PREDICTIVE FACTORS FOR MORTALITY, RECURRENT BLEEDING AND NEED FOR SURGERY IN NON-VARICEAL UPPER GASTROINTESTINAL (GI) BLEEDING IN CORRELATION WITH ROCKALL SCORE

BY

DR NORIDAH NORDIN

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ABBREVIATIONS

AUC	Area under Curve
APC	Argon Plasma Coagulation
APTT	Activated Partial Prothrombin time
BICAP	Bipolar Electrocoagulation
COX	Cyclooxygenase
DU	Duodenal Ulcer
ECG	Electrocardiogram
F 1/2/3	Forrest 1/2/3
GU	Gastric Ulcer
GI	Gastrointestinal
H_2R	Histamine Receptor
IHD	Ischaemic Heart Disease
INR	International Normalized Ratio
IQR	Inter Quartile Range
OGDS	Oesophagoduodenoscopy

UGIB	Upper Gastrointestinal
NSAID	Nonsteroidal Anti-inflammatory Drugs
ROC	Receiver Operating Characteristic
SD	Standard Deviation

ABSTRAK

Latar belakang:

Sistem skor Rockall telah digunakan dengan meluas di seluruh dunia termasuk Malaysia Skor in berguna untuk meramal kematian, tetapi ada kontroversi dalam meramal kejadian pendarahan yang berulang dan keperluan pembedahan.

Tujuan:

Tujuan kajian ini adalah untuk melihat korelasi skor Rockall dan akibat pendarahan usus atas dan menentukan faktor-faktor yang dapat meramalkan ketiga-tiga akibat pendarahan dan kumpulan risiko Rockall.

Tatacara:

Ini adalah peninjauan penilaian ke atas 250 orang pesakit dengan pendarahan usus yang bukan varis yang dimasukkan ke wad HUSM di antara 2004 hingga 2006

Keputusan:

Min umur adalah 62.1 $\pm$16 tahun. Terdapat lebih lelaki 57.6% (144) daripada perempuan 42.4% (106). Kebanyakannya Melayu 209 (83.6%)orang, selainnya adalah Cina 30 (12%) orang, Siam 8(3.2%) orang dan India 3(1.2%) orang. 24 pesakit (9.6%) mendapat pendarahan yang berulang, 11(4.4%) memerlukan pembedahan dan 9 pesakit (3.6%) meninggal dunia. Kebanyakan pesakit 213(85.2%) mempunyai skor Rockall ≤ 5 iaitu kumpulan berisiko rendah dan 37 (14.8%) mempunyai skor Rockall > 5 iaitu kumpulan berisiko tinggi. Skor Rockall yang tinggi di dalam kumpulan berisiko tinggi mempunyai perhubungan yang signifikandengan kematian ($P < 0.001$), pendarahan yang berulang (P value = 0.01) dan keperluan pembedahan (P = 0.013).

Faktor-faktor yang berhubung dengan kematian di dalam analisis univariate adalah umur yang meningkat (p=0.001), penyakit hati yang kronik (p=0.008), sepsis (p<0.001), warfarin (p=0.019)

Keadaan tidak sedar (p<0.001), darah di dalam tiub ryles (p=0.019), haemoglobin rendah (p=0.030, min ± SD=6.4±2.0 g/dl)) urea tinggi (p=0.040, min ± SD = 22.5±13.4). Di dalam analisis multivariate faktor yang ada hubung kait signifikan dengan kematian adalah sepsis (p=0.021, OR=9.9, 95%CI 1.413-69.513). Faktor yang ada hubung kait dengan pendarahan berulang di dalam analisis univariate adalah penyakit jantung iskemik (p=0.032), penyakit hati yang kronik (p=0.042), sepsis p=(0.004), aspirin (p=0.022), mempunyai simtom anemia (p=0.002), keadaan tidak sedar (p=0.008), darah di dalam tiub ryles (p=0.024), haemoglobin rendah (p=0.006, min± SD= 6.8±1.6), urea tinggi(p=0.028, min±SD=21.0±14.9), creatinine tinggi(p=0.029 min±SD = 290.4± 230.7). Faktor yang berhubung kait dengan pendarahan yang berulang di dalam analisis multivariate adalah creatinine. (p=0.012, 95% CI 1.0-1.0).Faktor yang berhubung kait dengan keperluan pembedahan adalah simtom sakit di epigastrik (p=0.005), mempunyai simtom anaemia (p=0.018), tekanan darah diastolic (p=0.031, min±SD, 63.8±10.3), epigastrium sakit (p=0.015), haemoglobin rendah (p=0.001, min±SD=6.4 ±1.3). Faktor yang berhubung kait dengan kumpulan berisiko tinggi adalah umur yang meningkat (p=0.010), penyakit jantung iskemik (p=0.007), penyakit peptik ulser (p=0.018), penyakit buah pinggang yang chronic (p=0.004), penyakit hati yang chronic (p=0.039), sepsis (p<0.001), ubat kampung (p=0.046), keadaan tidak sedar(p=0.014), haemoglobin rendah(p=0.022, min±SD=7.3±2.4), APTT (p=0.026, min±SD=37.9±9.4). Faktor yang berhubung kait dengan kumpulan berisiko tinggi dalam analisis multivariate adalah kesan pendarahan di dalam perut (p<0.001, OR=0.063, 95%CI =0.26-0.152), Sepsis (p=0.013, OR=0.149, CI 0.034-0.664) dan warfarin (p=0.028, OR=0.182, CI = 0.040-0.832)

Skor Rockall yang tinggi di dalam kumpulan berisiko tinggi mempunyai perhubungan yang signifikandengan kematian ($P < 0.001$), pendarahan yang berulang (P value = 0.01) dan keperluan pembedahan ($P = 0.013$).

Garis lengkungan ROC (Receiver Operating Characteristic) untuk kematian menunjukkan kawasan di bawah garis lengkungan adalah 0.87, untuk pendarahan berulang adalah 0.72 dan untuk keperluan pembedahan adalah 0.65.

Kesimpulan:

Kajian ini menunjukkan skor Rockall adalah berguna untuk meramal kematian tetapi tidak kejadian pendarahan yang berulang dan keperluan pembedahan tetapi analisis kumpulan menunjukkan ketinggian skor Rockall boleh meramal kematian, kejadian pendarahan yang berulang dan keperluan pembedahan. Kebanyakkan pesakit pendarahan usus atas adalah di dalam kumpulan berisiko rendah.Sepsis adalah satu faktor yang penting untuk meramal akibat pendarahan usus atas. Kajian prospektif skor Rockall di dalam pesakit sepsis dengan penyakit pendarahan usus atas adalah di cadangkan.

ABSTRACT

Background:

Rockall score was widely used around the world including Malaysia. The score was useful in predicting mortality but there were controversies regarding its use to predict recurrent bleeding and need for surgery.

Objectives:

The objectives of this study were to see the correlation between Rockall score and outcome of GI bleed and to determine factors that predict the three outcomes and association with Rockall risk group.

Methods:

This was a retrospective observational study of 250 patients with non variceal GI bleed who were admitted to HUSM between 2004 until 2006.

Results:

The mean age was 62.1 $\pm$16 years. There were more males 57.6% (144) than females 42.4% (106). Most patients were Malays 209 (83.6%) others were Chinese 30 (12%), Siamese 8(3.2%) and Indians 3(1.2%). Mortality rate was 3.6% (9 patients), recurrent bleeding rate was 9.6% (24 patients) and rate for patients that need operation was 4.4%(11 patients). 85.2% (213 patients were in the high risk group (Rockall score ≤ 5) and 14.8% (37 patients) were in the high risk group. The high risk group was significantly associated with mortality ($p < 0.001$), recurrent bleeding (p value = 0.01) and the need for surgery ($p = 0.013$). Factors associated with mortality in univariate analysis were older age ($p=0.001$), chronic liver disease ($p = 0.008$), sepsis

(p< 0.001), warfarin (p=0.019), unconscious state (p<0.001), coffee ground in ryles tube (p=0.019), low haemoglobin (p=0.030, mean ± SD=6.4±2.0 g/dl)) raised urea (p=0.040, mean ± SD = 22.5±13.4). In multivariate analysis significant factor associated with mortality was sepsis (p=0.021, OR=9.9, 95%CI 1.413-69.513). Factors associated with recurrent bleeding in univariate analysis were ischaemic heart disease (p=0.032), chronic liver disease (p=0.042), sepsis p=(0.004), aspirin (p=0.022), symptoms of anaemia (p=0.002), unconscious state (p=0.008), coffee ground in ryles tube (p=0.024), low haemoglobin (p=0.006, mean± SD= 6.8±1.6), raised urea (p=0.028, mean±SD=21.0±14.9), raised creatinine (p=0.029 mean±SD = 290.4± 230.7). Factor associated with recurrent bleed in multivariate analysis was creatinine. (p=0.012, 95% CI 1.0-1.0).Factors associated with the need for surgery in univariate analysis were epigastric pain (p=0.005), symptomatic anaemia (p=0.018), diastolic blood pressure(p=0.031, mean±SD, 63.8±10.3), tender epigastrium (p=0.015), low haemoglobin (p=0.001, mean±SD=6.4 ±1.3). Factors that were associated with the high risk group were older age (p=0.010), ischaemic heart disease (p= 0.007), prior peptic ulcer disease (p=0.018), chronic renal failure (p=0.004), chronic liver disease (p=0.039), sepsis (p<0.001), herbs (p=0.046), unconscious state (p=0.014), low haemoglobin (p=0.022, mean±SD=7.3±2.4), APTT (p=0.026, mean=37.9±9.4). Factors associated with high risk group in multivariate analysis were stigmata of recent haemorrhage (p<0.001, OR=0.063, 95%CI =0.26-0.152), Sepsis (p=0.013, OR=0.149, CI 0.034-0.664) and warfarin (p=0.028, OR=0.182, CI = 0.040-0.832)

The receiver Operating Characteristic (ROC) curve for mortality showed area under the curve of 0.87, for recurrent bleeding 0.72 and the need for surgery 0.65.

Conclusion:

The study showed Rockall score was useful to predict mortality but not recurrent bleeding and need for surgery however the risk grouping analysis showed that higher Rockall score can predict mortality, recurrent bleed and need for surgery. Most upper GI bleeders was in the low risk group. Sepsis was found to be an important factor to predict outcomes. A further prospective study on the use of Rockall score in sepsis patient in upper GI bleed should be proposed.

CHAPTER 1

INTRODUCTION

1. INTRODUCTION

1.1 OVERVIEW OF NON VARICEAL UPPER GASTROINTESTINAL BLEEDING (UGIB)

1.1.1 Epidemiology

In the United Kingdom, the annual incidence for UGIB is 50 to 150 per 100,000 of the population. The incidence is approximately 72 per 100,000 in Malaysia (Cheng JLS 2001)

1.1.2 Definition

Gastrointestinal bleeding (GI) refers to any bleeding that originates from the gastrointestinal tract. The upper gastrointestinal bleeding indicates the location of the bleeding between the mouth and the outflow tract of the stomach. Non variceal upper gastrointestinal bleeding includes bleeding other than those caused by esophageal varices. The degree of bleeding can range from nearly undetectable to acute massive bleeding and life threatening bleeding.

1.1.3 Aetiology

About 90% of the cases of non variceal upper GI bleeding arise from Mallory-Weiss tears, peptic ulcer disease, and anteroerosive gastritis.

Mallory-Weis tear is an acute tear at the gastro-oesophageal junction as a result of severe vomiting or retching, often after excessive alcohol intake.

Other cause includes malignancy. Carcinoma and lymphoma of the stomach commonly bleed at an advanced ulcerated stage, and occasionally present with an acute haemorrhage.

1.1.4 Pathophysiology

The bleeding is a result of mucosal and blood vessel wall erosion with subsequent hemorrhage. Peptic ulcer bleeding occurs predominantly from duodenal ulcer or gastric ulcers. The severity of the bleed is dependent on the size of the vessel affected. Simple oozing is caused by damage to small submucosal vessels less than 0.1 mm in diameter. More severe arterial bleeding indicates a large vessel between 0.1 and 2 mm in diameter in the base of the ulcer. Large ulcers arising from the posterior part of the duodenal cap can erode the gastroduodenal artery and provoke brisk bleeding. The passage of blood through the gastrointestinal tract was broken down and results in malaena that is the black tarry stool. It can be observed with as little as 50 mL of blood in the stomach.

Hematochezia (bright red blood per rectum) may be observed in up to 15% of cases of UGIB. Its presence suggests a large blood loss of greater than 1 liter and is therefore associated with a less favorable prognosis.

1.1.5 Risk factors for upper gastrointestinal bleeding

The major risk factor for the development of peptic ulcers is the presense of Helicobacter Pylori. Other important risk factor are exposure to nonsteroidal anti-inflammatory drugs (NSAIDS) (E stodolnik, 1987). The occurrence of injury may depend on clinical factors, type and dose of NSAID used. The use of NSAIDs have also been found to be a risk factor for ulcer rebleeding. The risk of ulcer bleeding increases significantly when both risk factors are present. Selective cyclooxygenase-2 inhibitors has less gastroduodenal ulcer and ulcer complications compared to conventional NSAID. (Kolars 2007)

Other important risk factors are patients who are using steroids, patients that are on aspirins, on anticoagulants, and those who have significant comorbid medical illness. Also those who are at risks are of advanced age, or have a prior history of peptic ulcer disease. (Hernandez–Diaz S, 2001).

1.1.6 Clinical presentation

Upper GI bleeding typically presents with either hematemesis which is vomiting of bright red blood or coffee ground contents, or melaena (black tarry stools). Others can also present with epigastric pain or anaemic symptoms without hematemesis or malaena. Severe upper GI bleeding can present with haemodynamic changes such as dizziness, dyspnea and altered sensorium with tachycardia and hypotension.

1.1.7 Initial Management

Initial management of patients with upper GI bleeding should include an assessment of the patient's hemodynamic state and evaluation of the severity of the bleeding episode.

The need for resuscitation and intervention to stop bleeding depends on the presence or absence of the signs of shock rather than the haemoglobin level .

- tachycardia over 100 b.p.m.
- hypotension with systolic blood pressure less than 100 mm Hg and mean arterial pressure less than 80mmHg
- a postural drop of over 20 mm Hg.

The presence of any of these signs of shock indicates the need for active resuscitation Aggressive hemodynamic resuscitation with fluid replacement and blood volume should be initiated early.

The blood samples should be sent for full blood count, urea and electrolytes, prothrombin time and a cross-match for 6 units of packed red cells. Packed red cells are required if the haemoglobin level is less than 100 g/litre in the absence of chronic anaemia or if it is estimated that more than 20% of intravascular volume has been lost. In massive gastrointestinal bleeding, O negative blood may be required. In addition to that, any significant coagulopathy should be corrected with fresh frozen plasma.

Furthermore an airway protection should be established with endotracheal intubation in patients with ongoing hematemesis or compromised mental status. This will minimize aspiration.

The adequacy of resuscitation may be assessed from central venous pressure monitoring and measurement of the hourly urine output, aiming for a value of more than 0.5 ml/kg/hour.

1.1.8 Endoscopic diagnosis

Upper gastrointestinal endoscopy represents the primary diagnostic tool of choice in the management of GI bleeding as it provides a direct visualization for an accurate diagnosis. Also it provides an opportunity for therapeutic intervention. Early endoscopy within 12 to 24 hours of initial presentation is strongly recommended in all cases of UGIB (Joseph K Lim, 2005).

Oesophagogastrocopy can be associated with occasional life-threatening complications including perforation, hemorrhage, and various cardiopulmonary events but it is uncommon. In the upper gastrointestinal bleeders, especially in the elderly with active bleeding, the risks may be higher. In these patients, sedatives should be used with caution and with the minimal dose necessary to produce the desired effect. Oxygen saturation should be monitored and nasal O_2 should be used if hypoxia exists. Also ECG should be performed and cardiac monitoring carried out during the procedure. Resuscitative equipment should be readily available. Careful explanation of the procedure is mandatory for good patient cooperation and safety.