Severity and Outcomes of Upper Gastrointestinal Bleeding With Bloody Vs. Coffee-Grounds Hematemesis

Loren Laine, MD[1,2], Stig B. Laursen, MD, PhD[3], Liam Zakko, MD[1], Harry R. Dalton, DPhil, DipMedEd[4], Jing H. Ngu, MBChB, PhD[5], Michael Schultz, MD, Dr Habil (Germany)[6] and Adrian J. Stanley, MBChB, MD[7]

OBJECTIVES: **Numerous reviews indicate bloody hematemesis signifies more severe bleeding than coffee-grounds hematemesis. We assessed severity and outcomes related to bleeding symptoms in a prospective study.**

METHODS: **Consecutive patients presenting with hematemesis or melena were categorized as bloody emesis (*N*=1209), coffee-grounds emesis without bloody emesis (*N*=701), or melena without hematemesis (*N*=1069). We assessed bleeding severity (pulse, blood pressure) and predictors of outcome (hemoglobin, risk stratification scores) at presentation, and outcomes of bleeding episodes. The primary outcome was a composite of transfusion, intervention, or mortality.**

RESULTS: **Bloody and coffee-grounds emesis were similar in pulse ≥100 beats/min (35 vs. 37%), systolic blood pressure ≤100 mm Hg (12 vs. 12%), and hemoglobin ≤100 g/l (25 vs. 27%). Risk stratification scores were lower with bloody emesis. The composite end point was 34.7 vs. 38.2% for bloody vs. coffee-grounds emesis; mortality was 6.6 vs. 9.3%. Hemostatic intervention was more common (19.4 vs. 14.4%) with bloody emesis (due to a higher frequency of varices necessitating endoscopic therapy), as was rebleeding (7.8 vs. 4.5%). Outcomes were worse with hematemesis plus melena vs. isolated hematemesis for bloody (composite: 62.4 vs. 25.6%; hemostatic intervention: 36.5 vs. 13.8%) and coffee-grounds emesis (composite: 59.1 vs. 27.1%; hemostatic intervention: 26.4 vs. 8.1%).**

CONCLUSIONS: **Bloody emesis is not associated with more severe bleeding episodes at presentation or higher mortality than coffee-grounds emesis, but is associated with modestly higher rates of hemostatic intervention and rebleeding. Outcomes with hematemesis are worsened with concurrent melena. The presence of bloody emesis plus melena potentially could be considered in decisions regarding timing of endoscopy.**

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

Am J Gastroenterol 2018; 113:358–366; doi:10.1038/ajg.2018.5; published online 30 January 2018

INTRODUCTION

Guidelines recommend risk stratification of patients presenting with upper gastrointestinal bleeding (UGIB) into higher- and lower-risk categories (1–3). A variety of baseline characteristics are used to risk stratify patients with UGIB. Multiple reviews state that bloody hematemesis indicates more severe bleeding than hematemesis of coffee-grounds material (4–6)—generally without citing references that provide supporting evidence. International consensus recommendations on the management of nonvariceal UGIB state that fresh red blood in emesis predicts increased mortality (2,3), citing a single study reporting increased mortality with presence vs. absence of "hematemesis" (7). American Society for Gastrointestinal Endoscopy (ASGE) guidelines state that "hematemesis" is among the most predictive individual

[1]Section of Digestive Diseases, Yale School of Medicine, New Haven, Connecticut, USA; [2]Section of Digestive Diseases, VA Connecticut Healthcare System, West Haven, Connecticut, USA; [3]Department of Medical Gastroenterology, Odense University Hospital, Odense, Denmark; [4]Gastrointestinal Unit, Royal Cornwall Hospital, Cornwall, UK; [5]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore, Singapore; [6]Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand; [7]Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow, UK. **Correspondence:** Loren Laine, MD, Section of Digestive Diseases, Yale School of Medicine, P.O. Box 208019, New Haven, Connecticut 06520-8019, USA. E-mail: loren.laine@yale.edu
Received 26 September 2017; accepted 12 December 2017

factors associated with need for urgent hemostatic intervention (8), citing studies reporting that red blood in the nasogastric aspirate—but not hematemesis—predicts high-risk endoscopic findings (9,10).

Given this background, physicians may make triage and management decisions, based in part on the belief that bloody emesis indicates more severe bleeding with worse outcome than coffee-grounds emesis. However, scant information is available to confirm this notion.

We therefore evaluated the hypothesis that patients presenting with bloody emesis more often have severe bleeding at presentation and have worse clinical outcomes than those with coffee-grounds emesis. The hypothesis is based on the concept that red blood in emesis often indicates ongoing active bleeding, whereas coffee-grounds emesis may represent bleeding that has stopped (4,8)—and persistent bleeding is postulated to result in greater blood loss with greater likelihood of hemodynamic compromise at presentation. Furthermore, actively bleeding lesions at endoscopy generally require endoscopic therapy and have poorer outcomes (1,2). To evaluate the hypothesis, we assessed, in a prospective series of patients who presented to emergency departments with overt UGIB, the association of the presenting symptom of UGIB with (i) severity of the UGIB episode at presentation based on hemodynamic parameters of heart rate and blood pressure, (ii) predictors of outcomes at presentation including hemoglobin and risk stratification instruments, and (iii) outcome of the UGIB episode after presentation based on need for blood transfusion, need for hemostatic intervention, or death.

METHODS

Study population

The study was performed at the Yale-New Haven Hospital (USA), Glasgow Royal Infirmary (Scotland), Royal Cornwall Hospital Truro (England), Odense University Hospital (Denmark), Singapore General Hospital (Singapore), and Dunedin Hospital (New Zealand). Ethical approval was obtained from West of Scotland Ethics committee (reference 14/WS/0012; project number: 145837) and each center obtained approval from their local research committee or review board.

Consecutive, unselected patients were included if they presented to the hospital from March 2014 to March 2015 with hematemesis and/or melena. The methods and primary results of the study regarding comparison of risk stratification scores have been published previously (11). Information regarding patients' presenting symptoms as well as baseline characteristics and outcomes detailed below were recorded prospectively.

Assessment and management of patients

All patients were initially assessed in the emergency department or acute assessment unit of the participating hospitals. Patients were followed for 30 days irrespective of whether discharged from the emergency department or admitted to the hospital. The policy in all centers was to administer high-dose proton pump inhibitor therapy starting with an initial intravenous bolus to patients with ulcers and high-risk ulcer stigmata who required endoscopic therapy and to other selected patients depending on clinical judgment. For patients with suspected variceal bleeding, the policy in all centers was to initiate intravenous vasoactive medications and antibiotics before endoscopy.

The endoscopic practice in all centers for patients with high-risk stigmata of nonvariceal bleeding was to administer injection therapy, thermal contact therapy, and/or clips; epinephrine was not used alone. Band ligation was performed for esophageal variceal bleeding and injection of tissue adhesive or transjugular intrahepatic portosystemic shunt was performed for gastric variceal bleeding. The protocol for red cell transfusion was to transfuse below a hemoglobin threshold of 70–80 g/l. Exceptions to this practice were made at the discretion of the treating physician if the physician felt a higher transfusion threshold was appropriate (e.g., hemodynamic instability in severe UGIB).

Predefined variables and outcome measures

Multiple predefined characteristics and outcome measures were collected for each patient and placed in a deidentified electronic database. The presenting UGIB symptoms included bloody hematemesis (defined as emesis containing fresh blood), coffee-grounds hematemesis (defined as emesis containing brownish granular material), and melena (defined as black tarry stool). Characteristics at presentation included site, sex, age, altered mental status (Glasgow coma scale score <14 or designation of disorientation, lethargy, stupor, or coma), major comorbidities (ischemic heart disease, heart failure, renal failure, liver cirrhosis, current malignancy), syncope, nonsteroidal anti-inflammatory drug use, antithrombotic agent use (low-dose aspirin, thienopyridine, or anticoagulant), heart rate, blood pressure, laboratories (hemoglobin, blood urea nitrogen, international normalized ratio, albumin), and risk stratification scores (Glasgow–Blatchford (12), admission Rockall (13), and AIMS65 (ref. (14))). Endoscopic diagnoses were also recorded.

Predefined outcomes included blood transfusion, hemostatic intervention (endoscopic, surgical, or interventional radiology), 30-day mortality, and the composite of transfusion, hemostatic intervention, or mortality. The primary outcome for the study was this composite end point. We also recorded clinical evidence of rebleeding, using previously defined criteria (11,15), and hemostatic intervention for rebleeding.

Patients were categorized into three groups based on presenting UGIB symptoms: bloody hematemesis (with or without melena), coffee-grounds hematemesis without bloody hematemesis (with or without melena), and melena without hematemesis. Indicators of severity of the UGIB episode at presentation were heart rate (presented as mean and dichotomized as ≥100 vs. <100 beats per min) and systolic blood pressure (presented as mean and dichotomized as ≤100 vs. >100 mm Hg). Predictors of outcome at presentation were hemoglobin (presented as mean and dichotomized as ≤100 vs. >100 g/l) and the risk stratification scores. We included hemoglobin, although it may not indicate the acuity or severity of a bleeding episode at initial presentation before equilibration, because it has been reported to predict clinical outcomes (7). The

breakpoints for heart rate, blood pressure, and hemoglobin were based on values from the Rockall (13) and Glasgow–Blatchford (12) scores. Sensitivity analyses for these variables were also performed using different thresholds for dichotomization: heart rate at 110 beats per min, blood pressure at 90 mm Hg, and Hgb at 80 g/l.

Statistical analysis

The primary analysis was comparison of outcomes in patients with bloody emesis vs. those with coffee-grounds emesis; secondary analyses were comparisons of patients with melena without hematemesis vs. those with bloody emesis and vs. those with coffee-grounds emesis. Univariable comparisons of continuous data (presented as mean±s.e.) were performed with a *t*-test and of proportional data with Pearson's χ^2 test.

Multivariable logistic stepwise regression analysis was also performed to assess associations of the presenting UGIB symptoms with the study outcomes (statistical analyses were performed with JMP Pro software, Version 11, SAS, Cary, NC). A model was constructed designed to achieve excellent goodness of fit and stop at the minimum Bayesian Information Criterion value, providing parsimony in variable selection. The following variables were included for comparison of bloody emesis vs. coffee-grounds emesis: sex, syncope, hemoglobin, blood urea nitrogen, international normalized ratio, albumin, and site. Variables were selected similarly for comparison of melena vs. bloody emesis (age, sex, syncope, heart rate, blood pressure, hemoglobin, blood urea nitrogen, international normalized ratio, and albumin) and comparison of melena vs. coffee-grounds emesis (hemoglobin, urea, and albumin). All 3 models had excellent goodness of fit (lack of fit test P=1.0).

In addition, sensitivity analyses of the primary outcome for the three comparisons were performed using a different method to build the multivariable model (backward stepwise regression analyses with variables removed if $P \geq 0.10$ during backward steps) and revealed no qualitative change in results. *Post hoc* analyses were done comparing results in the bloody and coffee-grounds emesis groups for those with vs. without concurrent melena. In addition, *post hoc* sensitivity analyses of the multivariable analyses were performed adding melena to the models to assess the impact of concurrent melena.

Analyses were performed using listwise deletion. Because rates of missing data were very low, proportions of patients shown for each presenting characteristic used the denominator of the total patients. Proportions for predefined outcomes provide the number of patients with data available as the denominator used in the analysis.

RESULTS

A total of 3,012 patients presenting with UGIB were enrolled. Of these, 33 patients did not have one of the three presenting symptoms recorded, leaving 2,979 (98.9%) for analysis: 1,209 had bloody hematemesis (302 also had melena), 701 had coffee-grounds hematemesis without bloody hematemesis (242 also had melena), and 1,069 had melena without hematemesis. Baseline characteristics of the groups are shown in **Table 1**. Patients in the bloody emesis group tended to be younger (mean age 53.5 vs. 67.3 vs. 68.6 years) with fewer major comorbidities (46% vs. 56% vs. 60%) and less antithrombotic use (25% vs. 38% vs. 48%) than those with coffee-grounds emesis or melena without hematemesis. The mean time interval from presentation to endoscopy among hospitalized patients was 21±1 h for bloody emesis, 23±1 hour for coffee-grounds emesis (P=0.14 vs. bloody emesis), and 29±1 h for melena (P<0.01 vs. coffee-grounds and blood emesis).

Table 1. Selected baseline characteristics related to presenting symptoms of bleeding

	Bloody emesis (*N*=1,209)	Coffee-grounds emesis (*N*=701)	Melena without hematemesis (*N*=1,069)
Female sex	465 (38%)[a]	326 (47%)	458 (43%)[b]
Age (years) mean±s.e.	53.5±0.6[a]	67.3±0.7	68.6±0.499[b]
Syncope	88 (7%)	50 (7%)	111 (10%)[a,b]
Altered mental status	115/1,207 (10%)[a]	94 (13%)	76 (7%)[a,b]
Major comorbidity	552 (46%)[a]	391 (56%)	640 (60%)[b]
Nonsteroidal anti-inflammatory drugs	139 (11%)	90 (12.8%)	161 (15%)[b]
Antithrombotic drugs	298 (25%)[a]	252 (38%)	497 (48%)[a,b]
BUN (mmol/l) mean	9.0±0.3[a]	11.7±0.4	12.6±0.3[b]
INR	1.3±0.1	1.3±0.0	1.6±0.1[a,b]
Albumin (g/l)	36.6±0.2	36.2±0.3	34.9±0.2[a,b]

BUN, blood urea nitrogen; INR, international normalized ratio.
[a]P<0.05 vs. coffee-grounds emesis.
[b]P<0.05 vs. bloody emesis.

Characteristics reflecting the severity of the bleeding episode and the predictors of outcome at presentation are shown in **Table 2**. Mean heart rate and proportion of patients with tachycardia were virtually identical in those with bloody and coffee-grounds emesis—and significantly higher than in patients presenting with melena alone. The mean systolic blood pressure and the proportion with hypotension were similar in the three groups. The proportions of patients with reduced hemoglobin (at thresholds of both 100 and 80 g/l) were similar in the bloody and coffee-grounds emesis groups, but more than double in the melena group compared with the hematemesis groups. The mean scores using three separate risk stratification tools (Glasgow–Blatchford, Rockall, and AIMS65) were all significantly lower in the bloody emesis group than the coffee-grounds emesis group.

Predefined outcomes for bloody emesis vs. coffee-grounds emesis are shown in **Table 3**. The proportion of patients with the primary end point (transfusion, intervention, or death) was 3.5% lower in the bloody emesis group, but the difference was not significant on univariable or multivariable analysis. The proportions receiving blood transfusion were similar, although multivariable

Table 2. Indicators of bleeding severity and predictors of outcome at presentation related to presenting symptoms of bleeding

	Bloody emesis (*N*=1,209)	Coffee-grounds emesis (*N*=701)	Melena without hematemesis (*N*=1,069)
Indicators of bleeding severity at presentation			
Heart rate (beats per min) mean±s.e.	93±1	93±1	87±1[a,b]
Heart rate ≥100 beats per min	420 (35%)	256 (37%)	258 (24%)[a,b]
Heart rate ≥110 beats per min	256 (21%)	146 (21%)	137 (13%)[a,b]
Blood pressure (mm Hg) mean±s.e.	127±1	129±1	126±1[c]
Blood pressure ≤100 mm Hg	149 (12%)	82 (12%)	158 (15%)
Blood pressure ≤90 mm Hg	67 (6%)	37 (5%)	67 (6%)
Predictors of outcome at presentation			
Hemoglobin g/l	121±1[d]	117±1	97±1[a,b]
Hemoglobin ≤100 g/l	298 (25%)	190 (27%)	598 (56%)[a,b]
Hemoglobin ≤80 g/l	121 (10%)	88 (13%)	356 (33%)[a,b]
Blatchford score (0–23) mean±s.e.	5.1±0.1[a]	6.1±0.2	8.5±0.1[a,b]
Pre-endoscopic Rockall score (0–7) mean±s.e.	2.3±0.1[a]	3.0±0.1	3.0±0.1[b]
AIMS65 score (0–5) mean±s.e.	0.82±0.03[a]	1.08±0.04	1.16±0.03[b]

[a]*P*<0.0001 vs. coffee-grounds.
[b]*P*<0.0001 vs. bloody.
[c]*P*=0.002 vs. coffee-grounds.
[d]*P*=0.004 vs. coffee-grounds.

Table 3. Outcomes related to presenting symptoms of bloody emesis vs. coffee-grounds emesis

	Bloody emesis (*N*=1,209)	Coffee-grounds emesis (*N*=701)	OR (95% CI) from multivariable analysis
Blood transfusion, hemostatic intervention, or mortality	418/1,204 (34.7%)	267/699 (38.2%)	1.15 (0.87–1.54)
Blood transfusion	316/1,196 (26.4%)	191/698 (27.4%)	1.55 (1.11–2.16)
Hemostatic intervention	234/1,206 (19.4%)[a]	101/700 (14.4%)	1.76 (1.31–2.37)
Mortality	80/1,208 (6.6%)[a]	65/701 (9.3%)	0.73 (0.49–1.10)
Rebleeding	91/1,171 (7.8%)[a]	31/696 (4.5%)	2.03 (1.28–3.24)
Hemostatic intervention for rebleeding	43/1,171 (3.7%)	14/696 (2.0%)[a]	2.04 (1.06–3.91)

CI, confidence interval; OR, odds ratio.
[a]*P*<0.05 for bloody emesis vs. coffee-grounds emesis on univariable analysis.

analysis indicated the odds of transfusion were higher with bloody vs. coffee-grounds emesis (odds ratio (OR)=1.55, 1.11–2.16). The proportion with hemostatic intervention was higher with bloody emesis than coffee-grounds emesis on univariable and multivariable analyses. Mortality was 2.7% lower in the bloody emesis group (*P*=0.04 on univariable analysis), but the difference was not significant on multivariable analysis (*P*=0.13). Rebleeding and hemostatic intervention for rebleeding were higher in those with bloody emesis. We found no significant interactions of the symptom of bloody emesis with other factors (including melena, hemoglobin, blood urea nitrogen, heart rate, systolic blood pressure, syncope, and Glasgow–Blatchford score) in prediction of the primary outcome or the need for hemostatic intervention.

Sensitivity analyses were done for the primary analysis excluding those who did not undergo endoscopy for assessment of the composite end point and of hemostatic intervention: the proportions with the composite end point remained similar on comparison of bloody emesis (371/762 (48.7%)) and coffee-grounds emesis (211/437 (48.3%)), whereas the proportion with hemostatic intervention remained higher with bloody emesis (234/764 (30.6%)) than coffee-grounds emesis (101/438 (23.1%)).

The *post hoc* comparisons of patients with vs. without melena in the bloody and coffee-grounds emesis groups are shown in **Table 4**. Patients with melena had lower mean systolic blood pressure and markedly lower mean hemoglobin. In addition, patients with melena were more likely to receive blood transfusions, undergo hemostatic intervention, rebleed, or undergo hemostatic intervention for rebleeding. The adjusted ORs for sensitivity analyses in which melena was added to the multivariable models comparing bloody vs. coffee-grounds emesis were similar to those without melena in the model for the composite end point (1.23, 0.92–1.64), blood transfusion (1.67, 1.19–2.35), hemostatic intervention (1.98, 1.47–2.69), mortality (0.72, 0.48–1.08), rebleeding (2.15, 1.34–3.44), and intervention for rebleeding (2.18, 1.13–4.21). The proportion with variceal bleeding was higher with concurrent melena, but remained higher for bloody vs. coffee-grounds emesis with melena (37/302 (12.3%) vs. 16/241 (6.6%)) and without melena (57/907 (6.3%) vs. 7/458 (1.5%)).

Secondary analyses comparing melena with bloody emesis are shown in **Table 5**. The proportion of patients with the primary outcome of transfusion, intervention, or mortality was nearly twice as high with melena vs. bloody emesis. This difference was driven by the twofold higher proportion receiving transfusions in the melena group. These differences were not significant on multivariable analysis—due to inclusion of hemoglobin in the model: when hemoglobin was removed from the model the *P* value for

Table 4. Comparison of hematemesis groups with vs. without melena

	Bloody emesis		Coffee-grounds emesis	
	Melena (*N*=302)	No melena (*N*=907)	Melena (*N*=242)	No melena (*N*=459)
Heart rate (beats per min) mean±s.e.	95±1	92±1	96±1	92±1[a]
Blood pressure (mm Hg) mean±s.e.	123±1	128±1[a]	120±2	134±1[a]
Hemoglobin g/l	105±2	127±1[a]	104±2	125[a]
Blatchford score (0–23) mean±s.e.	8.4±0.3	4.0±0.1[a]	8.9±0.2	4.6±0.2[a]
Pre-endoscopic Rockall score (0–7) mean±s.e.	2.8±0.1	2.1±0.1[a]	3.1±0.1	3.0±0.1
AIMS65 score (0–5) mean±s.e.	1.1±0.1	0.7±0.0[a]	1.1±0.1	1.0±0.0
Transfusion, intervention, or mortality	186/298 (62.4%)	232/906 (25.6%)[a]	143/242 (59.1%)	124/457 (27.1%)[a]
Blood transfusion	156/297 (52.5%)	160/899 (17.8%)[a]	114/241 (47.3%)	77/457 (16.8%)[a]
Hemostatic intervention	109/299 (36.5%)	125/907 (13.8%)[a]	64/242 (26.4%)	37/458 (8.1%)[a]
Mortality	30/302 (9.9%)	59/906 (5.5%)[a]	18/242 (7.4%)	47/459 (10.2%)
Rebleeding	38/295 (12.9%)	53/876 (6.1%)[a]	17/241 (7.1%)	14/455 (3.1%)[a]
Hemostatic intervention for rebleeding	18/295 (6.1%)	25/876 (2.9%)[a]	11/241 (4.6%)	3/455 (0.7%)

[a]*P*<0.05 vs. melena.

Table 5. Outcomes related to presenting symptoms of melena vs. bloody emesis

	Melena without hematemesis (*N*=1,069)	Bloody emesis (*N*=1,209)	OR (95% CI) from multivariable analysis
Blood transfusion, hemostatic intervention, or mortality	646/1,068 (60.49%)[a]	418/1,204 (34.7%)	1.05 (0.80–1.39)
Blood transfusion	571/1,062 (53.8%)[a]	316/1,196 (26.4%)	1.10 (0.67–1.21)
Hemostatic intervention	227/1,069 (21.2%)	234/1,206 (19.4%)	0.66 (0.51–0.85)
Mortality	59/1,069 (5.5%)	80/1,208 (6.6%)	0.55 (0.35–0.84)
Rebleeding	83/1,065 (7.8%)	91/1,171 (7.8%)	0.76 (0.52–1.11)
Hemostatic intervention for rebleeding	38/1,065 (3.6%)	43/1,171 (3.7%)	0.76 (0.46–1.28)

CI, confidence interval; OR, odds ratio.
[a]*P*<0.05 for melena vs. bloody emesis on univariable analysis.

comparison of bloody emesis vs. melena was again *P*<0.0001 for the composite end point and for transfusion. Hemostatic intervention and mortality were similar for melena and bloody emesis, although multivariable analysis indicated lower odds with melena (hemostatic intervention OR=0.66, 0.51–0.85; mortality OR=0.55, 0.35–0.84). The proportion with rebleeding and intervention for rebleeding were similar for melena and bloody emesis.

Secondary analyses comparing melena with coffee-grounds emesis are shown in **Table 6**. The primary outcome and blood transfusion were much more common with melena than with coffee-grounds emesis. The difference lessened on multivariable analysis—also due to inclusion of hemoglobin in the model: removal of hemoglobin from the model again led to *P*<0.0001 for the composite end point and blood transfusion. Hemostatic intervention was also more common with melena, although this difference was not significant on multivariable analysis. Mortality was lower with melena than coffee-grounds emesis on both univariable and multivariable analyses. The proportion with rebleeding and intervention for rebleeding were higher with melena than coffee-grounds emesis, although adjusted ORs from the multivariable analysis crossed unity.

Endoscopic findings related to presenting symptom of bleeding are shown in **Table 7**. The *post hoc* comparison of characteristics that may impact the decision to perform endoscopy in the 934 patients not undergoing endoscopy vs. the 2,043 who did undergo endoscopy revealed the following: age ≥65 years (42 vs. 55%), heart rate ≥100 beats per min (28 vs. 33%), systolic blood pressure ≤100 mm Hg (8 vs. 16%), hemoglobin ≤100 g/l (17 vs. 45%), cirrhosis (6 vs. 14%), and ischemic heart disease (15 vs. 21%).

Table 6. Outcomes related to presenting symptoms of melena vs. coffee-grounds emesis

	Melena without hematemesis (*N*=1,069)	Coffee-grounds emesis (*N*=701)	OR (95% CI) from multivariable analysis
Blood transfusion, hemostatic intervention, or mortality	646/1,068 (60.5%)[a]	267/699 (38.2%)	1.30 (0.97–1.73)
Blood transfusion	571/1,062 (53.8%)[a]	191/698 (27.4%)	1.49 (1.07–2.07)
Hemostatic intervention	227/1,069 (21.2%)[a]	101/700 (14.4%)	1.18 (0.88–1.57)
Mortality	59/1,069 (5.5%)[a]	65/701 (9.3%)	0.58 (0.37–0.91)
Rebleeding	83/1,065 (7.8%)[a]	31/696 (4.5%)	1.53 (0.96–2.46)
Hemostatic intervention for rebleeding	38/1,065 (3.6%)	14/696 (2.0%)	1.30 (0.67–2.51)

CI, confidence interval; OR, odds ratio.
[a]*P*<0.05 for melena vs. coffee-grounds emesis on univariable analysis.

Table 7. Endoscopic findings related to presenting symptoms of bleeding

	Bloody emesis (*N*=1,209)	Coffee-grounds emesis (*N*=699)	Melena without hematemesis (*N*=1,069)
Normal endoscopy	95 (7.9%)	51 (7.3%)	146 (13.7%)[a,b]
Upper gastrointestinal erosions	231 (19.1%)	154 (22.0%)	190 (17.8%)[a]
Mallory–Weiss tear	45 (3.7%)[a]	11 (1.6%)	7 (0.7%)[b]
Gastric/duodenal ulcers	141 (11.7%)[a]	120 (17.2%)	304 (28.4%)[a,b]
Esophageal ulcer	28 (2.3%)	12 (1.7%)	15 (1.4%)
Varices	94 (7.8%)[a]	23 (3.3%)	24 (2.2%)[b]
Cancer	28 (2.3%)	10 (1.4%)	32 (3.0%)[a]
Vascular ectasia	8 (0.7%)	6 (0.9%)	30 (3.0%)[a,b]
Other cause/evidence of bleeding without site identified	96 (7.9%)	49 (7.0%)	93 (8.7%)
No endoscopy	443 (36.6%)	263 (37.6%)	228 (21.3%)[a,b]

Two patients in the coffee-grounds emesis group did not have endoscopic results recorded.
[a]*P*<0.05 vs. coffee grounds.
[b]*P*<0.0001 vs. bloody emesis.

The proportion of normal endoscopies was similar with bloody and coffee-grounds emesis—about half the proportion with melena alone. Although an infrequent finding, Mallory–Weiss tears were more common with bloody emesis than coffee-grounds emesis or melena. Gastric or duodenal ulcers were least common with bloody emesis (11.7%), intermediate with coffee-grounds emesis (17.2%), and most common with melena (28.4%). In contrast, variceal bleeding was 4.5 and 5.6% higher with bloody emesis than coffee-grounds emesis and melena. Finally, vascular ectasias were infrequent, but more common with melena than with bloody or coffee-grounds emesis.

The proportion of patients who received endoscopic therapy for variceal bleeding was 77 (7.2%) for bloody emesis vs. 20 (2.9%) for coffee-grounds emesis (*P*=0.0008). In contrast, the number of patients requiring endoscopic therapy for gastric or duodenal ulcers was similar in the bloody and coffee-grounds emesis groups: 68 (6.4%) and 50 (7.2%).

DISCUSSION

This multinational prospective observational study of ~3,000 patients revealed that patients presenting with bloody emesis do not have more severe bleeding episodes at presentation than patients presenting with coffee-grounds emesis as assessed by heart rate and blood pressure. In addition, scores for three validated UGIB risk stratification instruments commonly used at presentation to predict outcomes all indicated a lower risk in patients with bloody emesis, likely at least in part because these patients tended to be younger with fewer comorbidities. Finally, clinical outcome was not worse with bloody emesis compared with coffee-grounds emesis based on our primary composite end point of need for blood transfusion, need for hemostatic intervention, or death. We believe this composite is the most clinically relevant end point because its three elements represent the key clinical concerns in management of patients with UGIB. Patients who do not require blood transfusion, do not need hemostatic

intervention, and do not die generally have an uncomplicated, relatively benign course.

Hemostatic intervention, which included endoscopic therapy in all patients, was more common with bloody emesis than coffee-grounds emesis. Hemostatic intervention with endoscopic therapy is directly related to the finding of high-risk lesions, such as varices or ulcers with active bleeding, nonbleeding visible vessels, or clots. A higher proportion of high-risk lesions is reported when endoscopy is performed sooner after presentation (16). However, the time to endoscopy after presentation was not significantly shorter in the bloody emesis group than the coffee-grounds emesis group.

Given the scant information on outcomes with bloody emesis, some have used the appearance of nasogastric aspirates as surrogates to draw conclusions about hematemesis (8). Prior studies have reported that bloody nasogastric aspirate is associated with high-risk endoscopic findings. Adamopoulos *et al.* (9) reported that red blood in the nasogastric aspirate was associated with active bleeding at endoscopy on multivariable analysis (OR=16.4, 4.8–56) of 190 patients (181 with nonvariceal UGIB). However, the authors did not compare red blood vs. coffee grounds in the aspirate or present data on the association of active bleeding with coffee-grounds aspirates or emesis. They did find that hematemesis was not significantly associated with active bleeding, but do not state whether this represented all hematemesis including coffee-grounds emesis. Aljebreen *et al.* (10) evaluated 520 patients with acute nonvariceal UGIB and a nasogastric aspirate. They identified an increase in high-risk endoscopic findings (spurting, oozing, non-bleeding visible vessel) with bloody vs. coffee-grounds aspirate (74/163 (45%) vs. 49/213 (23%)).

These prior reports on nasogastric aspirates in nonvariceal UGIB raised the possibility that bloody emesis might similarly be associated with high-risk endoscopic findings that necessitate endoscopic therapy more frequently than coffee-grounds emesis. In our study, the 5% increase in hemostatic intervention with bloody vs. coffee-grounds emesis related largely to the higher proportion of patients with varices in the bloody emesis group. Varices generally mandate endoscopic therapy, and the proportion of patients receiving endoscopic therapy for varices was 4.3% greater in patients with bloody vs. coffee-grounds emesis (7.2 vs. 2.9%). In contrast, we identified no difference in the proportion of patients with ulcers requiring endoscopic therapy for high-risk stigmata with bloody vs. coffee-grounds emesis.

The mortality in our study was lower with bloody emesis than with coffee-grounds emesis, although the difference was not significant on multivariable analysis. Prior studies have primarily evaluated outcomes related to appearance of gastric aspirates and have not compared bloody vs. coffee-grounds emesis. Survey data submitted by 269 ASGE members on 2,225 patients presenting with UGIB in 1978–1979 found that mortality was higher with bloody nasogastric aspirate than coffee-ground aspirate (18 vs. 10%) as was transfusion of >5 units of blood (41 vs. 26%) and surgery (23 vs. 13%) (17). Because this study occurred before the advent of modern endoscopic and pharmacologic therapy, its applicability to current practice is uncertain. Corley *et al.* (18) reported that bloody nasogastric aspirate (OR=1.1, 1.0–1.3) and bloody hematemesis (OR=1.2, 1.1–1.3) were associated with an increased risk of a composite end point of rebleeding, surgery, or death in a study of 335 admissions. Finally, Blatchford *et al.*(7), in a prospective study of 1,882 patients, found that hematemesis was associated with increased mortality on multivariable analysis (OR=2.0, 1.1–3.5) whereas coffee-grounds emesis was not associated with increased or decreased mortality; the article does not make clear whether the hematemesis group included patients with coffee-grounds emesis. Nevertheless, the last three studies only compared the presence vs. the absence of a bloody aspirate, bloody emesis, or hematemesis, but did not compare bloody vs. coffee-grounds aspirate or emesis.

Rebleeding was more common with bloody emesis than with coffee-grounds emesis. Although we provided criteria to investigators for rebleeding, this can be a rather subjective diagnosis that may vary among the multiple investigators recording outcomes at different centers. Assessment of rebleeding requiring hemostatic intervention may be a more useful indicator of patients with clinically meaningful rebleeding. We found that this outcome was also more common among those with bloody emesis than coffee-grounds emesis.

A higher proportion of patients with melena in our study had the primary composite outcome of transfusion, intervention, or death as compared with patients with hematemesis (bloody or coffee-grounds emesis) due to the much higher rate of blood transfusion with melena. Patients with melena were more likely to present with a low hemoglobin: one-third of those with melena presented with hemoglobin ≤80 g/l as compared with 10% of those with bloody emesis. Therefore, patients with melena were much more likely to receive blood transfusions. We have previously shown that this may relate to the fact that UGIB patients with symptoms of only melena delay their presentation to emergency departments, allowing their hemoglobins to drift down to lower levels (19).

Mortality appeared to be lower with melena than with hematemesis in our study. Potential reasons for why mortality might be lower with melena than hematemesis include that melena may be more likely to represent a slower, more chronic bleeding process and may occur with a smaller amount of bleeding—as little as 50–80 ml (20). Prior studies (**Supplementary Table S1** online) provide conflicting results regarding the prognosis of patients with melena. In the ASGE survey from 1978 to 1979, melena was associated with a lower mortality than hematemesis (9.4 vs. 13.6%) without significant differences for transfusion of >5 units or surgery (17). More recent studies have reported melena to be associated with less further bleeding (21); increased rebleeding (22); an increase in a composite end point of blood transfusion, central line insertion, endoscopic therapy, surgery or death (23); and no association with a composite end point of rebleeding, surgery, or death (18)—but have not identified an increase or decrease in mortality (7,8,21–23). Variations in definitions of clinical characteristics, populations, sample size, rigor of data collection, and analysis may explain some of these differences.

When hematemesis, whether bloody or coffee-grounds, occurred with melena, patients had a lower systolic blood pressure at presentation and a markedly lower hemoglobin as compared with hematemesis without melena. Furthermore, the presence of

concurrent melena was associated with nearly a threefold greater likelihood of transfusion and hemostatic intervention, and a doubling of rebleeding. Sensitivity analyses suggest that the relative impacts of bloody vs. coffee-grounds emesis on outcomes are similar regardless of the presence or absence of melena. Nevertheless, concurrent melena and hematemesis (whether bloody or coffee-grounds emesis) appear to be associated with more severe UGIB and worse outcomes than isolated hematemesis

Limitations exist in our study. The reliability of patient or provider reports of bloody vs. coffee-grounds emesis has not been documented to our knowledge, although in real-world practice, decisions are made based on the histories obtained and exams performed by providers. Broad representation of patients from around the world may be viewed as a strength of our study, but also may lead to variation in patients and practices. All participating centers agreed on management practices, but this was an observational study without study-mandated treatment and hence variations may exist.

Furthermore, although guidelines recommend endoscopy within 24 h in most patients admitted with UGIB, and all study investigators accept these recommendations, the mean time to endoscopy was ~24 h. Thus, the results of our observational study suggest that many patients around the world do not undergo endoscopy within the recommended time frame. We cannot say whether outcomes would be different if a higher proportion of patients had upper endoscopies performed within 24 h of presentation.

We designed the study to provide information relevant to a practitioner seeing a patient at presentation. Some studies may exclude patients from analysis based on characteristics identified at a later time (e.g., only non-variceal UGIB, only those having endoscopic evaluation). However, because such characteristics are not available to providers at the time of presentation, these restricted analyses do not simulate real-world practice and artificially focus on just a select subset of patients. Excluding patients based on factors not known at the time of presentation may introduce bias and may provide an inaccurate assessment of patients at the time of presentation

In conclusion, patients with bloody emesis do not have more severe bleeding episodes at presentation than those with coffee-grounds emesis. Patients with bloody emesis do have a modest 5% higher rate of endoscopic therapy (largely due to their higher rate of varices) and also rebleed more frequently compared with those with coffee-grounds emesis. However, mortality and the composite end point, outcomes commonly used in development and validation of risk stratification tools, are not increased with bloody emesis as compared with coffee-grounds emesis. Concurrent hematemesis and melena is associated with more severe bleeding at presentation and worse outcomes than isolated hematemesis. Consideration for early endoscopy (within 12 h) has been suggested with presenting characteristics such as hemodynamic instability, Glasgow–Blatchford score ≥12, and cirrhosis (1,24). Given our findings, the presence of bloody emesis plus melena potentially could be incorporated along with these other high-risk factors in decisions regarding timing of endoscopy.

CONFLICT OF INTEREST

Guarantor of the article: Loren Laine, MD.

Specific author contributions: L.L.: study concept and design; acquisition, analysis, and interpretation of data; drafting of manuscript. S.B.L. and A.J.S.: study design; acquisition and interpretation of data; critical revision of manuscript. L.Z., H.R.D., J.H.N., and M.S.: acquisition of data, critical revision of manuscript. All authors approved the final draft submitted.

Financial support: none.

Potential competing interests: none.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Bloody emesis is said to represent more severe upper gastrointestinal bleeding than coffee-grounds emesis.
- ✓ Scant evidence supports this belief.

WHAT IS NEW HERE

- ✓ Bloody emesis was not associated with more severe bleeding episodes at presentation or an increased mortality as compared with coffee-grounds emesis.
- ✓ Patients with bloody emesis required endoscopic therapy more often than those with coffee-grounds emesis (due to their higher rate of varices) and had more rebleeding.
- ✓ Concurrent melena and hematemesis (whether bloody or coffee-grounds) is associated with more severe bleeding at presentation and worse outcomes than isolated hematemesis.

REFERENCES

1. Laine L, Jensen DM. ACG Practice Guidelines: management of patients with ulcer bleeding. Am J Gastroenterol 2012;107:345–60.
2. Barkun AN, Bardou M, Kuipers EJ *et al.* International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2010;152:101–13.
3. Barkun A, Bardou M, Marshall JK *et al.* Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2003;139:843–57.
4. Saltzman JR. Approach to upper gastrointestinal bleeding in adults. UpToDate. Last updated 24 July 2017 http://www.uptodate.com/contents/approach-to-acute-upper-gastrointestinal-bleeding-in-adults
5. Cappell MS, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin North Am 2008;92:491–509
6. Kim BSM, Li BT, Engel A *et al.* Diagnosis of gastrointestinal bleeding: a practical guide for clinicians. World J Gastrointest Pathophysiol 2014;5:467–78.
7. Blatchford O, Davidson LA, Murray WR *et al.* Acute upper gastrointestinal haemorrhage in west of Scotland: case ascertainment study. BMJ 1997;315:510–4.
8. Hwang JH, Fisher DA, Ben-Menachem T *et al.* The role of endoscopy in the management of acute non-variceal upper GI bleeding. Gastrointest Endosc 2012;75:1132–8.
9. Adamopoulos AB, Baibas NM, Efstathiou SP *et al.* Differentiation between patients with acute upper gastrointestinal bleeding who need early urgent upper gastrointestinal endoscopy and those who do not. A prospective study. Eur J Gastroenterol Hepatol 2003;15:381–7.
10. Aljebreen AM, Fallone CA, Barkun AN. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. Gastrointest Endosc 2004;59:172–8.

11. Stanley AJ, Laine L, Dalton H *et al.* Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. BMJ 2017;356:i6432.
12. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet 2000;356:1318–21.
13. Rockall TA, Logan RFA, Devlin HB *et al.* Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996;38:316–21.
14. Saltzman JR, Tabak YP, Hyett BH *et al.* A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. Gastrointest Endosc 2011;74:1215–24.
15. Laine L, Spiegel B, Rostom A *et al.* Methodology for randomized trials of patients with nonvariceal upper gastrointestinal bleeding: recommendations from an international consensus conference. Am J Gastroenterol 2010;105:540–50.
16. Tsoi KKF, Ma TKW, Sung JJY. Endoscopy for upper gastrointestinal bleeding: how urgent is it? Nat Rev Gastroenterol Hepatol 2009;6:463–9.
17. Silverstein FE, Gilbert DA, Tedesco FJ *et al.* The national ASGE survey on upper gastrointestinal bleeding. II. Clinical prognostic factors. Gastrointest Endosc 1981;27:80–93
18. Corley DA, Stefan AM, Wolf M *et al.* Early indicators of prognosis in upper gastrointestinal hemorrhage. Am J Gastroenterol 1998;93:336–40.
19. Laine L, Laursen SB, Dalton HR *et al.* Relationship of time to presentation after onset of upper gastrointestinal bleeding with patient characteristics and outcomes: a prospective study. Gastrointest Endosc 2017;86:1028–37.
20. Daniel WAJr, Egan S. The quantity of blood required to produce a tarry stool. JAMA 1939;113:2232.
21. Jaramillo JL, Galvez C, Carmona C *et al.* Prediction of further hemorrhage in bleeding peptic ulcer. Am J Gastroenterol 1994;89:2135–8.
22. Katschinski B, Logan R, Davies J *et al.* Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci 1994;39:706–12.
23. Cameron EA, Pratap JN, Sims TJ *et al.* Three-year prospective validation of a pre-endoscopic risk stratification in patients with acute upper-gastrointestinal haemorrhage. Eur J Gastroenterol Hepatol 2002;14:497–501
24. Garcia-Tsao G, Abraldes JG, Berzigotti A *et al.* Portal hypertensive bleeding in cirrhosis: risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. Hepatology 2017;65:310–35.