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Upper Gastrointestinal Bleeding Due To Peptic Ulcer, Management and Complication: Overview

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Abstract: **Upper-gastrointestinal bleeding (UGIB) secondary to peptic ulcer disease (PUD) is a severe medical condition that is related to considerable morbidity, high health care costs, and reduced lifestyle, patients believed to have UGIB secondary to PUD need immediate medical attention.. Main goal of this current study was to focus on the complications and management of Upper-gastrointestinal bleeding (UGIB) which is secondary to peptic ulcer disease (PUD), through reviewing the literature concerning this condition. In MEDLINE/PubMed, Cochrane Library, Embase and Web of Science databases search was performed for all studies published throughout the past 3 decades up to December 2016. This search was without language restriction, and involving articles with human subject discussion. We search for relevant articles which were discussing the upper-gastrointestinal bleeding (UGIB) which caused by peptic ulcer disease, and mainly those studies which review and evaluate the management of UGIB. Management of the patient providing with obvious bleeding earnings in a step-wise manner. The first step is assessment of hemodynamic status and initiation of resuscitative steps as required. Patients are risk stratified based upon scientific functions such as hemodynamic status, comorbidities, age, and preliminary laboratory tests. The majority of patients need to receive an upper endoscopy within 24 h or less, and endoscopic functions of the ulcer help in directing further management.**

Keywords: **Upper-gastrointestinal bleeding (UGIB), MEDLINE/PubMed, peptic ulcer disease.**

1. INTRODUCTION

Upper-gastrointestinal bleeding (UGIB) secondary to peptic ulcer disease (PUD) is a severe medical condition that is related to considerable morbidity, high health care costs, and reduced lifestyle [(1,2)]. Patients believed to have UGIB secondary to PUD need immediate medical attention [(3,4)]. In spite of advances in management, the risk for mortality amongst patients with this condition varies from 2.2 % upward to 14 % [(5,6,7)]. Upper intestinal bleeding, specified as bleeding from the duodenum, stomach, or esophagus, is responsible for 50% or more of these hospitalizations [(8)]. The case death rate among hospitalized patients with upper gastrointestinal bleeding has decreased over the past 20 years and varieties from 2.1 to 2.5% in U.S. nationwide database research studies [(9,10)] to 10% in big, prospective European observational research studies [(9,10)]. The rate of death among patients who are already hospitalized for another condition when upper intestinal bleeding develops is around 3 to 4 times as high as the rate among patients who are admitted to the healthcare facility for upper gastrointestinal bleeding [(11)]. Peptic ulcers, which are primarily due to Helicobacter pylori infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), occur in the stomach or duodenum and are the most regular cause of upper gastrointestinal bleeding [(10)]. Disintegrations in the esophagus (which are brought on by gastroesophageal reflux disease) or in the stomach or duodenum (which are regularly due to NSAIDs) are also common sources of upper gastrointestinal bleeding. Disintegrations are breaks confined to the mucosa (the most superficial layer of the intestinal system) and must not trigger serious bleeding due to the fact that veins and arteries are not generally present in the mucosa [(10,11)].

Historical and epidemiologic data recommend that PUD is a reasonably modern disease of industrialized nations [12]. Autopsy data showed practically no cases of death secondary to PUD in the early 1800's, but by the mid 1800's PUD ended up being acknowledged as a major factor to death in Westernized nations like North America and England [12]. Aspirin was just introduced in the early 1900's and thus, the epidemic increase of PUD is hypothesized to have been caused by a virulent strain of Helicobacter pylori [12].

Purpose:

Main goal of this current study was to focus on the complications and management of Upper-gastrointestinal bleeding (UGIB) which is secondary to peptic ulcer disease (PUD), through reviewing the literature concerning this condition.

2. METHODS

In MEDLINE/PubMed, Cochrane Library, Embase and Web of Science databases search was performed for all studies published throughout the past 3 decades up to December 2016. This search was without language restriction, and involving articles with human subject discussion. We search for relevant articles which were discussing the upper-gastrointestinal bleeding (UGIB) which caused by peptic ulcer disease, and mainly those studies which review and evaluate the management of UGIB.

3. RESULTS

- ***Overview of morbidity and incidence of UGIB due to PUD:***

Inconsistencies in reported results among previous studies may be discussed by numerous factors. The public health of PUD has actually evolved and is no longer primarily owned by H. pylori [3,13]. An aging society has resulted in an increase in using non-steroidal anti-inflammatory drugs (NSAIDs) consisting of aspirin [14]. This contributed to UGIB secondary to PUD ending up being more typical amongst the senior population. As elderly patients typically have more comorbidities and more complicated PUD, they may also experience even worse results than young PUD patients [15]. Health care systems have provided more reliable treatment for PUD, but these advances in health systems may be limited to large city centres [16]. Several studies have shown that the incidence of UGIB secondary to PUD diminished to completion of the 20th century and has actually mainly stabilized during the turn of the 21st century. In Sweden the incidence decreased from 64/100000 in 1987 to approximately 35/100000 in 1999, but was steady as much as 2005 [17]. Incidence was stable in the United States from 1999-2004 [14]. Spain reported a constant decrease in occurrence from approximately 55/100000 in 1996 to approximately 25/100000 in 2005 [5]. The reducing incidence of UGIB secondary to PUD from the late 20th century to the early 21st century might be partially discussed by the reduced occurrence of H. pylori [18].

Death continues to be a widespread result for UGIB secondary to PUD. In our research study, total in-hospital death for Alberta, Canada, was 8.5%. Nevertheless, the risk of death varies between nations: Korea (2.2% in 2006-2007) [6]. United States (2.5% in 2006) [4] Turkey (2.8% in 2009) [19], Spain (3.1% in 1996-2005) (5), Sweden (6.2% in 2005) [7], Denmark (11% in 2010-2011) [20] and the Netherlands (14% in 2000) [21]. Heterogeneity in between countries might be discussed by the period of study, the age distribution of populations, occurrence of comorbidities, and differences in UGIB management practices, which may be affected by factors such as accessibility of endoscopy and utilization of pharmacotherapies such as proton pump inhibitors and prokinetics. Methodological factors might additionally describe heterogeneity, including various definitions of mortality.

- ***Specific UGIB due to PUD studies showing complications and management approches:***

We identified large study [1] which involved all hospitalizations for UGIB secondary to PUD in Alberta, Canada from 2004 to 2010 (n = 7079) utilizing the International Classification of Diseases Codes (ICD-10). And aimed to assess the occurrence, surgical treatment, death, and readmission of upper gastrointestinal bleeding (UGIB) secondary to peptic ulcer disease (PUD) the qualities of patients in this study are demonstrated in (**Table 1**) [1].

Total risk of surgical intervention amongst patients with UGIB secondary to PUD was 4.3%. The odds of surgery were higher in patients who were younger (changed OR ≥ 65 vs < 65: 0.74; 95%CI: 0.58-0.94) (**Table 2**). Only 0.6% of our population underwent an interventional radiological treatment to control bleeding (**Table1**). While 76% of those who underwent interventional radiology avoided surgical treatment, going through interventional radiology was related to increased odds of surgical treatment (adjusted OR = 7.18; 95%CI: 3.48-14.84). The general risk of in-hospital death was

8.5% (Table 1). In-hospital death was connected with sex (adjusted OR woman vs male: 1.28; 95%CI: 1.07-1.53), age (changed OR ≥ 65 vs < 65: 1.68; 95%CI: 1.37-2.06), comorbidities (changed OR ≥ 3 comorbidities vs no comorbidities: 9.51; 95%CI: 7.28-12.43), and interventional radiology (changed OR = 2.41; 95%CI: 1.07-5.41) (**Table 2**) [(1)].

Risk of 30-d readmission with UGIB secondary to PUD significantly increased from 3.1% to 5.2% in between 2004 and 2010 (changed OR each year: 1.07; 95%CI: 1.01-1.14). The odds of readmission were higher among older patients (changed OR ≥ 65 vs < 65: 1.57; 95%CI: 1.21-2.04) and patients living in rural areas (adjusted OR rural vs metropolitan: 2.30; 95%CI: 1.79-2.95). Patients who got an upper endoscopy were at lower chances of hospital readmission (adjusted OR = 0.58; 95%CI: 0.45-0.74) (**Table 1**) [(1)]. An upper endoscopy treatment was carried out in over 70% of our study population. Methodological considerations might describe the absence of endoscopy reporting in this administrative database. The subpopulation that was validated consisted of 15% incorrect positives and some of these patients did not undergo upper endoscopy. Additionally, within our database some true cases of UGIB secondary to PUD went through endoscopy, but the CCI treatment code was missing out on from the database (3% in our recognition subpopulation). Reassuringly, our predictors of surgical treatment, in-hospital mortality, and 30-d readmission remained much like our main analysis when we restricted our study population to patients with a concurrent upper endoscopy procedural code [(1)].

patients with a bleeding duodenal ulcer had a worse prognosis than those with a bleeding gastric ulcer. Duodenal ulcers were associated with greater chances of death, readmission, and surgical treatment to healthcare facility. Bleeding duodenal ulcers were related to a higher risk of mortality and surgery. Duodenal ulcers may be associated with an even worse prognosis since ulcers located within the duodenum can be technically more difficult to manage; particularly, for endoscopy carried out in backwoods with decreased volume of experience in handling UGIB secondary to PUD [(1)].

Table1: Characteristics of patients admitted to hospital with incidence of gastrointestinal bleeding secondary to peptic ulcer disease *n* (%) (1)

	All hospitalized patients with UGIB Secondary to PUD	**Patients admitted for UGIB Secondary to PUD**
	***n* =7079**	***n* = 4713**
Female	2784 (39.3)	1841 (39.1)
Age ≥ 65 yr	4307 (60.8)	2720 (57.7)
Rural	1318 (18.6)	883 (18.7)
Underwent upper endoscopy	5422 (76.6)	3466 (73.5)
Underwent interventional radiology treatment	42 (0.6)	26 (0.6)
Underwent both interventional radiology and surgery[1]	10 (23.8)	7 (26.7)
Comorbidities		
No comorbidities	3016 (42.6)	2491 (52.9)
1-2 comorbidities	2329 (32.9)	1460 (31.0)
≥ 3 comorbidities	1734 (24.5)	762 (16.2)
In-hospital mortality	601/7079 (8.5)	175/4722 (3.7)
30-d readmission with UGIB secondary to PUD[2]	301/6478 (4.7)	229/4538 (5.1)
Surgical intervention	305/7079 (4.3)	200/4722 (4.2)

[1]Percentage reflects the proportion of patients who underwent surgery among those patients undergoing an interventional radiology intervention;

[2]Those who died in hospital were excluded from the calculation for readmission. UGIB: Gastrointestinal bleeding; PUD: Peptic ulcer disease.

Table2: Adjusted odds ratio (95%CI) among all hospitalized patients with a gastrointestinal bleeding secondary to peptic ulcer disease; admitted for any cause (*n* = 7079) [(1)]

	In-hospital mortality (95%CI)	30-d readmission (95%CI)[1]	Surgical intervention (95%CI)
One-year increase (yr)	0.98 (0.94-1.02)	1.07 (1.01-1.14)	0.98 (0.93-1.04)
Female to male	1.28 (1.07-1.53)	1.16 (0.91-1.47)	0.94 (0.74-1.20)
Age ≥ 65 yr to age < 65 yr	1.68 (1.37-2.06)	1.57 (1.21-2.04)	0.74 (0.58-0.94)
Rural to urban	0.90 (0.71-1.14)	2.30 (1.79-2.95)	0.90 (0.66-1.22)
Perforation to no perforation	3.14 (2.03-4.85)	1.59 (0.76-3.33)	Not applicable
Surgery[2]	2.23 (1.56-3.20)	1.16 (0.62-2.15)	Not applicable
Interventional radiology[2]	2.41 (1.07-5.41)	0.70 (0.09-5.16)	7.18 (3.48-14.84)
Upper endoscopy[2]	1.08 (0.86-1.35)	0.58 (0.45-0.74)	0.86 (0.66-1.13)
Charlson comorbidities[3]			
1-2 comorbidities	3.13 (2.36-4.16)	1.14 (0.86-1.49)	1.07 (0.81-1.41)
≥ 3 comorbidities	9.51 (7.28-12.43)	1.20 (0.88-1.64)	1.04 (0.77-1.41)

[1]Those who died in hospital were excluded from the calculation for readmission;

[2]Those who had the procedure performed compared to those who did not;

[3]Patients who had no comorbidities was used as the reference group. UGIB: Gastrointestinal bleeding; PUD: Peptic ulcer disease.

Other case-crossover study [(22)] was determined and included in our evaluation, including Adults presenting to medical facilities with their first UGIB secondary to PUD from 2004-- 2010. The goal of the study was to evaluate if everyday increases in air contamination concentrations were favorably related to upper intestinal bleeding (UGIB) secondary to peptic ulcer disease (PUD). This research study [(22)] revealed that there are no statistically considerable associations were observed for any of the specific toxins based upon same-day, or 1-day lag impacts within the Calgary discovery accomplice. When the air contamination exposures were examined as 3-, 5-, and 7-day averages, some contaminants were inversely related to UGIB in the discovery cohort; for example, 5-day averages of nitrogen dioxide (OR=0.68; 95 % CI: 0.53 - 0.88), and particle matter <2.5 μm (OR=0.75; 95 % CI: 0.61-- 0.90). However, these findings could not be recreated in the duplication mate [(22)].

- ***Treatment approaches of UGIB:***

Standards advise that patients with ulcers and high-risk endoscopic findings get an intravenous proton-pump inhibitor bolus (at a dose of 80 mg) followed by a continuous infusion (8 mg per hour) for 72 hours [(23,24)]. A meta-analysis [(25)] of randomized trials revealed that this technique, as compared to endoscopic treatment alone, substantially decreased risks of additional bleeding, the need for surgical treatment, and mortality [(25)]. A current meta-analysis revealed that periodic oral or intravenous proton-pump inhibitor treatment resulted in outcomes that were non-inferior to those after continuous infusion [(27)]; this suggests that periodic proton-pump inhibitor might be utilized in place of constant infusion [(24)]. The most suitable intermittent dosing is not known, but an initial oral or intravenous bolus of 80 mg followed by 40 to 80 mg two times daily for 72 hours has actually been recommended [(24)]. Based on other designs of hemorrhage [(27)], the first step in management of patients presenting with overt upper intestinal bleeding (UGIB) is assessment of hemodynamic status and initiation of resuscitative steps as needed. In addition to intravenous fluids, transfusion of red blood cells might be required. Randomized trials in euvolemic patients without existing bleeding [(28)] and in cirrhotic with UGIB [(29)] indicate that transfusions should be provided to preserve hemoglobin ≥ 7 g/ dl. A restrictive transfusion policy is likewise

supported by an older randomized trial of 50 patients without known varices where patients transfused ≥ 2 units within 24 h of admission had significantly more re-bleeding than those not transfused unless Hgb was < 8 g/ dl [30]. Greater hemoglobin levels might have to be targeted in patients with other health problems (e.g., coronary artery disease) [31] and in those with intravascular volume depletion (i.e., hypotension and tachycardia) in whom the hemoglobin is" synthetically" elevated prior to repletion with intravascular fluid. Intubation might be considered to prevent and protect the air passage goal in patients with extreme ongoing hematemesis and/ or transformed mental status; it may also be required in some patients (e.g., those with comorbidities) to securely and effectively provide sedation for endoscopy [1].

Endoscopic therapy:

Most patients who are hospitalized with upper intestinal bleeding should undergo endoscopy within 24 hours, after proper resuscitation and transfusion, as required, to a hemoglobin level greater than 7 g per deciliter. In some observational studies, timely endoscopy, as compared to endoscopy after 24 hours, has been associated with decreases in the need for surgery, length of hospitalization, and mortality [23,24,32,33].

A lot of patients with a low scientific risk (normal high blood pressure and heart rate and no major coexisting conditions) must go through endoscopy as soon as possible during routine medical hours. Approximately 40 to 45% of patients who undergo endoscopy within 2 to 6 hours have low-risk endoscopic findings that permit discharge, consequently reducing expenses [34,35]. An observational research study and a subgroup analysis of a randomized trial suggest that endoscopy within 12 to 13 hours in patients with high scientific risk (Glasgow - Blatchford rating ≥ 12, bloody nasogastric aspirate, hypotension, and tachycardia) might be connected with improved results [23]. Endoscopic features of ulcers are key in forecasting risk and determining management methods (**Figure 1**) [23].

A randomized trial involving patients with rebleeding after endoscopic therapy showed that surgery was avoided in 73% of cases and adverse events were substantially less common with endoscopic treatment than with surgical therapy [36]. If repeat endoscopic treatment stops working, transcatheter arterial embolization or surgery is performed. Issues of bleeding or perforation happen in around 0.5% of patients who undergo endoscopic treatment [25]. Endoscopic treatment likewise may be used for vascular ectasias, Dieulafoy's lesions, neoplasms, and actively bleeding Mallory - Weiss tears [24]. In patients with ulcers or disintegrations, biopsy specimens should be acquired from lesion-free locations of the gastric body and antral mucosa for assessment of H. pylori infection [23,24].

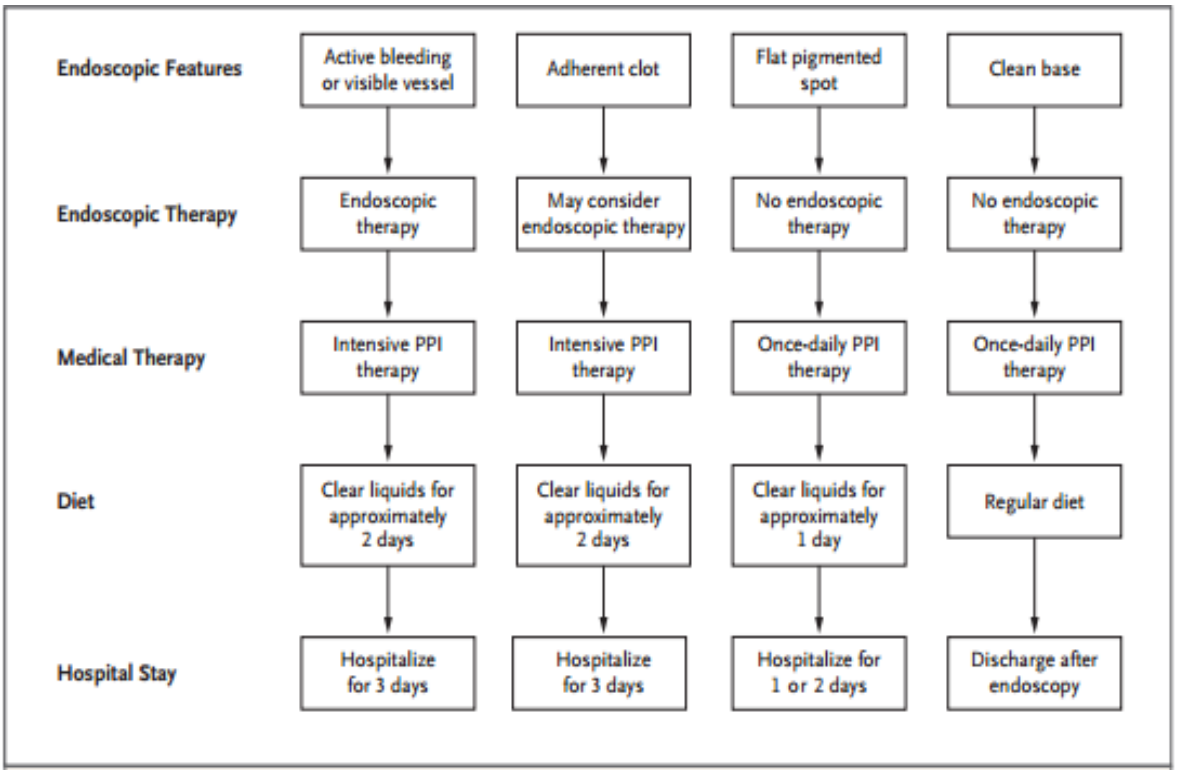

Figure1: Recommended endoscopic and medical management based on stigmata of hemorrhage in ulcer base. PPI, proton pump inhibitor. [23]

Prevention of Recurrent Ulcer Bleeding and management of risk factors:

Rebleeding is common after ulcer recovery if strategies to prevent reoccurrence are not utilized. A systematic evaluation of research studies with a 12-month follow-up revealed a 26% rebleeding rate among patients with H. pylori-- associated bleeding ulcers who did not get treatment for H. pylori infection [(37)]. Strategies to prevent recurrent ulcer bleeding depend upon the cause of the ulcer. The 3 significant causes are H. pylori infection, the use of NSAIDs (consisting of aspirin), and an idiopathic cause (**Figure 2**) [(37)].

Patients with H. pylori infection must get treatment to get rid of the germs. A meta-analysis of randomized trials of such therapy showed considerably less rebleeding in patients who got this therapy than in patients who did not get treatment for H. pylori infection and in those who got maintenance antisecretory treatment [(37)]. Obliteration of H. pylori need to be validated after treatment with a breath test, a stool test, or, if repeat endoscopy is carried out for another reason, gastric biopsy. Patients must not receive bismuth or prescription antibiotics for at least 4 weeks and ought to not get proton-pump inhibitors for a minimum of 2 weeks prior to testing to prevent incorrect unfavorable results; histamine H2 -receptor villains are acceptable. In a methodical evaluation of studies with a mean follow-up of 11 to 53 months,34 the incidence of rebleeding was only 1.3% among patients with validated obliteration of H. pylori [(37)].

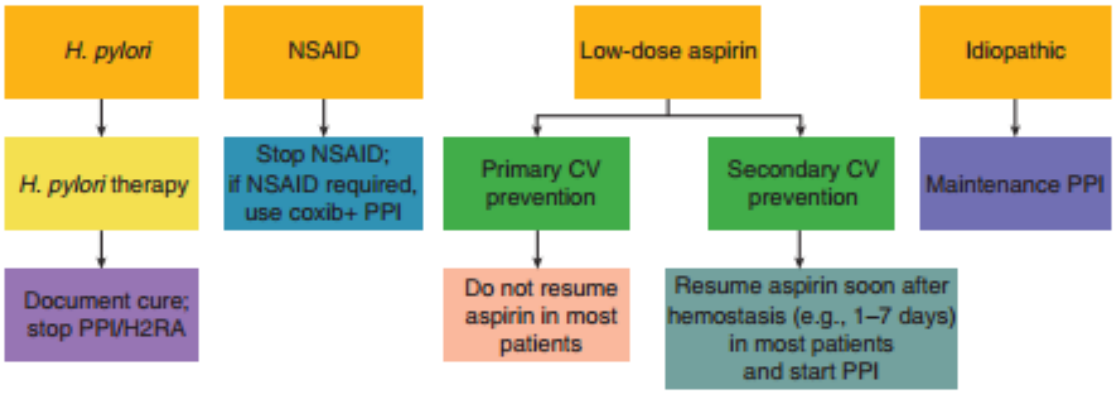

Figure2: Recommended management to prevent recurrent ulcer bleeding based on etiology of ulcer bleeding. CV, cardiovascular; H2RA, histamine-2 receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor. [(37)]

4. CONCLUSION

Management of the patient providing with obvious bleeding earnings in a step-wise manner. The first step is assessment of hemodynamic status and initiation of resuscitative steps as required. Patients are risk stratified based upon scientific functions such as hemodynamic status, comorbidities, age, and preliminary laboratory tests. The majority of patients need to receive an upper endoscopy within 24 h or less, and endoscopic functions of the ulcer help in directing further management. Those with high-risk findings of active bleeding or non-bleeding noticeable vessel ought to get endoscopic therapy and those with an adherent embolism may receive endoscopic therapy; these patients need to then receive intravenous PPI treatment with a bolus followed by continuous infusion. Those with flat spots or clean-based ulcers do not need endoscopic treatment or intensive intravenous PPI therapy. Reoccurring ulcer bleeding after endoscopic therapy need to be treated with a second endoscopic treatment, but if bleeding still repeats or persists treatment with surgical treatment or interventional radiology is undertaken.

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