

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
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PhD Thesis
Abstract

DIAGNOSIS AND THERAPEUTIC ALGORITHM
OF UPPER GASTROINTESTINAL BLEEDING

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CONTENT :

A. OVERVIEW

Abbreviations

CHAPTER 1:

INTRODUCTION

CHAPTER 2:

2. Etiopathogenesis of UGIB

2.1 Etiological classification

2.2 Non-variceal upper gastrointestinal bleeding

2.2.1 Definitions

2.2.2 Etiology

2.2.3 Risk factors

2.3 Variceal upper gastrointestinal bleeding

CHAPTER 3:

3. Physiopathology of upper gastrointestinal bleeding

3.1 Hemodynamic classification of UGIB

3.2 Hemodynamic principles and causes of portal hypertension

CHAPTER 4:

4. Positive diagnosis of UGIB

4.1 Clinical examination

4.2 Paraclinic and imagistic explorations

CHAPTER 5:

5. Diagnosis of severity of UGIB

5.1 Clinical criteria

5.2 Assessing the severity of bleeding

CHAPTER 6:

6. Diagnosis of evolution of UGIB

CHAPTER 7:

7. Etiological diagnosis of UGIB

CHAPTER 8:

8. Management of UGIB

- 8.1 Conservative treatment

- 8.2 Endoscopic therapy

- 8.3 Surgical treatment of UGIB

B. PERSONAL CONTRIBUTION

CHAPTER 9:

- 9.1 Motivation of choosing the theme

- 9.2 Material and method

CHAPTER 10:

10. Results

- 10.1 Demographic elements

- 10.2 Etiopathogenic elements

- 10.3 Diagnosis of UGIB

- 10.4 Treatment of UGIB

- 10.5 Evolution, complications and mortality of UGIB

CHAPTER 11:

11. Discussing the results

CHAPTER 12:

12. Conclusions

References.

Key words: Upper gastrointestinal bleeding (UGIB), hematemesis, melena, upper digestive endoscopy

Introduction

Upper gastrointestinal bleeding is defined as proximal bleeding by Treitz ligament [1]. Upper gastrointestinal bleeding is one of the most common causes of hospitalization in the world. In the United States, there are 250,000 to 300,000 hospital presentations and 15,000 to 30,000 deaths each year from UGIB [2, 3]. In England, this is a common medical emergency, with an annual incidence of 100 to 100,000. [4, 5].

Treating and preventing UGIB costs more billions of dollars a year [6]. The annual incidence of hospitalization for UGIB is 1 in 1,000 people in America [7]. It has a mortality of 7% to 10% [8]. Mortality has fallen sharply in the last 30 years despite the introduction of endoscopic therapy that reduces the rate of rebleeding [8]. This phenomenon has been attributed to the increasing percentage of UGIB occurring in older people who have a much worse prognosis than other patients due to their frequent use of platelet antiaggregants or anticoagulant, as well as frequent comorbidities [9,10]. Approximately 45% of patients hospitalized for UGIB are over 60 years [11]. Endoscopic therapy has led to a recent decline in the need for blood transfusion or UGIB surgery [1]. UGIB mortality is much higher for patients bleeding after hospitalization than for admitted patients due to gastrointestinal bleeding [1, 12, 13].

Motivation of choosing the theme

UBIB is one of the most common causes of hospitalization in the world. Treating and preventing UGIB costs billions of dollars a year. Patient assessment and appropriate management before performing upper digestive endoscopy are essential to reduce morbidity and mortality.

There are several hypotheses that may be responsible for the lack of improvement in mortality from gastroduodenal ulcer bleeding. Simultaneously with the decline in gastroduodenal ulcer prevalence of *Helicobacter pylori*, the incidence of aspirin use or non-steroidal anti-inflammatory drugs (NSAIDs) in the etiology of the ulcer is increasing. Another problem is attributed to the increasing percentage of UGIB occurring in the elderly patients, a group with a reserved prognosis than in other patients, due to increased use of platelet antiaggregants or anticoagulants as well as

their frequent comorbidities. One of the potential directions for improvement in the management of gastrointestinal hemorrhages is to identify patients at risk for unfavorable outcomes that could improve initial triage, primary endoscopic hemostasis plan, and postendoscopic management.

Endoscopic therapy has made progress in the accuracy of the etiologic diagnosis of certainty within the first 24 hours, while offering the possibility of performing a definitive or temporary hemostasis, depending on the etiology, thus decreasing the rebleeding rate, the need for blood transfusions, and the need for surgery.

The thesis envisages the following objectives:

- the study of the main causes of UGIB, the incidence of their morbidity and evolution for a period of six years, as well as the weight of modification of the different endoscopic means, pharmacological or surgical therapeutically means.
- correlation of morbidity changes through UGIB with different demographic factors (sex, age groups, urban or rural environment).
- study of the current diagnosis and treatment algorithm of nonvariceal and variceal UGIB, on the studied group of patients;
- the influence of modern diagnostic and treatment strategies on morbidity and mortality through UGIB.

The thesis represents a retrospective, unicentric clinical-statistic study, performed on 462 cases of UGIB of diverse etiology, admitted, investigated and treated in the First Surgery Clinic, the Intensive Care Unit and the Gastroenterology Laboratory of the Craiova County Emergency Clinical Hospital within a 6-year period (2009-2014).

Results

Gender - male predominance: 315 males (68.18%) vs. 147 women (31.82%) with male / female ratio (sex ratio) = 2.14. This predominance of male gender is maintained in both primary etiopathogenic forms of UGIB, with the difference that it is more pronounced for non-variceal UGIB (256 men / 108 women, sex ratio = 2.37) versus variceal UGIB (59 men / 39 women, sex ratio + 1.59),(Table 1).

Sex	Male	Female	Total cases
Number of UGIB cases	315	147	462

Table 1. Distribution of patients with UGIB according to sex.

Age -UGIB have been encountered at all ages; with extreme limits ranging from 21 to 84 years and an average of 63 years. Analysis of the distribution by age group showed that most UGIB (349 cases = 75.54%) belonged to age groups over 50 years, respectively 23% age group 51-60 years, 24% age group 61-70 years and 29% age group including elderly patients over 70 years of age. The same distribution was also found in patients with non-variceal UGIB, while in variceal UGIB patients the incidence was increased in the age group 51-60 years (30.61%), followed in order by the adjacent age groups, respectively 25.51% for the seventh decade and 19.38% for the fifth decade (Table 2).

Age group	20-30 years	31-40 years	41-50 years	51-60 years	61-70 years	>70 de years	Total cases
Number of UGIB cases	10	33	70	107	111	131	462

Table 2. Distribution of UGIB cases according to age group

Environment of origin as such, if not correlated with dietary habits, alcohol consumption, profession, etc. has no significant etiopathogenic significance. In the studied clinical material, 319 patients (69%) come from rural areas and the remaining 143 (31%) from the urban area, which is maintained for both etiopathogenic, variceal and non-variceal UGIB, without significant differences between the two etiopathogenic forms in absolute numbers, fact confirmed

by the statistical analysis, respectively Chi square test, which shows a p-value of 0.107751 (p <0.03)

Environment of origin	Rural	Urban	Total cases
Number of UGIB cases	319	143	462

Table 3. Distribution of patients according to their origin of environment

Etiological forms:

Although UGIB represent an anatomical clinic entity with multifactorial etiopathogenesis in recent years, for diagnosis and therapeutic reasons, two basic types of UGIB have been identified: variceal bleeding secondary to portal hypertension and non-variceal hemorrhage, which include the rest of UGIB, having a etiology that includes a wide range of conditions. In our study 98 variceal UGIB (21.21%) and 364 (78.79%) nonvariceal UGIB were recorded.

Non-variceal UGIB- 364 (78.79%) cases were the majority of cases. The main causal injuries in the nonvariceal UGIB etiology were: gastroduodenal ulcer 192 cases (52.75%), acute gastritis 132 cases (36.26%), Mallory Weiss syndrome 12 cases (3.30%), gastric neoplasm 23 cases (6.32%) and neoplasm of esogastric junction 5 cases (1.37%).

Variceal UGIB (98 cases = 21.21%) were due to bleeding rupture of esophageal varices secondary to portal hypertension in cirrhosis, viral etiology in 15 (19%) cases, alcoholic etiology in 57 (73%) cases and metabolic in 6 %) cases.

Diagnosis of UGIB is complex (clinical and paraclinical) carried out following an algorithm that involves the following steps:

- diagnosis of digestive hemorrhage (positive diagnosis);
- the diagnosis of severity;
- the evolutionary diagnosis;
- the etiological diagnosis.

Hours/days interval	< 6 hours	6-24 hours	1- 2 days	2-3 days	3-4 days	>4 days	Can't specify	Total cases
Number of UGIB cases	54	136	86	92	58	33	3	462

Table 4. Beginning-admission interval of UGIB

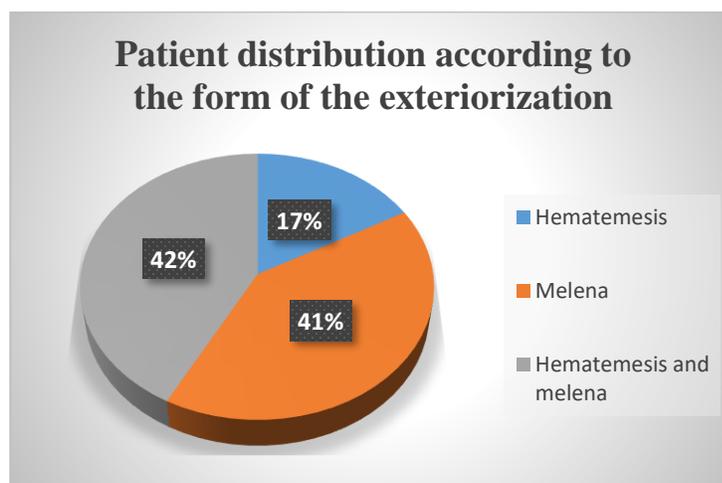


Chart 1. Patient distribution according to the form of the exteriorization

Diagnosis of gravity and of evolutivity are useful for assessing the amount of lost blood as well as for establishing the priority of therapeutic gestures in the management of each case. The severity diagnosis was based on hemodynamic constants (blood pressure, heart rate, diuresis) and hematological (Hemoglobin, Hematocrit) and revealed the high rate of severe and very severe hemorrhages (53.46%, Grade III and IV). The same distribution is maintained among variceal hemorrhages, where the severity of severe bleeding (severe UGIB / moderate UGIB = 62/36), while for nonvariceal hemorrhages the ratio of severe bleeding / moderate-mild bleeding is close to 1 (185 / 179). However, these differences are statistically insignificant ($p < 0.05$).

UGIB grade	Grade I	Grade II	Grade III	Grade IV	Total cases
	Hb 10-12 g/dL	Hb 8-10 g/dL	Hb 5-8 g/dL	Hb <5 g/dL	
Number of UGIB cases	59	156	186	61	462

Table 5. Distribution of patients with UGIB according to severity of bleeding.

Upper digestive endoscopy has been the main mean of etiological diagnosis, providing endoscopic hemostasis, which has greatly reduced surgical indications and has led to significant improvement in UGIB prognosis. It was performed in 232 (50.21%) cases, of which 23 (9.92%) variceal UGIB and 209 (90.08%) nonvariceal UGIB. EDS was performed with early urgency (first 8 hours) in 7 cases (3%), in the first 24-48 hours in 160 cases (69%), in the first 3 days in 48 (20%) cases and with scheduled endoscopy, usually after stopping bleeding in the rest of the cases (Table 6).

Hours/days interval	<8 hours	48 hours	3 - 4 days	> 4 days	Total cases
Number of UGIB cases	7(3%)	160(69%)	46(20%)	19(8%)	232

Table 6. Admission-Endoscopy interval of UGIB

Upper digestive endoscopy highlighted source of bleeding: esophageal varices 23 cases, gastric ulcer 70 cases, duodenal ulcer 58 cases, acute gastritis 53 cases, gastric cancer 13 cases, Mallory-Weiss syndrome 12 cases and stomal ulcer 2 cases.

Conservative medical treatment is first-line treatment, mandatory in all UGIB; with him begins any therapeutic attempt and may be the only therapeutic method or an adjunct to surgical treatment, used pre-, intra- and postoperatively.

Volemic therapy with isotonic saline and macromolecular solutions after a preliminary balance of losses was carried out in principle in all cases, at least until the severity of bleeding and the need for blood transfusion are settled.

Iso-group blood transfusion is the only method to compensate hematic capital losses and improve tissue oxygenation, despite its known avatars (transfusion-specific accidents and transmission of hepatitis B and C virus or other transmissible diseases). In our study, iso-group blood transfusion was indicated in all severe UGIB with hemoglobin values below 8 g / dl. The rhythm and the amount of blood transfused ranged from 1 to 10 units, depending on the bleeding severity and bleeding evolution (stopped, continuous or repeated bleeding).

Antisecretory therapy is part of the obligatory therapeutic gestures in all UGIB, regardless of etiology; it favors hemostasis and prevents rebleeding by diminishing the corrosive action of hydrochloric-peptic secretion on the gastric and duodenal mucosa, thus preventing the lysis of the clot or the appearance of new superficial ulcers. Antisecretory therapy has been used in principle in all cases in the form of histamine H₂- receptor antagonists monotherapy (152 cases - 33%) or proton pump inhibitors (176 cases - 38%) or associated therapy (134 cases- 29%) using the combination of the two types of antisecretory.

Endoscopic hemostasis was performed in 46 cases representing 19.82% of endoscopically investigated cases and 9.95% of total UGIB. The following endoscopic hemostasis methods were used: electrothermocoagulation in 21 patients (9%), elastic bands ligatures in 11 patients (5%), adrenaline injection in visible vessel of ulcers in 10 patients (4%), and Mallory Weiss lesions 2 patients (1%) and 2 endoclips in bleeding ulcers (1%).

Surgical treatment, once the main mean of hemostasis, was performed in 48 (10.38%) cases, a percentage which fits in the limits of literature data; of these 6 were variceal UGIB and 42 non-variceal ulcerative disease (Table 7).

Surgical interventions	Number of UGIB
Gastrectomy 2/3 type Pean with gastro-duodeno anastomosis	8
Polar superior esogastrectomy with eso-gastro anastomosis	3
Ulcer excision with pyloroplasty and vagotomy	3
Total gastrectomy with eso-jejuno anastomosis	5
Hemostasis in situ	23
Transgastric ligature of eso-gastric varices	6
Total cases	48

Table 7. Surgical treatment of UGIB

The **evolution of UGIB** was favorable in 374 (81%) cases, where conservative therapy, inclusive endoscopic hemostasis, led to bleeding stopping. In 88 cases (19%), there was a negative response to conservative therapy: bleeding continued in 37 (8%) cases or repeated several days after stopping conservative treatment in 51 (11%) cases, selected cases those requiring iterative endoscopic hemostasis or surgical hemostasis.

The uncommon gravity of UGIB is also supported by high **mortality**. There were 58 deaths, with a general mortality rate of 12.5%. The mortality rate is different for the two UGIB etiopathogenic forms, being 40.81% (40 deaths) in variceal UGIB, again emphasizing their severity, compared to 4.94% (18 deaths in non-variceal UGIB). The rate of postoperative mortality was also high - 16.66% (8 deaths).

Conclusions:

1. UGIB is a major medical-surgical emergency, striking a still high mortality and significant social costs.
2. The UGIB incidence was 28.6%, most common among male patients (68%), belonging to age groups of over 50 years (76%) coming from rural areas (69%).
3. Non-variceal hemorrhages were the major etiopathogenic form of UGIB (79%).

4. Gastro-duodenal ulcer (107 cases) and acute gastritis (44 cases) were the main cause of bleeding in non-variceal UGIB.
5. The UGIB diagnosis is a complex one, developed by an algorithm that includes positive diagnosis, gravity diagnosis, evolutionary and etiological diagnosis.
6. Severe hemorrhages (Grade III and IV) accounted for over half of the cases (53.46%), the ratio of severe/mean-mild UGIB being net in variceal UGIB (63/36) versus non-variceal UGIB (185/179).
7. EDS is the elective method of etiological diagnosis and hemostasis - it was performed in 50.2% of cases.
8. The management of UGIB is a complex, conservative and surgical medical, the weight of the two therapeutic attitudes depending on the etiopathogenic type of hemorrhage, the causal lesion, the severity and the evolution of the bleeding and the therapeutic response.
9. Endoscopic therapy performed in 46 patients used according to causal lesion the following therapeutic procedures: electrothermocoagulation in 21 patients (9%), elastic ligatures in 11 patients (5%), injection of adrenaline in vascular ulcers visible at 10 patients (4%) and Mallory Weiss injuries in 2 patients (1%) and 2 endoclips in bleeding ulcers (1%).
10. UGIB are still struggling with a high rate of postoperative morbidity (29.6%) and a general (12.5%) and postoperative (16.6%) mortality.

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