients with a score of “0” could be considered for OPD early endoscopy.<sup>29, 39</sup> It is important to state that the cutoff value of score “0” has both a sensitivity and specificity of 100% to predict the need for treatment in acute upper GI bleeding with a negative predictive value of 100%.<sup>28</sup> The sensitivity for the cutoff value of 2 or less still remains 100%,<sup>28</sup> while the negative predictive value decreases to 98.1%.<sup>35</sup>

**Table 2: Glasgow-Blatchford Scoring system**

Glasgow-Blatchford Score	
Admission risk factor	Score
<b>BUN (mg/dL)</b>	
< 6.5	0
≥ 6.5 < 8.0	2
≥ 8.0 < 10.0	3
≥ 10.0 < 25.0	4
≥ 25	6
<b>Hemoglobin (g/L) for men</b>	
≥ 13.0	0
≥ 12.0 < 13.0	1
≥ 10.0 < 12.0	3
< 10.0	6
<b>Systolic blood pressure (mm Hg)</b>	
≥ 100	0
100 – 109	1
90 – 99	2
< 90	3
<b>Other Factors</b>	
Pulse ≥ 100 (per min)	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

Adapted from reference<sup>27</sup>

Both systems are very well applicable and sensitive,<sup>40</sup> however, the sensitivity and the accuracy of the Glasgow-Blatchford Scoring system has been reported to be higher in some recent studies,<sup>33, 41, 42</sup> and it is regarded as the most accurate scoring system for assessment of patients with upper GI bleeding and predicting the need for endoscopy and 30-day mortality rate.<sup>41</sup>

#### Time to endoscopy & literature review

The National Institute for Health and Care Excellence (NICE) guideline recommendations include risk assessment by Glasgow-Blatchford Score and Full Rockall score (after endoscopy) with early endoscopy (during the first 24 hours) for all patients, and immediate endoscopy for the patients with severe acute GI bleeding after resuscitation.<sup>4,40</sup>

The Scottish guideline for GI bleeding recommends hospital admission and early endos-

copy for the patients at the age of 60, witnessed hematemesis and hematochezia, liver disease, or known varices and hemodynamic disturbance (systolic blood pressure (SBP) < 100 mm Hg and pulse rate > beats 100/min).<sup>25</sup> International Consensus Recommendations on the Management of Patients with Non-variceal Upper Gastrointestinal Bleeding recommends that early endoscopy (in the first 24 hours of presentation) for most patients with upper GI bleeding.<sup>42,43</sup> Guidelines of the American Society of Gastrointestinal Endoscopy (ASGE) recommends early endoscopy (within the first 24 hours of presentation) after risk stratification, both variceal and non-variceal upper GI bleeding.<sup>44, 45</sup>

While almost all guidelines support the early endoscopy with the definition of “within the first 24 hours of presentation”, the effectiveness, risks, and cost-benefit effect of performing the endoscopy in a shorter interval must be evaluated.<sup>23,26,40,42,44,46</sup> The time interval for “early endoscopy” varies from 2 to maximum 24 hours after initial presentation.<sup>23,24, 47-49</sup> The terms of “urgent”, “emergency”, and “very early” endoscopy have been used interchangeably with different time interval definitions in the literature, and urgent (or as soon as possible) endoscopy definition varies from arrival time to 6 hours after initial presentation.<sup>24,26,42</sup>

One retrospective study on 500 patients with non-variceal upper GI bleeding from 2004 to 2006 showed that endoscopy within 6 hours compared with 6-24 hours was not associated with a different mortality rate, need for blood transfusion, and surgery.<sup>26</sup> A study on 169 patients with acute non-variceal GI bleeding that had either systolic blood pressure less than 100 mm Hg or pulse rate more than 100 beats per minute showed no significant difference in adverse outcomes or transfusion requirements in patients receiving endoscopy in the first 6 hours compared with the first 6-24 hours.<sup>50</sup> Another meta-analysis with 528 patients showed no significant difference in mortality (OR; 0.70 [CI; 0.14 to 3.57]), surgery (OR; 1.16 [CI; 0.39 to 3.51]), or re-bleeding (OR; 0.71 [CI; 0.28 to 1.81]) among the high risk patients who had undergone endoscopy in the first 12 hours compared with 12-24 hours after initial presentation.<sup>42</sup>

One study on 689 high-risk patients found no significant difference in the mortality rate among the patients who had undergone endoscopy within 3 hours after presentation compared with 3-24 hours ( $p = 0.67451$ ).<sup>24</sup>

Some retrospective analyses comparing urgent endoscopy (within first 8 hours) versus early endoscopy (8-24 hours) found no difference in clinical outcomes.<sup>42</sup> Interestingly, one study on 6,749 patients in the U.K found no difference between the mortality of the patients with GI bleeding who were admitted on the weekend vs. weekday (OR = 0.93; [95% CI; 0.75-1.16]),<sup>51</sup> but another similar study in the U.S. on 391,119 patients found a higher rate in-hospital mortality among patients that had been admitted on weekends (OR = 1.21; [95% CI, 1.09 –1.35]).<sup>52</sup> In contrast to the above findings, some different results have been reported in the literature, as well. One study found that the presence of fresh blood in nasogastric tubes, hemoglobin level less than 8 g/dL, hemodynamic instability, and WBC count more than 12000/mcL are independent predictors of active bleeding and the need for the endoscopy to be performed within the first 12 hours of the initial presentation ( $p < 0.050$ ).<sup>53</sup> A study by Lim and colleagues<sup>54</sup> on 394 high-risk upper GI bleeding revealed that the all-cause in-hospital mortality was significantly lower in the group of patients who had an endoscopy done within the first 13 hours of presentation compared with the other group that had undergone endoscopy in 13-24h (0% vs. 44% ;  $p < 0.001$ ).

NICE guidelines on acute upper GI bleeding recommend performing endoscopy immediately in unstable patients with severe acute upper GI bleeding immediately after resuscitation.<sup>40,43</sup> American Association for the Study of Liver Disease (AASLD) practical guidelines on prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis recommend that endoscopy should be done within the 12 hours of presentation to diagnose and treat variceal bleeding (Class I, Level A).<sup>55</sup> One study on 210 patients with acute variceal bleeding and stable hemodynamic parameters found no significant association between time to endoscopy and mortality (OR = 1.0 [95% CI; 0.92-1.08],  $p =$

0.91),<sup>56</sup> while another retrospective analysis on 311 consecutive acute variceal bleeding cases found that delayed endoscopy (more than 15 hours after presentation) was an independent risk factor for mortality (OR = 3.67 [95% CI; 1.27-10.39]).<sup>57</sup>

## DISCUSSION

Acute upper GI bleeding as a major life-threatening condition is one of the most common medical emergencies. It costs billions of dollars annually and estimated a crude overall in-hospital mortality of 10%.<sup>58,59</sup>

Endoscopy not only can offer identification of the source of bleeding but also can be used in the hemostatic treatment of lesions with active bleeding. This type of treatment can stop bleeding in patients with high-risk lesions and can reduce the need for surgery, as well. It is proposed that endoscopic hemostatic treatment can reduce further bleeding in high-risk lesions.<sup>60</sup> It is recommended that endoscopy was performed within 24 hours after the presentation for patients with acute upper GI bleeding.<sup>61</sup> Various study findings have demonstrated that urgent endoscopy (the definitions of which have varied among studies, ranging from within 2 hours to within 12 hours after presentation) in unselected patients with acute upper GI bleeding did not decrease mortality.<sup>62,63</sup>

In recent years, many improvements have been made to endoscopic devices. New technology and more sophisticated instruments allow us to perform advanced diagnosis and therapeutic procedures in the management of GI bleeding. However, despite improvements in endoscopic devices and associated modalities, the mortality rate has not changed in the past decade and has been reported to range between 6% and 12%.<sup>64-66</sup> Therefore, emphasizing the need for improvement in this area is worthy. Some studies have reported that mortality was unchanged for the past 50 years.<sup>59</sup> In order to improve patients' care, authors believe it is now time to focus on other aspects of management as well as the technical aspects. The importance of "risk assessment" and "time to endoscopy" in the management of GI bleeding is well evident. Therefore, the authors decided to review the current guidelines and recommendations with a focus on risk assessment and time to endoscopy



for the management of acute upper GI bleeding.

It is recommended that patients with acute upper GI bleeding undergo endoscopy within 24 hours; however, for the time range shorter than 24 hours, it has not been adequately explained. In one study, James and colleagues assigned patients with overt signs of acute upper GI bleeding and a Glasgow–Blatchford score of 12 or higher (scores range from 0 to 23, with higher scores indicating a higher risk of further bleeding or death) to undergo endoscopy within 6 hours (urgent-endoscopy group) or between 6 and 24 hours (early-endoscopy group). Findings revealed that among 516 patients who were enrolled in the study, the 30-day mortality was 8.9% (23 of 258 patients) in the urgent-endoscopy group and 6.6% (17 of 258) in the early-endoscopy group (difference, 2.3 percentage points; 95% CI, -2.3 to 6.9). Findings revealed further bleeding within 30 days in 28 patients (10.9%) in the urgent endoscopy group and in 20 (7.8%) in the early-endoscopy group (difference, 3.1 percentage points; 95% CI, -1.9 to 8.1). When initial endoscopy was performed, ulcers with active bleeding or visible vessels were seen in 105 out of the 158 patients (66.4%) with peptic ulcers in the urgent-endoscopy group, and 76 of 159 (47.8%) in the early endoscopy group, as well. After the initial endoscopy, 155 patients (60.1%) in the urgent-endoscopy group and 125 (48.4%) in the early-endoscopy group underwent endoscopic hemostatic treatment.<sup>67</sup> This study revealed that for patients with acute GI bleeding who were predicted to be at high risk for further bleeding or death, endoscopy was performed within 6 hours after gastroenterology consultation. This medical evaluation that used the Glasgow–Blatchford Score as a measure of risk would forestall further bleeding and improve outcomes as compared with endoscopy performed between 6 and 24 hours after consultation.

Abougergi and co-workers performed a longitudinal study of upper GI hemorrhage (UGIH) hospitalizations by using the nationwide inpatient sample.<sup>59</sup> They found that the non-variceal UGIH mortality rate decreased from 4.5% in 1989 to 2.1% in 2009. Also, the findings of the study revealed that non-variceal UGIH incidence decreased from 108 to 78 cases/100,000

persons in 1994 and 2009, respectively. It is reported that in-hospital upper endoscopy and endoscopic therapy rates increased from 70% and 10% in 1989 to 85% and 27% in 2009, respectively, and the early endoscopy rate increased from 36% in 1989 to 54% in 2009, as well. Although the median length of hospitalization decreased from 4.5 days in 1989 to 2.8 days in 2009, the median total hospitalization charges increased from \$9249 in 1989 to \$20,370 in 2009.

After an initial presentation of GI bleeding, risk stratification by either the Rockall scoring system or Glasgow-Blatchford Scoring system must be done. Glasgow-Blatchford Scoring system seems to be more applicable at the patient bedside, endoscopy independent, and was reported to be more accurate and sensitive. Patients with no history of melena, syncope, cardiac failure, and hepatic disease who have pulse rate < 100 beats per minute, systolic blood pressure  $\geq$  100 mm Hg, hemoglobin level  $\geq$  13.0 g/L for men or  $\geq$  12.0g/L for women, and BUN level < 6.5 mg/dL, have Glasgow-Blatchford Score of “0” and are categorized as low-risk patients. This group of patients could be considered for OPD early endoscopy with 100% sensitivity, specificity, and negative predictive value. Other patients must be considered as high risk and should be scheduled for early endoscopy in less than 24 hours of the initial presentation. In an international multicenter prospective study involving 3012 patients, a threshold score of 7 or higher was shown to provide the most accurate prediction of whether a patient will be determined to need endoscopic treatment. Findings revealed that the Glasgow Blatchford Score had high accuracy in predicting the need for hospital-based intervention or death. Scores of  $\leq$  1 appear the optimum threshold for directing patients to outpatient management. The area under the receiver operating characteristic curve of scores (AUROCs) for the other endpoints is less than 0.80; therefore their clinical utility for these outcomes seems to be limited.<sup>68</sup>

All patients who do not meet the above criteria are considered “high-risk patients”. Early endoscopy (within the first 24 hours of initial presentation) must be done for them. Most of the current evidence does not

show any significant effect of performing endoscopy in a shorter interval on mortality and outcome of the patients with non-variceal upper GI bleeding. However, two studies found a beneficial effect on mortality if the endoscopy is done in the first 12 hours after presentation. So the decision for the time of endoscopy within the first 24 hours should be made for each patient separately.

It is recommended that endoscopy be done immediately after resuscitation for severe acute upper GI bleeding. All patients with cirrhosis, history of liver disease, or at risk of variceal bleeding should have an endoscopy in the first 12 hours after each type of upper GI bleeding presentation. Finally, it must be emphasized that the two most common causes of upper GI bleeding are peptic ulcer disease and variceal bleeding. Hence, any recommendation should cover these underlying pathologies. Patients suspected of upper GI bleeding should be assessed carefully in an acute clinical setting. Despite some minor differences, all of the above guidelines and recommendations could be used as valuable tools to safely and accurately assess patients. Available logistics and individual circumstances should be considered in decision-making and management plans. More investigations and data from the large multicenter registries will be helpful in detecting the best time for endoscopy in the first 24 hours in the future.

## CONCLUSION

It must be emphasized that the two most common causes of upper GI bleeding are peptic ulcer disease and variceal bleeding. Patients suspected of upper GI bleeding in an acute clinical setting should be assessed carefully and resuscitated well. Taken together, despite some minor differences, all of the above guidelines and recommendations could be used as valuable tools to safely and accurately assess the patients. Available logistics and individual circumstances should be considered in decision-making and management plans. The majority of related studies in this field were relatively small, single-center, and mainly reflected GI bleeding incidence and treatment outcomes at tertiary-care

centers that must be covered in future studies. More investigations and data from the large multicenter registries will be helpful in the timely performing of endoscopy procedures.

## Author contributions:

Fardad Ejtehad, Gholam Reza Sivandzadeh, and Ramin Niknam contributed to idea generation, draft preparation, literature review, and preparing the manuscript equally. Ahmad Hormati, and Sajjad Ahmadpour, contributed to the literature review and preparing the manuscript.

## ETHICAL APPROVAL

There is nothing to be declared.

## CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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