

## NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: CLINICAL, THERAPEUTIC AND EVOLUTION ASPECTS. COMPARISON BETWEEN A TERTIARY MEDICAL CENTER AND A MUNICIPAL HOSPITAL.

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### Abstract

Upper gastrointestinal bleeding (UGIB) is one of the most common emergencies in gastroenterology practice. In recent years, the introduction of urgent upper gastrointestinal endoscopy (UGIE) and of the treatment with proton pump inhibitors (PPIs) in high doses has resulted in an improvement of the treatment outcome in patients with UGIB, but without a significant improvement in mortality rates.

In our study we compared the epidemiological, clinical, therapeutic, and prognostic aspects in patients with non-variceal UGIB admitted over a period of one year in a tertiary center where urgent UGIE is a routine procedure and in a municipal hospital where UGIE with endoscopic hemostasis is not available.

Patients admitted to the tertiary medical center had more clinical and endoscopic severity factors compared to those from the municipal hospital: they were older, with more frequent intake of NSAIDs, several comorbidities, some of them severe, and more severe posthemorrhagic anemia. The endoscopic examination revealed that active bleeding and stigmata of recent hemorrhage were more frequent in these patients. Urgent UGIE and, where necessary because of lesions, endoscopic hemostasis were performed in most of these patients.

Patients admitted to the municipal hospital were treated more frequently with high-dose intravenous PPIs.

Patients undergoing urgent UGIE and endoscopic therapy had a shorter duration of hospitalization. However, there were no differences regarding the need for surgery or mortality rates. The results of our study are consistent with the literature.

**Keywords:** non-variceal UGIB, emergency endoscopy, gastric antisecretory

### Introduction

UGIB is one of the most common emergencies in gastroenterology. The management of patients with UGIB has changed radically in recent decades with the introduction of gastric antisecretory therapy (H<sub>2</sub> receptor antagonists, in particular PPIs) and therapeutic endoscopy. However, despite progress in the treatment of patients with UGIB, mortality remained between 6 and 14% [1].

International consensus has attempted to regulate the approach of patients with UGIB to reduce mortality and improve costs involved in the management of these patients. Therefore, UGIE is recommended within the first 24 hours in most patients presenting with UGIB. Therapeutic endoscopy is indicated if bleeding lesions or stigmata of hemorrhage are detected. This must be associated with high-dose PPI therapy first administered intravenously (72h) and then orally [2].

Unfortunately, according to the latest study conducted by the Romanian Society of Endoscopy, urgent endoscopy and endoscopic homeostasis are not performed in

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most hospitals in Romania due to both the lack of material and equipment and the insufficient medical personnel necessary to ensure the number of doctors on duty.

### Aim.

This study aims to compare the evolution of patients with non-variceal UGIB hospitalized in two reference centers: a tertiary medical center that performs urgent upper gastrointestinal endoscopy and endoscopic hemostasis and a municipal hospital that does not perform urgent UGIE and has no facilities for performing endoscopic hemostasis.

Patients with non-variceal UGIB admitted to the two units were compared both in terms of clinical and paraclinical parameters and in terms of therapeutic approaches, the duration of hospitalization and mortality.

### Materials and methods

*Study design.* Records of all patients with UGIB admitted to the Municipal Hospital "Dr. Al. Simionescu" in Hunedoara, and the Third Medical Clinic in Cluj-Napoca in 2010 were retrospectively selected from the database.

*Patients.* The study included all the patients who presented in 2010 in the two centers mentioned above: Third Medical Clinic in Cluj (where there is a permanent number of doctors on duty to perform endoscopy) and the Municipal Hospital "Dr. Al. Simionescu" in Hunedoara (where there is an endoscopy department but no organized emergency endoscopy service) and in which the diagnosis of non-variceal UGIB was determined by means of UGIE. Patients who did not undergo UGIE and those for whom UGIE had determined that the sources of bleeding were gastric or esophageal varices or portal hypertensive gastropathy were excluded.

Patients with non-variceal UGIB were divided into

two groups according to the hospital where they were admitted: Cluj group (Group 1) and Hunedoara group (Group 2).

Patients in both groups were characterized based on demographic data and some clinical and paraclinical parameters. Patients were analyzed by gender and age.

*Clinical parameters.* Patients in the study were followed according to the type of bleeding (hematemesis, melena, haematemesis in association with melaena), the presence of hematemesis being an index of severity, the presence of shock, the existence and the type of comorbidities, and the presence of risk factors: treatment with NSAIDs, anticoagulants, antiplatelet agents and the occurrence of rebleeding.

*Laboratory data.* Laboratory data provided information on hemoglobin levels and coagulation parameters. Based on hemoglobin levels, patients were divided into the following groups: non-anemic, with mild anemia (Hb >10g/dl), with moderate anemia (Hb=7-10g/dl) and with severe anemia (Hb <7g/dl).

*Upper gastrointestinal endoscopy.* Urgent UGIE was considered the endoscopy performed within the first 24 hours of patient presentation. Patients were characterized by the following parameters: undergoing or not urgent UGIE, endoscopic diagnosis of the lesions, Forrest classification, undergoing or not endoscopic hemostasis.

*Drug therapy.* We tracked the type of antisecretory drugs used (H2 receptor antagonists, PPIs or combinations), the dosage and the route of administration (intravenous/oral /combination).

*The need for transfusion.* We analyzed the number of patients in the studied groups requiring transfusions, the type of transfusion (blood, plasma, platelets) and the number of units transfused.

**Table 1.** Analysis of demographic and clinical parameters and the transfusion requirements in the two groups, n (%)

Parameters	Tertiary medicabcenter (group 1)	Municipal hospital (group 2)	p	
Gender (male)	248(64.9)	39(67.2)	0.8	
Age	63(54; 74) years	62(46; 71) years	0.1	
comorbidities	gastroenterologic	90(23.6)	4(6.9)	0.007
	cardiovascular	203(53.1)	22(37.9)	0.04
	metabolic	58(15.2)	3(5.2)	0.06
	renal	3(7.9)	6(10.3)	0.4
	neuropsychiatric	75(19.6)	2(3.4)	0.005
	digestive/extradigestive neoplasias	18(4.7)/18(4.7)	2(3.4)/3(5.2)	1/0.7
Consumption of NSAIDs	61(16)	3(5.2)	0.04	
Hematemesis (±melena)/ melena	232(60.7)/150(39.3)	23(39.7)/35(60.3)	0.004	
Shock during admission	8(2.1)	0(0)	0.55	
anemia	non-anemic	64(16.8)	13(22.4)	<0.0001
	mild	65(17)	16(27.6)	
	moderate	151(39.5)	21(36.2)	
	severe	102(26.7)	8(13.8)	
Blood/plasma transfusion	160(41.9)/67(17.5)	18(31)/0(0)	0.1/0.001	

**Table 2.** Analysis of endoscopic parameters in the two groups, n (%)

Urgent UGIE				
	376(98.4)	27(46.6)	<0,0001	
Forrest Classification	I (A/B)	10/82(2.7/22.1)	0/5(0.0/5.7)	<0,0001
	II (A/B/C)	54/37/36(14.6/10/9.7)	4/4/2(7.4/7.4/3.7)	
	III	152(41)	39(72.2)	
	PPIs/PPIs 80mg	247(63.4)/52(13.6)	37(63.8)/15(25.9)	0.01
	intravenous/oral/combined	134(35.1)/142(37.2)/106(27.7)	39(67.2)/18(31)/1(1.8)	<0,0001

**Duration of hospitalization.** An important parameter was the duration of hospitalization for the patients in the two groups. We have also analyzed the need for and the duration of hospitalization in the intensive care units for the patients in the study.

**Surgical treatment.** We have compared the two groups of patients in terms of the need for surgery in the treatment of upper gastrointestinal bleeding.

**Mortality.** Patients in the 2 groups were compared in terms of the number and causes of death occurring during hospitalization in the two reference medical centers.

#### Statistical analysis.

Statistical analysis was performed using SPSS version 20.

Data were labeled as quantitative or nominal. Normality of distribution for quantitative variables was tested with Kolmogorov-Smirnov test. Differences between groups regarding a quantitative variable were assessed by using the Mann-Whitney test. Differences of percentage between groups regarding nominal data were assessed by chi-square test. The level of statistical significance was set at  $p < 0.05$ .

## Results

Group 1 included 382 patients with non-variceal UGIB and group 2 included 58 patients.

The main demographic, clinical and evolutive aspects of the two groups are shown in the table.

The predominance of males was obvious in both groups. There were no significant differences between the municipalities regarding male/female distribution ( $p = 0.8$ ).

Although patients examined in Cluj-Napoca in 2010 were older than those examined in Hunedoara, the difference was not significant ( $p = 0.1$ ). The age group consisting of patients over 80 years revealed statistically significant differences between the two groups ( $p = 0.04$ ).

Hematemesis was more frequent in the patients in group 1 than in those in group 2 who showed predominant melena associated with UGIB.

Rebleeding rate in group 1 (17.5%) was significantly higher than in group 2 (3.44%) ( $p = 0.01$ ).

Patients in group 1 had a significantly higher prevalence of comorbidities compared with those in group 2.

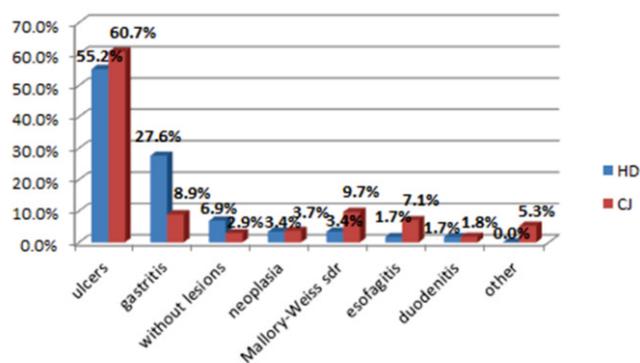
In our study, there were significantly more patients treated with NSAIDs in group 1 than in group 2 ( $p = 0.04$ ).

Patients in the group from Cluj had a higher percentage of moderate or severe anemia than those in the group from Hunedoara ( $p < 0.001$ ).

Among the main causes of non-variceal UGIB, we found statistically significant differences only in the case of erosive gastritis, which were significantly more frequent in group 2 ( $p = 0.0001$ ).

Emergency endoscopy was significantly more frequent in patients in group 1 who had more severe Forrest classes (IA, IB, IIA) compared with patients in group 2 who mainly had lesions without stigmata of recent hemorrhage (III) ( $p < 0.001$ ). Therapeutic endoscopy was performed in

45.1% of the patients in group 1, while it could not be performed in patients in group 2 ( $p < 0.001$ ).



**Figure 1.** The main causes of non-variceal UGIB in the two groups

Patients in group 1 received oral or combined antisecretory therapy more frequently than patients in group 2 who mostly received injected antisecretory therapy ( $p < 0.001$ ). Patients in group 2 were treated more frequently with PPIs compared with those in group 1 ( $p = 0.04$ ). Among patients treated with PPIs, those in group 2 received higher doses of PPIs (80mg) than patients in group 1 ( $p = 0.01$ ).

Patients who received transfusions of whole blood were older (67: 56, 76 years) than those who did not receive transfusion (61: 49, 72 years) ( $p < 0.001$ ).

The number of days of hospital stay in patients from Cluj (7: 4, 9 days) differed significantly from that of patients from Hunedoara (9: 7, 12 days) ( $p < 0.001$ ).

There was no significant difference between municipalities in the number of surgeries ( $p = 0.2$ ) or mortality ( $p = 1$ ).

## Discussion

The distribution of male and female patients in the groups studied was consistent with the data in literature, 2: 1 [3].

The group of patients in the tertiary medical center had a significantly higher percentage of patients aged over 80 years and of digestive, cardiovascular and neuropsychiatric comorbidities than the group of patients in the municipal hospital. Among digestive comorbidities the most frequent was liver cirrhosis of different causes. Studies have shown that the presence of cirrhosis in patients with non-variceal UGIB is an aggravating factor associated with increased mortality [4, 5].

There were more patients taking NSAIDs in the tertiary medical center. Various studies show that the use of NSAIDs does not worsen the prognosis of patients with UGIB [6].

UGIE was performed in the first 24 hours in a significantly larger number of patients in group 1 compared to group 2. Patients in the tertiary medical center had more frequent lesions with active bleeding or stigmata of recent

hemorrhage than patients in the municipal medical center, g the effects of urgent UGIE on the evolution of UGIB [2].which is explained by the fact that the latter underwent endoscopy after a few days of antisecretory therapy and by the fact that there were more patients with clinical signs of severe upper gastrointestinal bleeding (hematemesis, hematemesis and melena, severe anemia, etc.) in the tertiary medical center.

A meta-analysis carried out on 6 studies on the role of gastric antisecretory therapy showed that pre-endoscopic antisecretory therapy had significantly decreased the amount of lesions with high risk of rebleeding assessed by endoscopy, as well as the requirements for endoscopic hemostasis [7, 8].

Patients in both groups received antisecretory therapy in lower doses than those recommended by international consensus. There are studies showing that the use of lower doses (i.e. 2x40mg/day intravenous PPIs) than recommended have resulted in an increased length of hospital stay, number of surgical operations or mortality [9]. However, only few of the patients in our study were treated with 80mg PPIs/day, the rest receiving standard doses of gastric antisecretory therapy. The 80mg/day dose of PPIs was significantly more frequent in patients in the municipal hospital compared to those in the tertiary center.

Lower doses of PPIs and the route of administration (oral or intermittent intravenous) used in patients in our study might explain the higher rebleeding rate (17.5%) recorded in group 1 compared to that reported in the literature (4% and 6.7%, respectively) [2, 10].

Rebleeding rate recorded in patients in group 2 was 3.44%. Rebleeding rate difference between the two groups could be attributed to several factors: predominance of Forrest III lesions in patients in group 2, drug therapy consisting of intravenous and higher doses of PPIs in most cases in group 2, more frequent association of liver cirrhosis and severe anemia in patients in group 1 - disorders described in the literature as risk factors for rebleeding [11].

The number of surgical interventions in the treatment of UGIB and mortality did not differ between the two medical centers. Mortality rates recorded in our study were lower than those reported in the literature [1].

Duration of hospitalization was shorter in patients in the group undergoing urgent UGIE. Decreased length of hospital stay was also noted in other studies assessing the effects of urgent UGIE on the evolution of UGIB [2].

### Conclusions

The tertiary medical center with a permanent number of doctors on duty to perform emergency endoscopy deals with severe upper gastrointestinal bleeding cases. This explains the frequent rebleeding and mortality similar to the results obtained in the municipal hospital, despite the fact that most patients underwent urgent UGIE and those with

active bleeding or stigmata of recent bleeding underwent therapeutic endoscopy.

The correct administration of intravenous PPI therapy ompared with those admitted to the municipal hospital.can at least partially compensate for the lack of urgent UGIE and therapeutic endoscopy.

Patients who underwent urgent UGIE had fewer hospital days, but showed no differences in the need for surgery or mortality compared with those admitted to the municipal hospital.

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