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Comparison of Three Risk Scores to Predict Outcomes of Severe Lower Gastrointestinal Bleeding

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Abstract

Background & aims—Improved medical decisions by using a score at the initial patient triage level may lead to improvements in patient management, outcomes, and resource utilization. There is no validated score for management of lower gastrointestinal bleeding (LGIB) unlike for upper GIB. The aim of our study was to compare the accuracies of 3 different prognostic scores (CURE Hemostasis prognosis score, Charlston index and ASA score) for the prediction of 30 day rebleeding, surgery and death in severe LGIB.

Methods—Data on consecutive patients hospitalized with severe GI bleeding from January 2006 to October 2011 in our two-tertiary academic referral centers were prospectively collected. Sensitivities, specificities, accuracies and area under the receiver operating characteristic (AUROC) were computed for three scores for predictions of rebleeding, surgery and mortality at 30 days.

Results—235 consecutive patients with LGIB were included between 2006 and 2011. 23% of patients rebled, 6% had surgery, and 7.7% of patients died. The accuracies of each score never reached 70% for predicting rebleeding or surgery in either. The ASA score had a highest accuracy for predicting mortality within 30 days (83.5%) whereas the CURE Hemostasis prognosis score and the Charlson index both had accuracies less than 75% for the prediction of death within 30 days.

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Disclosures: None.

Conclusions—ASA score could be useful to predict death within 30 days. However a new score is still warranted to predict all 30 days outcomes (rebleeding, surgery and death) in LGIB.

Keywords

prognosis score; gastrointestinal bleeding; Charlson index; ASA score; CURE Hemostasis prognosis score

INTRODUCTION

Acute gastrointestinal (GI) hemorrhage is a common life threatening condition accounting for more than 120 hospitalizations per 100,000 admissions annually in the United States (1,2), with an estimated mortality rate from 5% to 15% (1,3).

It is reported that clinical use of risk scores may lead to improved patient risk stratification, triage, and management (4,5). However, there are limitations since most previous prognosis scores described for the management of GI bleeding have been designed for upper GI bleeding (UGIB) (4,5) to predict the risk of death and the need for intervention (transfusion, endoscopic or surgical therapy). For lower GI bleeding (LGIB), no risk score was designed, even though several studies identified possible prognostic factors (6–9). There is a need for a clinically applicable prognosis score that is suitable for risk stratification, triage, and management of all patients with severe GI hemorrhage including UGIB and LGIB.

We postulated that two prognosis scores not specifically designed for GI bleeding may be useful for predicting outcomes of patients with severe LGIB: the Charlson co-morbidity index and the American Society of Anesthesiologists (ASA) classification. The Charlson co-morbidity index was designed to predict ten-year mortality for patients with a range of co-morbid conditions (10) and has been reported to be correlated with mortality in acute UGIB (11). The ASA is a scoring system for assessing the fitness of patients for surgery, with five-category physical statuses (12). It has been reported in ulcer hemorrhage as an accurate predictor of death in patients with ulcer hemorrhage (13).

The Center for Ulcer Research and Education (CURE) Hemostasis prognosis score is a score designed for risk stratification, triage to level of care, and possible prognostication of all patients with severe GI bleeding by the CURE Hemostasis Reseach Unit and currently is used in our institutions (14,15).

The aim of our study was to compare the accuracy of these 3 different prognosis scores for the prediction of 30-day rebleeding, surgery, and deaths in patients with severe colon hemorrhage.

METHODS

All patients were enrolled in prospective CURE hemostasis studies of severe colonic hemorrhage which were approved by the institutional review boards (IRB) of the University of California, Los Angeles Medical Center and the Veterans Affairs Greater Los Angeles

Medical Center. This is a retrospective analysis of prospectively collected data by the CURE Hemostasis Research Group from a large database of these patients.

Patients

235 consecutive patients hospitalized with severe colon bleeding from January, 1 2006 to October, 31 2011 at our two-tertiary academic medical centers (UCLA Ronald Reagan Medical Center and VA Greater Los Angeles Medical Center) were prospectively enrolled and analyzed.

Inclusion criteria were 1) hospitalization for severe colon hemorrhage or development of GI hemorrhage after hospitalization for another non-bleeding indication, 2) age of 18 years or higher, 3) clinically significant GI bleeding with signs of severity (hypotension, shock, orthostatic changes in systolic blood pressure and/or pulse, or repeated bleeding); and 5) either a decrease of hemoglobin by more than 2 grams from baseline or transfusion of 2 or more units of packed red blood cell (PRBC).

The exclusion criteria were patients unable or unwilling to provide written informed consent or patients with unstable medical or surgical conditions which precluded urgent endoscopy and/or colonoscopy.

Data collected

Demographics on presentation, history of prior bleeds and transfusions, medications, co-morbidities, admission history, symptoms, and severity of bleeding (hypotension, syncope of shock) were prospectively collected by the investigators and a research coordinator for all patients during their hospitalization.

Clinical and laboratory data were prospectively recorded at the time of presentation. All patients had GI consultation and urgent colonoscopy +/− panendoscopy or push enteroscopy, for initial diagnosis of GI hemorrhage (15). In non-diagnostic cases, technetium labeled red blood cell scans, angiography, or capsule endoscopy were also performed. Endoscopic findings (source of bleeding, stigmata of recent hemorrhage-SRH, type and initial efficacy of endoscopic hemostasis) were prospectively assessed and recorded. The final diagnosis and localization were based on all these tests and SRH.

Outcomes (length of hospitalization, transfusion requirement, rebleeding rate, surgery, and death) were prospectively assessed and recorded until the patient's discharge and then at 30 days after endoscopic diagnosis by a research study coordinator. Rebleeding was defined by recurrent melena or hematochezia, with either hypotension, or shock and a decrease in hemoglobin concentration of at least 2g/dl and/or more PRBC transfusions after initial successful appropriate treatment and initial stabilization for 24 hours. Surgery was defined as the requirement of surgical treatment for continued bleeding or rebleeding after failure of endoscopic or pharmaceutical treatment.

The CURE Hemostasis prognosis score (14,15), ASA score and Charlson index were prospectively computed and recorded at the patient's admission. After the review of all the

235 files, Charlson index was available for 212 patients, the CURE Hemostasis prognosis score for 220 patients, and the ASA score for 235 patients.

Scores

The CURE Hemostasis prognosis score is a composite score of 6 items, which are: 1) age more than 65 years; 2) hypotension or shock on presentation; 3) any comorbidity, 4) any severe comorbidities, 5) rebleeding during the hospitalization (prior to the GI consultation); 6) PRBC transfusions of more than 5 units for initial resuscitation. Originally this score was created by the CURE Hemostasis Group to risk stratify patients, to triage to level of medical care on presentation, and to predict risk of rebleeding, need for endoscopic or other intervention, and mortality up to 30 days (14,15). Any co-morbidity that was listed for a major organ system by the primary managing team of physicians was included. Severity of co-morbidities was rated as mild, moderate, or severe by the primary care physicians or intensivists managing the patients in the hospital, based upon acuity, functional class, and their clinical/laboratory assessments.

The ASA physical status classification was developed for assessing the fitness of patients for surgery (12). The ASA score is a five-category physical status classification system: I) a normal healthy patient; II) a patient with mild systemic disease; III) a patient with severe systemic disease; IV) a patient with severe systemic disease that is a constant threat to life; and V) a moribund patient who is not expected to survive without the operation.

The items of Charlson co-morbidity index (10) are summarized in Table 1. Each condition is assigned a score of 1, 2, 3 or 6 depending on the risk of dying in the next 10 years associated with this condition.

Older dataset

In addition to the data available from 2006 to 2011, we also report data available from 1996 to 2005 for the CURE Hemostasis prognostic score only. Data on the Charlson and ASA scores were not collected during this study period. However, it is noteworthy that the inclusion and exclusion criteria, data collected on this older dataset, and the investigators of the CURE Hemostasis Research Group who collected the data were the same as for the database collected from 2006 to 2011.

Statistical analysis

All data were de-identified and entered into computer data files by experienced data managers. SAS software, version 9.1, (SAS Institute, Cary, NC) was used for data management and analyses. All analyses were performed in consultation with a biostatistician (JG).

We compared CURE Hemostasis prognosis score, ASA score, and Charlson index for predicting: 1) rebleeding rate, 2) surgical rate, and 3) mortality rate within 30 days. We did not consider a composite outcome but examined each outcome separately. Additional analysis and results for the CURE Hemostasis prognosis score only are also reported using a second (earlier) database, as explained above.

Descriptive statistics were expressed as percentage for discrete variables and as means and standard deviation for continuous variables. For a given binary 30 day outcome (rebleeding, death or surgery) and for each scoring system, a non-parametric receiver operator characteristic (ROC) analysis was carried out. The sensitivity, specificity, unweighted accuracy and area under ROC curve (AUROC) and their standard errors were calculated. The sensitivity was defined as the percent of the true positives that were correctly classified and specificity as the percent of the true negatives that were correctly classified. The unweighted accuracy was defined as the simple average of sensitivity and specificity. A threshold value for each score was chosen to maximize the unweighted accuracy.

For prediction of individual poor outcomes (rebleeding, surgery, or death) for high risk patients, the performance results were calculated and reported for each of the three scores. Also, for prediction of a good outcome (and no rebleeding, surgery, or death), a composite outcome was calculated and reported to assess the performance of each of the three scores for identifying a low risk group of patients with LGIB.

The p values for comparing the distributions of a given score were computed using the non-parametric Wilcoxon rank sum test. The Wilcoxon test was used instead of the unpaired t test since these scores are integers whose distribution was not always well approximated by the normal distribution.

RESULTS

Patients' characteristics

The characteristics of patients are presented in Table 2.

Diagnosis

The diagnoses were presumptive or definitive diverticular bleeding in 87 (37.0%) of patients, ischemic colitis in 31 (13.2%), delayed post polypectomy induced bleeding in 26 (11.1%), rectal ulcer in 21 (8.9%), internal hemorrhoids in 15 (6.4%), colon angiomas in 15 (6.4%), other colitis in 11 (4.7%), colonic cancer or polyp in 10 (4.3%), and other causes in 19 (8%). Stigmata of recent hemorrhage (SRH) were identified on urgent colonoscopy in 130 patients (55.3%). The SRH included active bleeding in 45 (19.2%), non-bleeding visible vessel in 29 (12.3 %), adherent clot in 47 (20%), flat spot in 9 (3.8%) and clean lesion in 105 (44.7%). Overall, 104 (44.3 %) patients underwent endoscopic hemostasis within 30 days for SRH and severe LGIB.

Patients' 30 day outcomes and risk scores

54 (23%) patients rebled, 14 (6%) needed surgery, and 18 (7.7%) patients died. Patients' outcomes and corresponding scores are summarized in Figures 1 to 3.

The CURE Hemostasis prognosis score was significantly higher in patients with rebleeding (3.8 ±1.3 vs. 2.9 ±1.1, $p<0.001$), surgery (3.9 ±1.3 vs. 3.0 ±1.2, $p=0.0141$), or death (3.9 ±1.0 vs. 3.0 ±1.2, $p<0.001$) than in patients without these outcomes within 30 days. The ASA score was also significantly different in patients with rebleeding (3.3 ±0.8 vs. 3.0 ±0.8, $p=0.0126$), surgery (3.6 ± 0.7 vs. 3.0 ±0.8, $p=0.0029$), or death (4.0 ±0.5 vs. 2.9 ±0.8,

p<0.001). The Charlson index was also significantly higher in patients with vs. than without rebleeding (4.4 ±3.1 vs. 3.2 ±3.2, p=0.0047), surgery (5.8 ±3.7 vs. 3.3 vs.3.1, p=0.010), or death (6.8 ±3.4 vs. 3.2 ±3.0, p<0.001).

Comparison of performances of risk scores

The best threshold was 3 for CURE Hemostasis prognosis score for all outcomes. For ASA score, the best threshold was 3 for surgery and death whereas it was 2 for predicting rebleeding, as determined by the AUROC's. For Charlson index, the best threshold was different for each outcome. It was 9 to predict rebleeding and 4 to predict 30 day mortality and surgery. The sensitivities, specificities and accuracies of each score for each outcome are summarized in Table 3.

Each score had less than 70% of accuracy for the prediction of rebleeding or surgery within 30 days in LGIB. For predicting mortality at 30 days, the CURE hemostasis prognosis score and the Charlson index had less than 75% accuracy. The accuracy of the ASA score was higher (83.5 %) for predicting death within 30 days in LGIB.

In the older dataset (1996–2005), the best threshold for the CURE Hemostasis prognosis score was different from the threshold of the recent dataset of 2006–2011 (2 vs. 3). The accuracies of the CURE Hemostasis prognosis score were similar to those in the current dataset with accuracies of less than 70% for outcomes at 30 days (Table 3).

The performance results for the three scores for prediction of a low risk group with a good outcome (e.g. no rebleeding, surgery, or death) are shown in Table 4. The sensativities and accuracies of all three scores were all less than 70%.

DISCUSSION

The frequency and severity of GI hemorrhage and its associated morbidity, mortality, and costs impose a significant burden on limited health care resources (14,16,17). Strategies applied early in the hospitalization to optimize patient outcomes while minimizing health care resource use are desirable (2). Improved medical decision making by computing risk scores, particularly at the initial patient triage level, may lead to improvements in patient management, outcome, and resource utilization (18–22).

In LGIB, no numerical risk score has been validated yet, even though early predictors of severity in LGIB have been reported (6,23). Strate *et al* (6) identified seven independent risks factors for severe acute LGIB: tachycardia, low systolic blood pressure, syncope, non-tender abdominal examination, bleeding per rectum within 4 first hours of medical assessment, use of aspirin, and more than two active co-morbid conditions.

In UGIB, several prognosis scores were reported (24–26) developed and validated in prospective multicenter studies. But these were only designed and validated for patients with UGIB. If accurate, a new score for predicting major clinical outcomes (rebleeding, surgery, or death within 30 days) of LGIB would be valuable for risk stratification.

We conducted this study to compare the accuracies of 3 scores to predict major outcomes: rebleeding, need for surgery and mortality at 30 days in severe LGIB. Unfortunately, we demonstrated that none of these scores had high enough accuracy to be recommended for routine clinical application. Expect for the ASA score with a good predictive ability for predicting death at 30 days, these scores had poor accuracies (less than 75%). We reported two different thresholds for the CURE Hemostasis prognosis score in two different data sets for the same outcomes and locations. Therefore, it would be difficult to apply this score universally. We also observed different thresholds for the ASA score and the Charlson index for predicting different outcomes. This lack of reproducibility is additional evidence for the limited performance characteristics of these scores for risk stratification or prediction. However, ASA score should be considered to predict 30-day death.

The Charlson index was designed to predict mortality in longitudinal studies at one and 10-years (10). In our study, we reported mortality rate for a much shorter period of time (within 30 days). In another prospective cohort study of 66 patients admitted to intensive care units with a primary diagnosis of GI bleeding, Gopalswamy *et al.*(27) reported that Charslon index correlated with long-term mortality (7 years). The Charlson index may be more accurate for long-term than short term mortality. The Charlson index is based upon co-morbid conditions which alone are not enough to accurately predict the 30 day outcomes of LGIB. Other potential risk factors (hemodynamic parameters, laboratory data, age, inpatient start of bleeding) should be considered to improve the accuracy of this or other scores for prediction of short term mortality.

The ASA score was an independent risk factor of death in a multivariate analysis in a multicenter prospective study including 144 patients with gastroduodenal ulcer hemorrhage (13). In another multicenter prospective study Marmo *et al.*(28) also reported ASA score as an independent predictor of 30-day mortality in a logistic regression analysis (OR 3.32, 95%CI 1.03–6.58) and in the same study an ASA score >3 was integrated in a score for predicting mortality of patients with non-variceal upper gastrointestinal bleeding. In our study, the ASA score had greater accuracy for prediction of death in LGIB than for prediction of rebleeding or surgery. Indeed, this score was designed to predict the mortality from surgery. One limitation is the difficulty in assessing a patient's score because individual parts of the score are subjective, and it is not always easy to categorize a patient, particularly in an emergency situation.

For possible prediction of a low risk group with good outcomes, we also analyzed and reported the performances of the three scores to predict any bad outcome. However, all had an accuracy of less than 70% and therefore are not recommended for risk stratification in clinical practice. A more accurate clinical scoring method is needed.

In conclusion, this study reports that the accuracies of the CURE Hemostasis prognosis score and the Charlson index were not high enough to recommend routine use in clinical practice for prediction of rebleeding, surgery, and death up to 30 days in patients with severe LGIB. The ASA score has a good predictive ability in prediction of mortality but not in prediction of rebleeding and surgery. The mortality rate of GI hemorrhage ranges from 5 to 15 %, even though the diagnosis and the management of acute GI hemorrhage have

undergone remarkable changes, and in improvements of therapeutic endoscopy and pharmacotherapeutics. Because there is substantial interest in the early risk stratification of patients with acute LGI hemorrhage to help in prognostication and triage to level of care, further studies are warranted to build and validate an appropriate prognostic score system. An ideal score would be highly accurate, easy to use during initial patient presentation and triage, prospectively and externally validated, reproducibly reliable, and a good predictor of different clinically relevant outcomes such as 30 day rebleeding, surgery and mortality.

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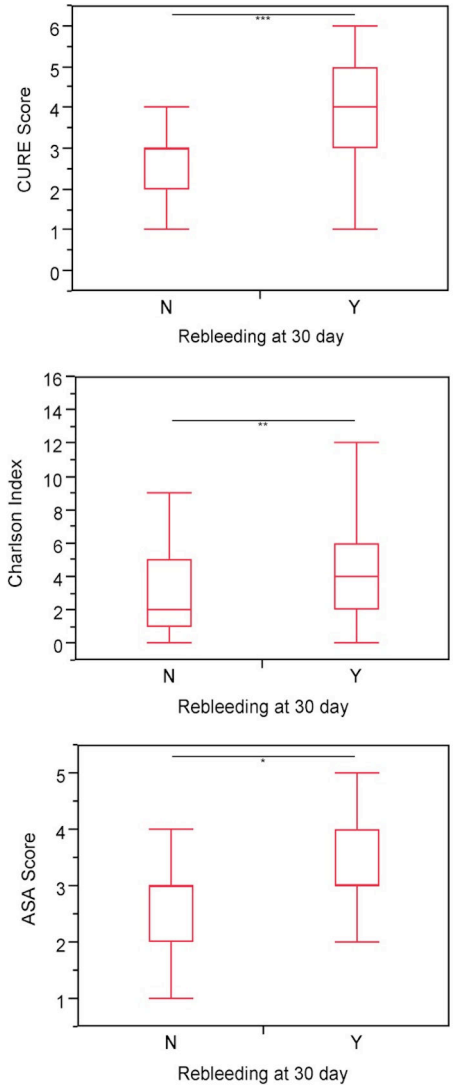

Figure 1.

Boxplots of mean scores for 30 day rebleeding of severe LGIB (A: CURE Hemostasis Prognosis score, B: Charlson Index, C: ASA score)

*P ≤ 0.05 **P ≤ 0.01 ***P ≤ 0.001

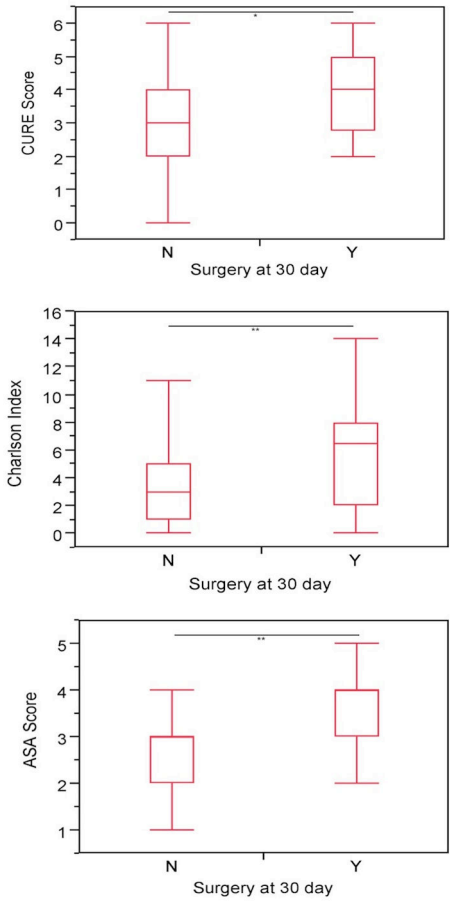

Figure 2.

Boxplots of mean scores for 30 day surgery of severe LGIB (A: CURE Hemostasis Prognosis score, B: Charlson Index, C: ASA score)

*P ≤ 0.05 **P ≤ 0.01

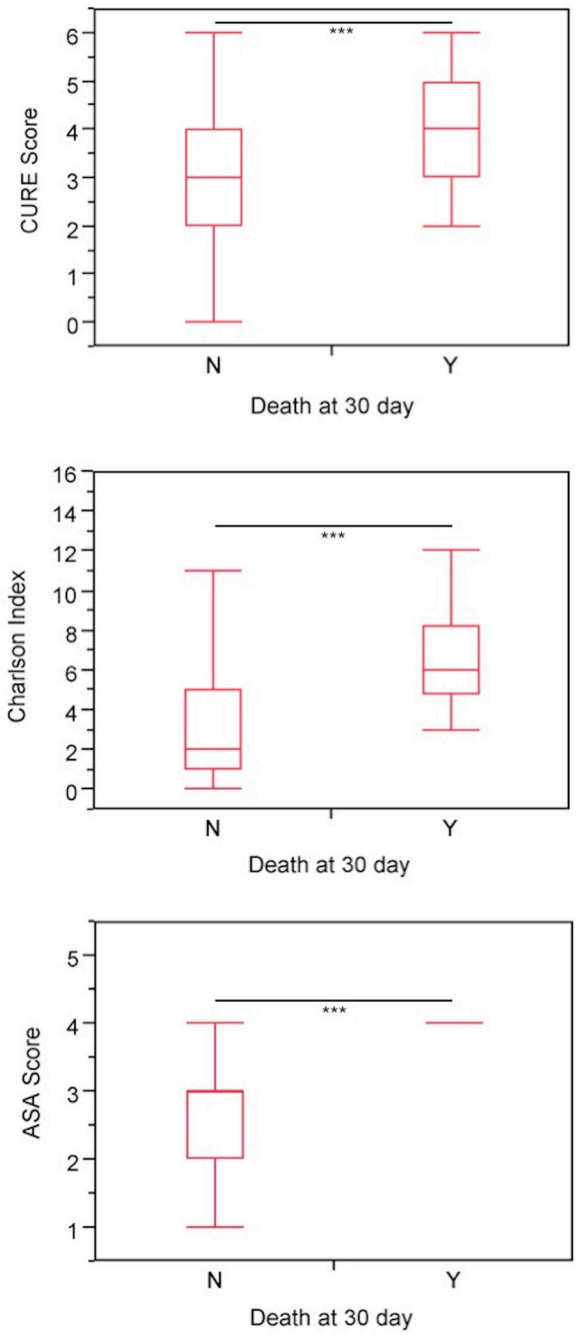

Figure 3.

Boxplots of mean scores for 30 day mortality of severe LGIB (A: CURE Hemostasis Prognosis score, B: Charlson Index, C: ASA score)

***P ≤ 0.001

Table 1

Charlson comorbidity index

Weight	Clinical condition
1	Myocardial infarct
	Congestive cardiac insufficiency
	Peripheral vascular disease
	Dementia
	Cerebrovascular disease
	Chronic pulmonary disease
	Conjunctive tissue disease
	Slight diabetes, without complications
	Ulcers
	Chronic disease of the liver or cirrhosis
2	Hemiplegia
	Moderate or severe kidney disease
	Diabetes with complications
	Tumors
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
6	Malignant tumor, metastasis
	AIDS

Table 2

Characteristics of patients at baseline

Age, mean (± SD)	68 years ± 14.0
Sex, no. % (M/F)	161/74 (68.5 %/31.5 %)
Inpatient, no. (%)	68 (28.9 %)
Nonsteroidal anti-inflammatory drugs and/or aspirin use, no. (%)	110 (46.8 %)
Anticoagulation use, no. (%)	46 (19.6 %)
Severe co-morbidities, no. (%)	
Cardiac	132 (56.4 %)
Hepatic	39 (16.6 %)
Pulmonary	65 (27.8 %)
Shock or hypotension, no. (%)	78 (33.2 %)
Hemoglobin count, mean (± SD)	8.7 g/dl ± 1.8
Platelet count, mean (± SD)	185,838/mm3 ± 101,626
Partial thromboplastin time, mean (± SD)	31.2 seconds ± 10.1

SD: standard deviation

Table 3

Performance of CURE Hemostasis prognosis score, ASA score, and Charlson index for predicting rebleeding, surgery, and death at 30 day in severe LGIB.

	CURE prognosis score in the old dataset 1996–2005	CURE prognosis score in the recent dataset 2005–2011	ASA score	Charlson index
Rebleeding at 30 day				
Sensitivity (%)	53.3 %	57.4 %	87 %	84.3 %
Specificity (%)	72.7 %	77.8 %	28 %	37.9 %
Accuracy (%)	63.0 %	67.6 %	57.5 %	61.1 %
AUROC ± SE	0.682 ± 0.053	0.706 ± 0.042	0.604 ± 0.040	0.630 ± 0.042
Surgery at 30 day				
Sensitivity (%)	52.2 %	64.3 %	64.3 %	71.4 %
Specificity (%)	72.1 %	71.8 %	75.3 %	69.9 %
Accuracy (%)	62.1 %	68.1 %	69.8 %	70.7 %
AUROC ± SE	0.652 ± 0.061	0.687 ± 0.084	0.721 ± 0.067	0.704 ± 0.078
Death at 30 day				
Sensitivity (%)	54.5 %	66.7 %	88.9 %	100 %
Specificity (%)	71.3 %	72.7 %	78.2 %	51.5 %
Accuracy (%)	62.9 %	69.7 %	83.5 %	75.7 %
AUROC ± SE	0.578 ± 0.097	0.725 ± 0.054	0.856 ± 0.033	0.813 ± 0.038

AUROC: Area under the receiver operator characteristic

Table 4

Performance of each score for predicting low risk patients (no rebleed, surgery or death at 30 days).

Composite Endpoint for prediction of low risk patients with no bad ouctomes (rebleeding-surgery and death) at 30 days				
Sensitivity (%)	50.0%	56.9%	45.8%	58.0%
Specificity (%)	74.3%	81.5%	81.5%	70.9%
Accuracy (%)	62.2%	69.2%	63.7%	64.4%
AUROC ± SE	0.645 ± 0.041	0.732 ± 0.036	0.684 ± 0.035	0.692 ± 0.037