Predictors of Non-Significant Endoscopic Findings in Patients with Suspected Upper Gastrointestinal Tract Hemorrhage

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Objectives: *The objective of the present study was to determine pre-endoscopic predictive factors of non-significant endoscopic findings in patients with suspected upper gastrointestinal tract hemorrhage (UGIH).*
Material and Method: *Medical records of 187 patients admitted with the primary diagnosis of UGIH were reviewed. Non-significant endoscopic findings were defined as "normal", "mild gastritis" or unspecified gastritis with a hospital stay of two days or less. Possible predictors of non-significant endoscopic findings included pertinent history, physical examination, nasogastric tube aspirate, routine laboratory findings, and units of infused packed red cells (PRC). Multiple logistic regression analysis was used to determine significant predictors.*
Results: *Predictors of non-significant endoscopic findings included the absence of comorbid diseases (OR: 6.4; 95%CI: 3.0-13.6), higher platelet count (OR: 1.7 per 100,000 increase; 95%CI: 1.1-2.5) and less PRC infusion (OR: 1.9 per unit decrease; 95%CI: 1.3-2.7).*
Conclusion: *Patients with UGIH who may have a negative EGD can be identified prior to endoscopy.*

Keywords: *Predictors, Non-significant findings, Endoscopy, Upper gastrointestinal hemorrhage*

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Acute upper gastrointestinal tract hemorrhage (UGIH) remains a major cause of morbidity and mortality[1,2]. Urgent esophagogastroduodenoscopy (EGD) is widely recommended for patients presenting with acute UGIH in the emergency department. EGD can provide definitive diagnoses of the cause of UGIH as well as treatment for actively bleeding lesions[3,4]. However, 80% of UGIH patients have an uncomplicated course[5]. If it is possible to identify these patients prior to EGD, then a less costly or less risky level of care can be provided without compromising outcome[6-8], for example by foregoing urgent EGD.

There is some evidence that 20% to 30% of patients presenting with UGIH can be safely managed in an outpatient setting[9-11]. Studies have been conducted to identify such patients with the hope of reducing hospitalization costs[6,12]. For example, many patients are hospitalized while awaiting EGD. The ability to recognize patients who may or may not need urgent EGD should reduce some of these costs[12]. It can be further proposed that a subgroup of these patients may not need EGD at all. These patients include those diagnosed as having suspected UGIH but with normal EGD findings or other "non-significant" findings such as "mild gastritis" or "mild duodenitis".

The objective of the present study was to determine which pre-endoscopic predictive factors can be used to distinguish between acute UGIH patients who do not have significant EGD findings and those who do.

Material and Method

Medical charts of patients who were admitted to the authors' hospital with the primary diagnosis of UGIH during the period between May 2003 and July 2004 were reviewed. Patients were included if they

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underwent urgent EGD (within 24 - 48 hrs after admission). Patients were excluded if they were hospitalized for other illnesses, if they had severe cardiopulmonary diseases, severe hematologic derangement and advanced cancer. A total of 187 patients were enrolled.

Data on pre-endoscopic predictive factors potentially able to help discriminate between UGIH patients without significant EGD findings and those with such findings were abstracted. These factors included age and sex, history associated with the current bleeding episode, documented history of comorbid diseases and medications used, results of pertinent physical examination, results of nasogastric (NG) tube aspirates, basic laboratory investigations, and units of blood components infused. Details of these factors and their measures are presented in Table 1.

The primary outcome of the present study was the EGD findings. These findings were abstracted from endoscopic report forms available both electronically and in the medical charts. "Non-significant" EGD findings were defined as either "normal" EGD findings, or findings of "mild gastritis", "mild duodenitis", "gastritis" along with a hospital stay no longer than 48 hrs. Other EGD findings were considered "significant".

"Bivariable" association between each predictive factor and the EGD finding of non-significant or significant lesions was tested using the t-test, Wilcoxon ranksum test, or chi-square test (including Fisher's exact test) as appropriate[13]. Factors found to be significantly associated with EGD findings on bivariable analysis were entered in a multiple logistic regression model. Factors remaining statistically significant in the model were retained in the final model. The discriminatory ability of the final multiple logistic regression model was measured using the Area Under the receiver operating characteristic Curve (AUC)[14]. Cross-validity of the model was assessed using the jackknife method[13]. Statistical significance was defined as a test p-value of 0.05 or less.

A simple clinical prediction rule was created based on the multiple logistic regression model, emphasizing high specificity. This was because in order not to perform an EGD, the clinician must be able to predict with near certainty that the EGD findings will be non-significant. Hence the prediction rule must be highly specific.

Results

Data were available for all 187 patients identified. There were 118 men (63%) and 69 women (37%) in the cohort. The mean age was 53.5 years (standard deviation, 17.9 years). Potential predictive factors for non-significant EGD findings are presented in Table 1, separately for patients with non-significant EGD findings and for those with significant findings. Fifty-five patients (29%) were found to have non-significant EGD findings. Details of the EGD findings are shown in Table 2. The most common EGD finding was gastritis (38%).

On bivariable analysis, sex, history associated with current UGIH episode, history of previous UGIH episodes and concomitant drug use, with the exception of aspirin, were not associated with EGD findings. Younger age was, however, associated with non-significant findings. Almost all comorbid diseases were significantly associated with significant EGD findings. A variable defined by the absence of any comorbid diseases was most significantly associated with non-significant EGD findings.

Interestingly, blood pressure at presentation was not associated with EGD findings although there was a tendency for patients with non-significant EGD findings to have higher blood pressure. Most of the patients in the present study were hemodynamically stable on presentation (66% and 60% of patients had a systolic and diastolic blood pressure greater than 100 and 60 mmHg, respectively). Physical findings of chronic liver disease, anemia and melena were associated with significant EGD findings, as was a bloody aspirate from the NG tube.

Blood counts were not associated with EGD findings, with the exception of platelet counts. Biochemical renal function tests were not associated EGD findings, although abnormal liver function tests were associated with significant EGD findings. Finally, the number of units of packed red cells (PRC) infused were significantly associated with EGD findings.

On multivariable analysis, the only remaining significant predictors of non-significant EGD findings were the absence of comorbid diseases or conditions, higher platelet counts and less PRC infusions (Table 3). It is interesting to note that physical findings, NG tube aspirates, and other routine laboratory tests were no longer significant in the multiple logistic regression model. The AUC of the model was 0.83, and the jackknife AUC was 0.81.

A simple clinical prediction rule was created, by which a clinician might exclude a UGIH patient from undergoing urgent EGD or not to undergo EGD at all. Based on the multiple logistic regression model, the simplest rule with the highest specificity was "the absence of comorbid diseases, with a platelet count

Table 1. Predictive factors for "non-significant" EGD findings

Predictive factors	Total (n = 187)	Significant EGD findings (n = 132)	Non-significant EGD findings (n = 55)	p-values
Age (years): mean (sd)	53.5 (17.9)	57.3 (16.8)	44.2 (17.1)	<0.001 a
Sex (male): number (%)	118/187 (63)	86/132 (65)	32/55 (58)	0.368 b
History				
Coffee ground emesis: number (%)	59/187 (32)	41/132 (31)	18/55 (33)	0.823 b
Hematemesis: number (%)	53/187 (28)	37/132 (28)	16/55 (29)	0.883 b
Melena: number (%)	129/187 (69)	95/132 (72)	34/55 (62)	0.171 b
Syncope: number (%)	93/187 (50)	67/132 (51)	26/55 (47)	0.664 b
Peptic ulcer disease: number (%)	66/187 (35)	45/132 (34)	21/55 (38)	0.594 b
First bleeding episode (yes): number (%)	121/187 (65)	81/132 (62)	40/55 (73)	0.138 b
Medications and substances				
NSAIDS use (yes): number (%)	42/187 (22)	27/132 (20)	16/55 (29)	0.161 b
ASA use (yes): number (%)	31/187 (17)	27/132 (20)	4/55 (7)	0.027 b
Anticoagulant use (yes): number (%)	5/187 (3)	5/132 (4)	0	0.143 b
Alcohol abuse (yes): number (%)	107/187 (57)	73/132 (55)	34/55 (62)	0.412 b
Comorbid conditions				
Existing renal disease (yes): number (%)	30/187 (16)	25/132 (19)	5/55 (9)	0.095 b
Existing lung disease (yes): number (%)	13/187 (7)	13/132 (10)	0	0.016 b
Existing CAD (yes): number (%)	68/187 (36)	58/132 (44)	10/55 (18)	0.001 b
Existing liver disease (yes): number (%)	31/187 (17)	28/132 (21)	3/55 (5)	0.008 b
Existing DM (yes): number (%)	35/187 (19)	32/132 (24)	3/55 (5)	0.003 b
No existing disease (yes): number (%)	77/187 (41)	36/132 (27)	41/55 (75)	<0.001 b
Vital signs				
SBP at ER (mmHg): median (range)	113 (60-222)	112 (60-222)	116 (80-210)	0.983 c
DBP at ER (mmHg):Median (range)	70 (6-139)	70 (6-139)	70 (43-115)	0.235 c
Heart rate at ER(per min.): median (range)	93 (58-164)	96 (58-164)	90 (60-124)	0.199 c
physical examination				
Signs of chronic liver disease (yes): number (%)	32/187 (17)	29/132 (22)	3/55 (5)	0.006 b
Pale conjunctiva (yes): number (%)	119/187 (64)	95/132 (72)	24/55 (44)	<0.001 b
Per rectal exam – melena (yes): number (%)	129/185 (70)	97/130 (75)	32/55 (58)	0.026 b
Clear NG tube aspirate (yes): number (%)	39/186 (21)	22/132 (17)	17/54 (31)	0.024 b
Lab findings				
Hemoglobin (gm%): mean (sd)	9.6 (2.7)	9.2 (2.6)	10.6 (2.5)	<0.001 a
White cell count (per 1000): median (range)	9.92 (1.16-28.2)	9.95 (1.16-28.2)	9.87 (4.89-19.30)	0.851 c
Platelet count (per 1000): median (range)	248 (54-645)	235 (54-645)	271 (98-515)	0.003 c
BUN (mg%): median (range)	29 (5-145)	29 (5-145)	25 (7-80)	0.330 c
Creatinine (mg%): median (range)	1.1 (0.5-11)	1.1 (0.5-11)	1.0 (0.6-3.6)	0.144 c
INR: mean (sd)	1.2 (0.4)	1.2 (0.4)	1.1 (0.1)	0.001 a
Normal LFT (yes): number (%)	150/187 (80)	101/132 (77)	49/55 (89)	0.049 b
PRC infused (U): median (range)	1 (0-8)	2 (0-8)	0 (0-5)	<0.001 c
FFP infused (U): median (range)	0 (0-4)	0 (0-4)	0 (0-4)	0.060 c

a p-values by independent samples t-test; b p-values by chi-square or Fisher's exact test as appropriate; c p-values by Wilcoxon ranksum test; ASA: acetyl salicylic acid; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; ER: emergency room; INR: international normalized ratio; LFT: liver function test; PRC: packed red cells; FFP: fresh frozen plasma

Table 2. EGD findings

EGD findings	Number (n = 187)	Percentage (%)
Normal	14	7
Gastritis	67	38
Esophagogastric varices	27	14
Gastric ulcer	45	24
Duodenal ulcer	21	11
Esophagitis/Mallory-Weiss tear	8	4
Gastric cancer	5	2

Table 3. Important predictors of non-significant EGD findings in the multiple logistic regression model

Predictive factor	Odds Ratio (OR)	95%CI for OR
No existing medical illnesses	6.4	3.0 to 13.6
Platelet count	1.7 per 100,000 increase	1.1 to 2.5
PRC infusion	1.9 per unit *decrease*	1.3 to 2.7

greater than 60,000 per mm^3 and no PRC transfusions predict non-significant EGD findings". This prediction rule has a sensitivity of 54.5% (30/55) and a specificity of 90.2% (119/132).

Discussion

The main result of the present study was that the best predictors of non-significant EGD findings were the absence of comorbid diseases, higher platelet counts and fewer PRC transfusions. The discriminatory ability of the predictive model was reasonable (AUC greater than 0.8) with good cross-validity (jackknife AUC greater than 0.8), although the prediction rule mentioned at the end of the results section was perhaps not very specific (90.2%).

Previous studies have focussed on the iden-tification of poor risk UGIH patients likely to experience adverse outcomes (e.g. hospital death and rebleeding)[5,11,15-17]. Predictions were based on a combination of clinical, laboratory and EGD criteria[5,11,15-17]. Other studies focussed directly on the need for treatment, including the need for endoscopic treatment[18,19]. Without the need for urgent endoscopy, it has become more practical to treat some UGIH patients on an outpatient basis[7,8,18,19]. Costs of treatment can be considerably reduced without compromising patient care[6-8].

The present study was conducted to directly address the question of the need for EGD based on EGD findings, without using indirect arguments based on the prediction of poor treatment outcomes or the need for treatment.

Studies on pre-endoscopic predictive factors for adverse outcomes of UGIH or the need for treatment rely on clinical and laboratory information. Many of these studies found very similar predictors, which include: large volume hematemesis, presence of melena, bloody NG tube aspirate, comorbid diseases (especially liver diseases), unstable hemodynamics on presentation and low hematocrit or hemoglobin on presentation[5,7,8,12,18,19]. One study mentioned low platelet counts as a significant risk factor[19], although other reports mentioned a high white cell count[12] as a significant risk. Blood transfusion requirement was not often mentioned as a predictor of adverse outcomes[5,6], although one study did find blood transfusion requirement to be important[15].

Presence of comorbid diseases is almost universally recognized as an important predictive factor of poor treatment outcomes in patients with UGIH[5,8]. In the present study, comorbid diseases also predicted EGD findings. It is not clear why platelet counts and blood transfusion requirement were also important predictors of EGD findings in the present study, while other significant predictors mentioned above were not. However, this statistical relationship (odds ratios less than 3 for both factors, see Table 3) was rather weak.

Perhaps the most important reason for the discordance between the findings in the present study and those of other studies mentioned above is related to differences in study populations and study outcomes. Patients in the current study were prognostically

well (a high proportion of patients had good hemodynamics on presentation), and a large proportion had low risk EGD lesions (29%)[6]. A high proportion of patients in the present study had EGD findings of "gastritis"[6,11,20]. The outcome of the present study was not treatment results but EGD findings. A difference between study results should be expected for the latter reason since patients with good prognoses (low risk of adverse outcomes) may nevertheless have "significant" EGD findings, such as a healing duodenal or gastric ulcer.

An application of the result of the present study, after independent (external) validation or confirmation, would be to use the clinical prediction rule to exclude patients with suspected UGIH from undergoing EGD. For example, the 54% sensitivity of the prediction rule, if true, would imply the exclusion of 32 patients from EGD examination and possibly from hospital admission in a hospital where 200 lower-risk UGIH patients are seen annually, and the prevalence of non-significant EGD findings is 29% as in the authors' hospital. This would translate into a cost savings of at least Baht 112,000 from the society's point of view, assuming that an EGD examination costs Baht 1,500 and the average cost of two days of uncomplicated hospital stay is Baht 2,000 per patient.

On the other hand, given the specificity of 90%, implementation of the prediction rule would also exclude 17 patients with significant upper GI tract lesions from EGD examination for the same group of 200 patients. These lesions may require treatment. Safety concerns may dictate that the risk of excluding these 17 patients outweighs the cost savings due to exclusion of the other 32. Therefore, strict use of the clinical prediction rule to exclude patients from EGD examination is not recommended, unless its specificity is substantially greater than 90%. However, the prediction rule may still help in the decision to exclude patients from EGD examination for certain low risk cases, such as young UGIH patients with a normal hematocrit. Safety issues can only be definitively resolved by a clinical trial not likely to be conducted in the near future[21].

Other applications of the prediction rule or use of the risk factors identified in the present study would be to classify UGIH patients into those with lower or higher risk of having significant upper GI lesions. Lower risk patients may not need to undergo urgent EGD if resources are limited. Similarly, in situations where endoscopic expertise is not available, patients classified as having lower risk may not need close observation or may even be treated as outpatients.

Although the use of the current result is limited, potential benefits of a clinical prediction rule might warrant larger studies in the future with the hope of improving specificity, perhaps by including more predictive factors. Other limitations of the present study include possible misclassification of patients in terms of predictive factors due to inaccurate notes or incomplete data in the medical charts, a common weakness of historical or retrospective studies. A prospective study validating the current findings or establishing new predictors should resolve some of these problems.

Conclusion

In the present study 29% of acute UGIH patients had non-significant EGD findings. The best predictors of non-significant EGD findings were the absence of comorbid conditions, higher platelet counts and less PRC transfusions. A clinical decision rule based on this finding which states that "the absence of comorbid conditions, with a platelet count greater than 60,000 per mm^3 and no PRC transfusions predict non-significant EGD findings" was found to be quite specific (90.2%) but not very sensitive (54.5%). However, the specificity of this clinical prediction rule is probably lower in actual application. Although the result of the present study was not accurate enough for use in excluding suspected UGIH patients from EGD examination, they are encouraging in the sense that future studies may yet better identify patients who can be so excluded. If true, this could translate into a significant cost and time savings for patients and all those involved. Patients can avoid an unpleasant and occasionally dangerous procedure, without compromising their care.

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ปัจจัยทำนายผลการตรวจที่ไม่ผิดปกติอย่างมีนัยสำคัญในการส่องกล้องกระเพาะอาหาร ในผู้ป่วยเลือดออกในทางเดินอาหารส่วนต้น

ปรีดา สัมฤทธิ์ประดิษฐ์, สุวัฒน์ ตั้งกิตติมศักดิ์, ภาณุวัฒน์ เลิศสิทธิชัย

เบื้องหลังและวัตถุประสงค์: เพื่อค้นหาปัจจัยที่ใช้ทำนายผลการส่องกล้องกระเพาะอาหารที่ไม่พบสิ่งผิดปกติอย่างมีนัยสำคัญ ในผู้ป่วยเลือดออกจากทางเดินอาหารส่วนต้น

วัสดุและวิธีการ: ศึกษาย้อนหลังกับเวชระเบียนของผู้ป่วย 187 คน ที่มารับการรักษาด้วยภาวะเลือดออกในทางเดินอาหารส่วนต้น นิยามของ "ผลการส่องกล้องกระเพาะอาหารที่ไม่พบสิ่งผิดปกติอย่างมีนัยสำคัญ" คือผลตรวจที่เป็น "ปกติ" หรือเป็น "กระเพาะอักเสบเพียงเล็กน้อย" หรือเป็น "กระเพาะอักเสบ" แต่อยู่ในโรงพยาบาลน้อยกว่า 2 วัน ปัจจัยที่ใช้ทำนายผลการตรวจดังกล่าวรวมถึงประวัติผู้ป่วย, การตรวจร่างกาย, การตรวจน้ำที่ได้จากการใส่ท่อล้างกระเพาะ, ผลการตรวจทางห้องปฏิบัติการและปริมาณเลือดที่ต้องทดแทน ได้คัดเลือกปัจจัยที่สำคัญที่สุดในการทำนายผลการส่องกล้อง โดยวิธี Multiple logistic regression

ผลการศึกษา: ปัจจัยในการทำนายผลการส่องกล้องที่ไม่ผิดปกติอย่างมีนัยสำคัญประกอบด้วย การไม่มีประวัติโรคแทรกซ้อนใด ๆ (OR: 6.4;95%CI: 3.0-13.6), จำนวนเกล็ดเลือดที่สูง (OR: 1.9 ต่อ 100,000 ที่เพิ่มขึ้น; 95%CI: 1.1-2.5) การได้รับเลือดทดแทนในปริมาณน้อย (OR: 1.9 ต่อจำนวนถุงที่ลดลง; 95%CI: 1.3-2.7)

สรุป: ก่อนการส่องกล้อง น่าจะทำนายได้ว่า ผู้ป่วยคนใดน่าจะมีผลตรวจกระเพาะอาหารที่ไม่พบสิ่งผิดปกติ