

Alimentary Tract

A simplified clinical risk score predicts the need for early endoscopy in non-variceal upper gastrointestinal bleeding



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ABSTRACT

Background: Pre-endoscopic triage of patients who require an early upper endoscopy can improve management of patients with non-variceal upper gastrointestinal bleeding.

Aims: To validate a new simplified clinical score (*T*-score) to assess the need of an early upper endoscopy in non variceal bleeding patients. Secondary outcomes were re-bleeding rate, 30-day bleeding-related mortality.

Methods: In this prospective, multicentre study patients with bleeding who underwent upper endoscopy were enrolled. The accuracy for high risk endoscopic stigmata of the *T*-score was compared with that of the Glasgow Blatchford risk score.

Results: Overall, 602 patients underwent early upper endoscopy, and 472 presented with non-variceal bleeding. High risk endoscopic stigmata were detected in 145 (30.7%) cases. *T*-score sensitivity and specificity for high risk endoscopic stigmata and bleeding-related mortality was 96% and 30%, and 80% and 71%, respectively. No statistically difference in predicting high risk endoscopic stigmata between *T*-score and Glasgow Blatchford risk score was observed (ROC curve: 0.72 vs. 0.69, $p = 0.11$). The two scores were also similar in predicting re-bleeding (ROC curve: 0.64 vs. 0.63, $p = 0.4$) and 30-day bleeding-related mortality (ROC curve: 0.78 vs. 0.76, $p = 0.3$).

Conclusions: The *T*-score appeared to predict high risk endoscopic stigmata, re-bleeding and mortality with similar accuracy to Glasgow Blatchford risk score. Such a score may be helpful for the prediction of high-risk patients who need a very early therapeutic endoscopy.

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1. Introduction

Upper gastrointestinal bleeding (UGIB) is a common life-threatening condition with a significant impact on health care resources. Ideally, all patients with UGIB should undergo

endoscopy within 24 h by a trained endoscopist supported by skilled assistant staff [1]. Although endoscopic therapy plays a pivotal role in UGIB management, the value of an early endoscopy is still debated. The definition of early endoscopy varies from 2 to 24 h from presentation [2], and retrospective studies did not show a clear advantage for an early as compared with a delayed endoscopy. Early endoscopy has been associated with a shorter hospital stay and reduced costs, although with no significant effect on mortality and need for surgery [3,4]. Use of prognostic scoring systems which include endoscopic findings is recommended by international guidelines to identify low-risk patients suitable for early discharge [1]. However, in order to decide the timing of

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endoscopy, risk assessment should be performed by scoring system including only clinical and laboratory variables. In UGIB patients the pre-endoscopic Blatchford risk score and the clinical Rockall score have been suggested to predict the need for clinical and endoscopic intervention and mortality, respectively [5,6]. Although the Blatchford score can accurately identify those low-risk patients not requiring a therapeutic endoscopy, it has not been designed to predict the need and the timing for an early endoscopy. In a pilot single-centre study, we showed that a new simplified pre-endoscopic clinical and laboratory score (*T*-score) may accurately predict the presence of active bleeding or high risk stigmata [7]. Aim of this multicentre study was to prospectively validate the accuracy of the *T*-score in predicting high risk endoscopic stigmata, re-bleeding and mortality in non-variceal bleeding patients as compared with the Glasgow Blatchford risk (GBR) score, which was previously tested in such a setting [8].

2. Methods

2.1. Study population

Overall, 30 Endoscopy Units with out of hours endoscopy service participated in this nationwide study. Consecutive patients admitted for UGIB, as well as inpatients presenting with UGIB, were considered for enrolment during a 6 month period. According to the study protocol, an early (≤ 2 h) upper endoscopy was to be performed in all the UGIB-patients in the study period, irrespectively of any clinical or other factors. All patients presenting with non-variceal UGIB were included, whilst those with oesophageal or gastric varices bleeding were excluded, as well those in whom upper endoscopy was performed beyond the 2-h limit. Baseline characteristics, comorbidities, haemodynamic, laboratory and endoscopy findings were systematically recorded. Patients were followed up for a total of 30 days in order to assess re-bleeding and mortality rates. The clinical outcome of inpatients was recorded by the referring physician whereas patients discharged were contacted by telephone. A bleeding-related death was defined as any death occurring within 30 days of the index bleeding episode. Recurrent bleeding was defined by recurrent hematemesis, melena or both with either shock or a decrease in haemoglobin concentration of at least 2 g/l after initial treatment and stabilization. Re-bleeding had to be confirmed by a repeat endoscopy. When the source of bleeding was not identified due to the presence of fresh blood in the stomach, case was recorded as bleeding but source not identified at EGD [9].

2.2. Pre-endoscopic clinical scores

Before the procedure, patients were stratified by the endoscopists according to 4 clinical variables: general conditions (poor, intermediate, good), pulse (< 90 beats/min, 90–110 beats/min, > 110 beats/min), systolic blood pressure (< 90 mmHg, 90–110 mmHg, > 110 mmHg), and haemoglobin level (< 9 g/dL, 9–10 g/dL, > 10 g/dL) [7–11]. General conditions were intended as a measure of the risk of an impending shock – defined as shock index > 0.8 calculated as ratio heart rate/systolic blood pressure [12] – or the presence of symptomatic comorbidities (cardiovascular, hepatic, chronic kidney disease, diabetes, malignancy). In detail, “poor conditions” included patients with impending shock or with ≥ 3 comorbidities, “good conditions” included patients with no debilitation and without postural hypotension and ≤ 1 comorbidity, whereas patients with 2 comorbidities and without postural hypotension were classified as with “intermediate conditions”. A numerical score was created for each of these parameters, the sum of all the parameters resulting in the total *T*-score. Patients were thereafter classified

according to arbitrarily defined *T*-score cut-off in 3 categories: a sum ≤ 6 corresponds to T1 (high-risk), a sum of 7–9 to T2 (intermediate-risk), and a cumulative value ≥ 10 to T3 (low-risk). The GBR score was also calculated for each patient, as previously reported (Appendix B) [7]. High risk endoscopic stigmata was defined as active bleeding (oozing or spurting), presence of an adherent clot or nonbleeding visible vessel on peptic ulcer [13], as well as on other bleeding lesions, such as Mallory-Weiss tears, Dieulafoy’s lesion, neoplasia, gastroduodenal erosions, or other vascular source. All patients gave their informed consent prior the endoscopic examination.

2.3. Study outcomes

Primary endpoint was the accuracy of *T*- and GBR-scores in predicting high risk endoscopic stigmata at an early endoscopy. Secondary end-points were the ability of these scores in predicting re-bleeding and mortality rates at 30 days of follow-up.

2.4. Statistical analysis

Continuous variables were analyzed by independent-sample *T* test and categorical variables were analyzed by Chi-square test. We assessed the validity of the scoring system by plotting receiver-operating characteristics (ROC) curves. *T*- and GBR-scores were compared in the prediction of high risk endoscopic stigmata. All statistical analyses were performed with SPSS version 13.0 (SPSS Inc., Chicago, IL). A *p* value < 0.05 was considered to be statistically significant.

3. Results

3.1. Study population

A total of 860 consecutive patients were considered for enrolment in the study period. Overall, 602 patients had an early EGD within 2 h with a median time of 89 min (inter-quartile range, IQR: 60–110 min), whilst the remaining 258 cases were excluded since the EGD was performed beyond the 2 h limit. At endoscopy, further 130 patients were excluded due to gastro-oesophageal varices bleeding. Therefore, 472 patients (316 males, 156 females; median age 74 years, IQR 60.5–82.3) with non-variceal UGIB were included in the final analysis, 319 (67.6%) being outpatients and 153 (32.4%) inpatients. Main clinical characteristics of the study population are shown in Table 1.

3.2. Endoscopic and clinical outcomes

The main endoscopic findings are provided in Table 2. At endoscopy, high risk endoscopic stigmata were detected in 145 (50.8%) out 286 ulcers, including active bleeding ($N = 70$), visible

Table 1
Clinical characteristics of the study population.

	N (%)	Median (IQR)
Males	316 (66.9%)	
Age (years)		74.0 (60.5–82.3)
Number of comorbidities	2 (2–3)	
In-hospital bleeding	153 (32.4)	
Time of endoscopy (min)		89 (60–110)
Melena	354 (75.0)	
Syncope	69 (14.6)	
Hemodynamic instability	70 (14.8)	
Haemoglobin (g/dl)		9.0 (7.5–10.6)
Urea (mmol/l)		8.8 (5.3–14.4)

IQR: interquartile range.

Table 2
Endoscopic finding at entry.

Findings	N (%)
Duodenal ulcer	172 (36.4)
Gastric ulcer (including anastomotic)	114 (24.1)
Gastroduodenal erosions	60 (12.7)
Esophagitis with bleeding	30 (6.3)
Mallory-Weiss tears	22 (4.7)
Dieulafoy's lesion	14 (3)
Neoplasia	23 (4.9)
Other vascular source	14 (3)
No lesion identified	23 (4.9)

vessel ($N=40$), and adherent clot ($N=35$). Recurrent bleeding was recorded in 42 patients (8.8%) and surgery was needed in 24 (5%). Overall, 35 (7.4%) patients died within 30 days from the bleeding episode.

3.3. Accuracy of *T*- and *GBR*-scores

Distribution of patients according to *T*- and *GBR*-score classes and the related high risk endoscopic stigmata prevalence is shown in Table 3. The area under-the-ROC for *T*-score in predicting high risk endoscopic stigmata was 0.72 (95% CI, 0.68–0.75), and no difference was found compared with that for *GBR* (0.69, 95% CI 0.66–0.76, $p=0.3$). In detail, a threshold of *T* score ≤ 6 (corresponding to *T*-score class 1) appeared to predict the presence of high risk endoscopic stigmata with sensitivity and specificity of 30% and 96%, respectively, corresponding to positive and negative predictive values of 74.5% and 76.4%, respectively. *T*- and *GBR*-scores had a similar area under-the-ROC for predicting mortality (0.78 vs. 0.76; $p=0.9$). In detail, the cut-off point that maximized the sum of the sensitivity and the specificity of the *T*-score for mortality was 8, corresponding to a 71% and 80% sensitivity and specificity, respectively, whilst the *GBR* score which optimized stratification was 9 (sensitivity 65%; specificity 77%). Areas under-the-ROC of *T*- and *GBR*-scores for re-bleeding were also similar (0.64 vs. 0.63; $p=0.8$) (Fig. 1).

4. Discussion

Although the incidence has significantly decreased in the last decade, UGIB is a frequent and severe clinical condition that has a major economic burden [14–16]. The rationale of an early endoscopy lies in offering therapeutic endoscopy to active bleeding or high-risk lesions and identifying patients that can be discharge early from hospital [4,17,18]. However, a policy of early endoscopy leads to a significant burden of costs. In contrast, pre-endoscopic triaging of patients could lead to a more efficient use of resources, optimizing patients' care and outcome while reducing costs. It is

still to be determined the best time to provide endoscopy and the most recent recommendations suggest that endoscopy should be performed within 24 h of presentation and prognostic scales to stratify patients according to their death and re-bleeding risks should be used [1]. However, in the daily practice, on call endoscopist is expected to decide whether to proceed immediately or delay the procedure up to 12 or 24 h. This decisional process has important legal aspects and often the endoscopist is found to rush in the endoscopy units during nights or over the week-end even for low risk cases.

We have previously shown in a population derived from a single tertiary referral centre that patients with high risk endoscopic stigmata can be identified using a simplified clinical score [7]. In this multicentre study we have confirmed these findings in an external independent population and shown that *T* score is useful in discriminating high risk patients who need endoscopic therapy. A strength of the present study is represented by the time of endoscopy which was performed in all cases within 2 h after admission or clinical evidence of acute UGIB while hospitalized. The prevalence of high risk endoscopic stigmata was similar to previous studies from different countries with larger sample size. An increased percentage of patients with high risk endoscopic stigmata was found in our study compared to another previous Italian prospective study, probably reflecting the different ratio between patients admitted from the Emergency Department and inpatients in the population studied and the earlier timing of endoscopy (mean time 89 min vs 8 h) [9].

We compared the *T* score with the *GBR* because the second one is the best known risk score that do not relies on endoscopic finding, and in a recent review it has been indicated as the advised score in predicting the need for endoscopic intervention [19]. In our population, the *T* score performed as the *GBR* and no difference was found when the AUROC for the presence of high risk endoscopic stigmata were compared. *T* score is a pre-endoscopy simple score that relies on patient's medical history and laboratory values routinely obtainable in the emergency setting. Although similar, there are differences between the two scores and *T* score is easier to calculate. Indeed, *T* score does not include blood urea nitrogen values and clinical signs such as syncope or melena, which sometimes could be difficult to define.

The *GBR* score can identify low-risk groups and patients who score 0 can be managed as outpatients and discharged without immediate EGD [6,8]. This was confirmed in our population were none of the patients who scored 0 showed high risk endoscopic stigmata, required endoscopic therapy, presented recurrent bleeding or died within 30 days. However, *GBR* is no longer useful in predicting who actually need endoscopic therapy when the score is 1 or more and this represents a significant limitation considering that more the 90% of patients will fall in this group. In this study a *T* score ≤ 6 was able to predict the presence of high risk endoscopic stigmata with a specificity of 96% and a PPV of 74.5%. In contrast,

Table 3
Frequency of high risk stigmata at endoscopy, re-bleeding and 30-day mortality in relation to different cut-off.

	T1 (54 pts)	T2 (225 pts)	T3 (193 pts)	<i>p</i> -Value*
T-score				
High risk endoscopic stigmata	43 (79.6%)	67 (29.7%)	35 (18.1%)	<0.0001
Re-bleeding	14 (26%)	23 (10.2%)	5 (2.5%)	<0.001
30-day mortality	11 (20.4%)	21 (9.3%)	3 (1.6%)	<0.0001
	GBR = 0 (7 patients)	GBR \geq 1 (465 patients)		
Glasgow Blatchford risk score				
High risk endoscopic stigmata	0 (0%)	139 (29.9%)		
Re-bleeding	0 (0%)	35 (7.5%)		
30-day mortality	0 (0%)	42 (9%)		

* Chi square-test for trend.

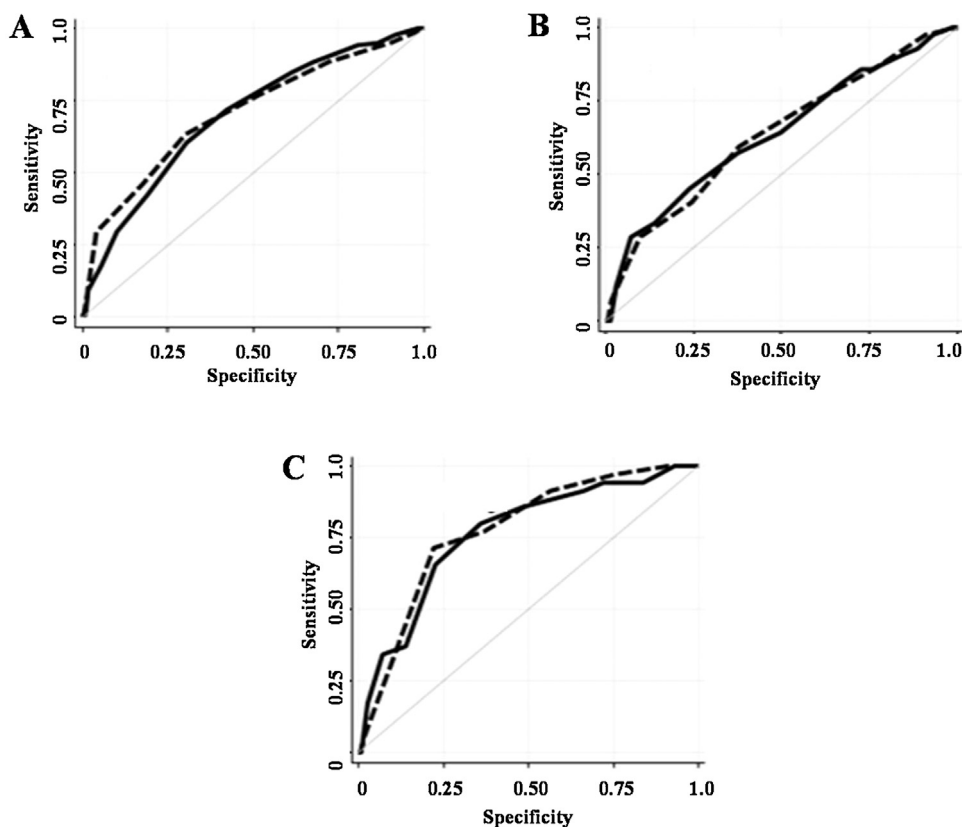


Fig. 1. Comparison between *T* (-) and Glasgow-Blatchford risk (---) scores with AUROC figures for the prediction of (A) high risk stigmata (*T* score = 0.72 and Glasgow-Blatchford risk = 0.69), (B) re-bleeding (*T* score = 0.64 and Glasgow-Blatchford risk = 0.63), and (C) 30 day mortality (*T* score = 0.78 and Glasgow-Blatchford risk = 0.76).

sensitivity was 30% and NPV was 76.4%. *T* score was developed in order to triage patients who are likely to have high risk endoscopic stigmata and therefore need intervention, and we suggest that this score is best used to identify high risk patients who would benefit an early endoscopy. Based on this clinical endpoint, we decided to set a cut-off point that maximized specificity at cost of sensitivity.

Several prognostic scores have been created to predict mortality in UGIB. Rockall et al. developed a high quality validated score that is widely used by clinicians to calculate the risk of death [5]. Bleeding-related 30-days mortality was the primary outcome of a recent validation study, which found that the PNEED score performed better than the Rockall and accurately predict mortality [20]. However, both the Rockall and the PNEED score include endoscopic variables. Although GBR was developed for prediction of clinical intervention after presentation of UGIB, a UK multicentre study showed that it is equivalent to Rockall score in identifying patients at risk of death [21]. In our population, the *T* score predicted 30-day bleeding-related mortality with a discriminant capacity of 78% which was equal to that of the GBR score. More recently, an easy to calculate nonweighted score, the AIM65 was shown to be superior to GBR in predicting mortality from UGIB [11]. However, this was a single centre retrospective study looking at inpatient mortality rather than 30-day bleeding-related mortality.

Our study presents some limitations. First the sample size was small. A recent systematic review pointed out that before the results from predictive score in UGIB studies could be extended to other patients, a population of at least 1000 patients should be considered [19]. However, in this prospective study the aim was to validate in an external population what previously found

among patients from a single tertiary referral centre. We included patients from 30 centres with the majority being community-based non-teaching hospital and outcomes such as re-bleeding, death and need for surgery were comparable to previously published studies [7,8,22,23].

Second, we did not include in the data collection use of antiplatelet and anticoagulants which could have potentially an impact on re-bleeding and bleeding-related death. However, in a recent study neither of these medications had a significant effect on mortality or recurrent bleeding risk [20]. Third, we include only patients who underwent EGD whereas patients discharged from the Emergency department have been missed, creating a bias. However, the proportion of this group is likely to be small since all patients presenting with UGIB usually are admitted and discharged only after an inpatient EGD.

The use of either *T* or GBR score may aid the triage of UGIB patients in predicting the need for intervention. A beneficial point of *T* score is that it can be used in real-time decision making by non-endoscopist physicians. Usually the initial triage decision in patients with UGIB is made by an emergency physician who may not be familiar with the Forrest classification and high risk endoscopic stigmata. Recently, it has been reported that the use of the Rockall and Blatchford scores was less accurate than clinical triage decision in determining the need of endoscopic therapy when used by emergency unit physicians [24]. In this context, the real-life data from this study support the use of our simplified clinical score in order to facilitate the identification of high risk patients who could benefit from an early endoscopy with therapeutic intervention, whilst upper endoscopy could be postponed in those patients a low risk. This should be assessed in a prospective randomized

control study comparing clinical outcomes of patients stratified or not by our scoring system in an emergency department or by a non-GI physician.

Conflict of interest

None declared.

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Appendix A.

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Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.dld.2014.05.006>.

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