RISK FACTORS FOR THE NEGATIVE COURSE OF GASTRODUODENAL GASTROINTESTINAL BLEEDING IN OBESE PATIENTS

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Summary

Obesity affects 18% of adults in Ukraine, which is one of the highest rates on the European continent. Treating gastrointestinal ulcer bleeding in obese patients is challenging due to 75% of them are taking at list one ulcerogenic or blood-thinning medications, and 25% use three or more because comorbidities. The problem of treating and predicting the outcomes of ulcerative bleeding in such patients is insufficiently studied.

This study aimed to assess treatment outcomes for acute ulcerative bleeding in sever obese patients, evaluate the effects of age and medication use, and compare these with outcomes in normal-weight patients.

To achieve this goal, a retrospective analysis included 82 sever obese and 282 normal-weight patients, focusing on early recurrences and mortality.

The study found that in obese patients under the age of 40, the mortality rate was more than three times higher (7.3%) compared to patients of normal weight (2.1%) (p – 0.0296). However, after the age of 40, no statistically significant difference in mortality was confirmed between the study groups (8.5% and 4.9%, respectively, p- 0.2864). Additionally, no increased risk of early rebleeding was observed in patients using non steroid anti inflammatory drugs or and/or drugs, affecting the rheological or coagulation properties of the blood (12.2% vs. 5%, p = 0.2527).

Thus, based on the obtained data, in Ukraine young age and obesity are risk factors for poor prognosis in treating gastrointestinal bleeding due to limited use of medications for comorbidities and resulting homeostasis issues. Despite this, they do not increase early rebleeding. The study suggests revising treatment strategies for young obese patients.

Key words: peptic ulcer disease, obesity, gastrointestinal bleeding.

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1. Introduction

The prevalence of obesity among the adult population in Ukraine is 18%, one of the highest rates in Europe. Treating patients with both gastrointestinal ulcer bleeding and obesity presents challenges, as by adulthood, 75% of these patients take at least one ulcerogenic

or blood-thinning medication, and 25% use three or more due to obesity-related conditions. The management and outcomes of ulcerative bleeding in such patients remain underexplored.

In Ukraine, the prevalence of obesity continues to rise, reaching 18% among adults and 8.7% among children by 2018 *(Biales, I. 2017), (Hu, 2009)*. The situation is further complicated by the fact that around 70% of such patients regularly take either nonsteroidal anti-inflammatory drugs (NSAIDs) or medications that affect blood coagulation (antiplatelet agents) to treat comorbid conditions caused by obesity *(Hu, 2009), (Lushchak, 2023)*. This, in turn, initiates the development of ulcerative bleeding, increases the risk of recurrence *(Lushchak, 2023)*, *(Peifer, S., 2020),* and impacts mortality rates *(Phelps, 2024, March 16), (Ren, Q., 2022)*. The exact frequency of ulcerative bleeding among obese patients in Ukraine is not well-documented, nor are there any specific data on mortality rates due to bleeding in obese patients.

The aim of the study is to evaluate the outcomes of combined treatment of acute ulcerative bleeding in obese patients, analyze the impact of age and the use of oral non-steroidal anti-inflammatory drugs, anticoagulants, and antiplatelet agents on the unfavorable course of the disease, and compare the treatment outcomes of obese patients with those of patients of normal weight.

A retrospective comparative analysis of clinical data on the treatment outcomes of early recurrences and mortality from gastrointestinal bleeding was conducted in 82 patients with morbid obesity and 282 patients with normal weight.

Objective. To evaluate treatment outcomes and identify negative prognostic factors for fatal outcomes in peptic and acute stress ulcer bleeding in obese patients. Additionally, to compare the obtained data with the treatment results of patients with normal weight.

2. Materials and Methods

The treatment data of 364 patients with gastric and duodenal ulcer bleeding, who were treated at the Department of Minimally Invasive Surgery at Kyiv City Clinical Hospital No. 7 (Kyiv City State Administration) and the Kyiv Regional Clinical Hospital No. 1 (Kyiv Regional Health Administration) from 2015 to 2023, were analyzed. The relationship between age and the use of medications for treating comorbidities associated with obesity, as well as the frequency of bleeding, recurrences, and mortality, was evaluated. Based on body mass index (BMI), the patients were divided into two groups: a control group with a BMI ≤ 25 kg/m² – 282 patients, and a study group – 82 patients with a BMI ≥ 30 kg/m². Both groups were further divided into six age categories: 18-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and a group of patients aged 70 years and older.

The effect of the use of oral NSAIDs (nimesulide, ibuprofen) and/or medications affecting blood coagulation or rheology (acetylsalicylic acid, clopidogrel) on treatment outcomes was also assessed. NSAID and/or antiplatelet use was observed in 101 patients (35.8%) in the control group and 49 patients (59.7%) in the study group ($p = 0.0001$).

Inclusion Criteria: Peptic ulcer disease complicated by bleeding (Forrest I or II), acute and stress ulcers complicated by active bleeding.

Exclusion Criteria: Gastric cancer, bleeding GIST tumors, bleeding from esophageal varices, Mallory-Weiss syndrome, and Dieulafoy's ulcers, BMI between 25 and 30 kg/m² (overweight).

The patients provided written informed consent to participate in the study, which was approved by the Bioethics Committee of the National Health University of Ukraine named after P. L. Shupyk. Norms of the "WMA Declaration of Helsinki" – paragraphs 7. 10. 12, 13, Medical

research is subject to ethical standards that promote and ensure respect for all human subjects and protect health and their rights.

Data processing. For statistical analysis, the free application GraphPad was used. Categorical data were calculated using Fisher's exact test, and continuous data using the t-test. A p-value of less than 0.05 was considered statistically significant.

3. Research Results

Among patients without obesity, the average age was 59.8 years, with a median of 62 years, while in the group of individuals with obesity, the average age was 46.5 years, with a median of 44 years. Accordingly, bleeding in patients with obesity occurs, on average, 16 years earlier. (Table 1).

Table 1

Distribution of Peptic Gastrointestinal Bleeding by Age Groups.

Age	Control Group 282		Study Group 82	
	BMI ≤ 25 kg/м² n (%)		BMI ≥ 30 kg/м² n (%)	
	181 (64,2%)	101 (35,8%) + NSAIDs/ACMs	33 (40,2%)	49 (59,8%) + NSAIDs/ACMs
≤ 29	20 (11%)	**10 (9,9%)#**	2 (6,1%)	**10 (20,4%)#**
30-39	32 (17,7%)	**17 (16,8%)#**	4 (12,1%)	**16 (32,7%)#**
40-49	42 (23,2%)	14 (14,1%)	9 (27,3%)#	12 (24,5%)
50-59	49 (27,1%)	25 (25,3%)	9 (27,3%)	5 (10,2%)
60-69	33 (18,2%)	28 (28,3%)#	8 (24,2%)#	5 (10,2%)
≥70	5 (2,8%)	7 (6,6%)	1 (3%)	1 (2%)

– statistically significant difference (p≤0.05) compared to the group not taking medications.

In the group of patients aged 18 to 39 with obesity and NSAIDs/antiplatelet therapy, the number of bleeding episodes was 26 cases (53%), while in the group with normal weight and NSAIDs/antiplatelet therapy, it was 27 cases (26.7%) (p = 0.003). In other age categories, the differences were not statistically significant.

The overall rate of recurrent bleeding was not statistically different, with 12.2% in the study group and 5% in the control group (p = 0.2564). The use of NSAIDs and/or antiplatelet agents in both groups did not influence early bleeding recurrence, with 14.3% versus 6.9% (p = 0.291) and 6.9% versus 3.8%, respectively (p = 0.4236).

Overall mortality was higher in the obesity group at 7.3%, compared to 2.1% in the normal weight group (p = 0.02). The use of NSAIDs and/or antiplatelet agents affected mortality rates, with 10% in the obesity group and 1.9% in the normal weight group (p = 0.04). In the subgroups without NSAID and/or antiplatelet use, the rates were 3% and 2.2%, respectively (p = 0.3922).

Thus, the use of medications for the treatment of comorbid conditions does not increase the risk of early recurrent bleeding but does increase the risk of fatal outcomes in patients with obesity. An important aspect of the study is that mortality in the normal weight group was accompanied by early recurrent bleeding in all cases, while no such trend was observed in the obesity group. This can be explained by the acute decompensation of comorbid conditions and the lack of compensatory resistance in the affected systems.

Table 2

Indicators of Recurrent Bleeding and Mortality among Study Groups.

Age	Control Group (N = 282)				Study Group (N = 82)			
	BMI ≤ 25 kg/м² n (%)				BMI ≥ 30 kg/м² n (%)			
	n (181)		n (101) NSAIDs/ACMs		n (33)		n (49) NSAIDs/ACMs	
	Recurrent Bleeding	Mortality	Recurrent Bleeding	Mortality	Recurrent Bleeding	Mortality	Recurrent Bleeding	Mortality
≤ 29	0 (0,6%)	0	1(1%)	0	0	0	2(4,1%)	1(2%)
30-39	1 (0,6%)	0	0(0%)	0	1(1,9%)	1(3%)	3(6,1%)	1(2%)
40-49	0	1(0,6%)	1(1%)	0	2(5,1%)	0	1(2%)	1(2%)
50-59	3(1,7%)	0	2(2%)	0	0	0	1(2%)	0
60-69	2(1,3%)	1(0,6%)	2(2%)	2(2%)	0	0	0	2(4%)
≥ 70	1(0,6%)	2(1,1%)	1(1%)	0	0	0	0	0
Total	7(3,8%)	4(2,2%)	7(6,9%)	**2(1,9%)#**	3(9,1%)	1 (3%)	7(14,3%)	**5(10%)#**

– p ≤ 0,05

+ – NSAIDs/ACMs

4. Discussion

The mortality rate due to gastroduodenal bleeding caused by peptic ulcer disease, despite the progress made in medical treatment over the past three decades, has remained largely unchanged and still ranges between 6-12% *(Ren, Q., 2022)*.

The multifactorial nature of this condition is partly due to the proven association between obesity and peptic ulcer disease *(van Lerdam, M. E. 2008)*, which contradicts the common notion that "a good mill grinds well," implying that for seamless nutrient translocation, leading to weight gain, the digestive organs must remain uncompromised. However, the situation is significantly complicated by comorbidities caused by obesity (musculoskeletal and cardiovascular diseases), which often require the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or medications that affect blood rheology and coagulation. Considering that 70% of obese patients take at least one of these medications, and 25% use three or more, such patients should be preemptively classified as being at high risk of mortality. Our study confirmed, at the local level, the validity of the hypothesis that patients with peptic gastrointestinal bleeding combined with obesity have a higher mortality rate.

Another factor, unfortunately perceived by many physicians as a positive prognostic indicator, is young age. The logic of predicting better outcomes in younger patients, due to a supposedly more stable homeostasis and therefore lower mortality risk, does not hold true. Unfortunately, reality shows the opposite: young patients often lack well-developed adaptive mechanisms, and the reactivity of their systems plays a negative role when it comes to sudden homeostatic changes caused by bleeding. Therefore, not only obesity but also the patient's age plays a critical role.

Thus, in patients with active peptic bleeding, young age, combined with obesity and the use of NSAIDs and/or antiplatelet agents, is a potential risk factor for fatal outcomes and requires earlier application of both therapeutic (urgent endoscopy) and surgical methods for long-term bleeding control (suturing, resection, etc.). In cases where the ulcer is located in the antral or pyloric region, bariatric bypass surgery may be considered for treating both the bleeding and the underlying obesity.

The small sample size and the limitations in patient selection in this retrospective study call for further analysis of this issue.

5. Conclusions

1. In obese patients under the age of 40, ulcerative gastrointestinal bleeding associated with the use of oral anti-inflammatory drugs or medications affecting blood rheology or coagulation is a risk factor for a fatal outcome compared to patients of normal weight (7.3% and 2.1%, respectively, p- 0.2864).
2. The incidence of early recurrent bleeding does not differ across age groups.
3. The use of non-steroidal anti-inflammatory drugs, oral anticoagulants, and antiplatelet agents is not a risk factor and does not increase the incidence of early recurrent bleeding.

References

1. Biales, I. (2017). Recent Advances in the Treatment of Ulcer Bleeding. F1000Res, 6, 1763. http://doi:10.12688/f1000research.11286.1.
2. Hu, D. P., Zhang, W., Bansback, N., et al. (2009). Prevalence of comorbidities associated with obesity and overweight: A systematic review and meta-analysis. BMC Public Health, 9, 88. http://doi:10.1186/1471-2458-9-88.
3. Lushchak, V. I., Kovasa, M., Abrat, O. B., Mykytyn, T. V., Tverdokhlib, I. Z., Strey, K. B., & Semchyshyn, H. R. (2023, September 25). Risks of obesity and diabetes development in the population of Ivano-Frankivsk region of Ukraine. EXCLI Journal, 22, 1047-1054. http://doi:10.17179/excli2023-6296.
4. Peifer, S., Pelton, M., Kini, L., Kwon, Y. G., Ofosu-Okromah, R., Acharya, Y., Chinchilli, V. M., Soybel, D. I., Oh, J. S., & Sentongo, P. (2020, February 17). Risk factors for perioperative mortality from complicated peptic ulcer disease in Africa: A systematic review and meta-analysis. BMJ Open Gastroenterol, 7(1), e000350. http://doi:10.1136/bmjgast-2019-000350.
5. Phelps, N. H., et al. (2024, March 16). Worldwide trends in underweight and obesity from 1990 to 2022: A pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. The Lancet, 403(10431), 1027-1050. http://doi:10.1016/S0140-6736(23)02750-2.
6. Ren, Q., Peng, K., Li, B., Zheng, Y., Guo, Q., Ji, R., Chen, Z., Wang, Y., & Zhou, Y. (2022). Obesity, peptic ulcer disease and metabolic status in the Wuwei Cohort of northwest China: A cross-sectional study. Asia Pac J Clin Nutr, 31(2), 294-304. http://doi:10.6133/apjcn.202206_31(2).0015. PMID: 35766565.
7. van Lerdam, M. E. (2008). Epidemiology of Upper Gastrointestinal Bleeding. Best Pract Res Clin Gastroenterol, 22(2), 209-224. http://doi:10.1016/j.bpg.2007.10.011.
8. Yaratakha, K., Talemal, L., Monaghan, B. V., Yu, D., Lu, H., & Poggio, J. (2023, December 29). Seasonal and geographical variations in peptic ulcer disease and related complications in the United States of America. J Res Health Sci, 23(4), e00595. http://doi:10.34172/jrhs.2023.130.
9. Yakovenko, V., Henn, L., Bettendorf, M., Zelinska, N., Solovyiova, H., Hofmann, H. F., & Gruhlih-Henn, Y. (2019, September 3). Risk factors for overweight and obesity in children in Ukraine and Germany. J Clin Res Pediatr Endocrinol, 11(3), 247-252. http://doi:10.4274/jcrpe.galenos.2019.2018.0157.
10. Ye, Z., Reyntjens-Blaser, A., & Lytvyn, L., et al. (2020, January 6). Clinical Guidelines for the Prevention of Gastrointestinal Bleeding in Critically Ill Patients. BMJ, 368, l6722. http://doi:10.1136/bmj.l6722. PMID: 31907223.