Journal of SURGICAL ARTS
CERRAHİ SANATLAR DERGİSİ
"A word can save a life"
jsurgarts.com
1308-0709

Clinical Practice Study

What determines mortality and morbidity rates in non-variceal, non-malignant upper gastrointestinal bleeding treated with urgent surgical operation?

Acil cerrahi operasyonla tedavi edilen varis dışı, malign olmayan üst gastrointestinal kanamalarda mortalite ve morbidite oranlarını ne belirler?

Haldun Kar, Necat Cin, Yasin Peker, Evren Durak, Halis Bağ, Cengiz Tavusbay, Fevzi Cengiz

İzmir Katip Celebi University, Ataturk Training and Research Hospital, Department of General Surgery, İzmir, Türkiye

Corresponding address: Dr. Haldun Kar, haldunkar@hotmail.com

How to cite: Kar H, Cin N, Peker Y, Durak E, Bağ H, Tavusbay C, Cengiz F. What determines mortality and morbidity rates in non-variceal, non-malignant upper gastrointestinal bleeding treated with urgent surgical operation. J Surg Arts 2022;15(1):18-24.

Received: 22.06.2022 Accepted: 26.07.2022

ABSTRACT

Despite the advances in treatment modalities, upper gastrointestinal (GI) bleeding is still a significant health issue. We aimed to assess the risk factors on mortality and morbidity rates in the patients that underwent surgery due to non-variceal and non-malignant bleeding from upper gastrointestinal tract.

We retrospectively examined records of 127 cases with non-variceal, non-malignant acute upper GI bleeding in the our University Hospital, General Surgery Clinic between January 1996 and December 2014.

Median age was 60 (16-88) years. The most frequent cause of upper gastrointestinal bleeding was duodenal ulcer observed in 93 (73.23%) patients. The most frequent presenting complaint was melena and hematemesis observed in 66 (52%) patients. Primary suturing, bilateral truncal vagotomy and pyloroplasty were the most frequent surgical procedure performed in 79 (62.20%) patients. There were 23 (27.71%) mortalities.

Statistically, mortality and morbidity rates were found to be significantly associated with female sex (OR 6.517, 95% CI 1.559 to 27.238, p=0.010), hematemesis at presentation (OR 10.378, 95% CI 1.889 to 57.005, p=0.007), presence of comorbidity (OR 14.131, 95% CI 2.197 to 90.904, p=0.005), and high urea levels (OR 0.937, 95% CI 0.952 to 0.994, p=0.013) prior to operation.

In conclusion, although surgical treatment is the most effective method to control active bleeding from the ulcer and to prevent recurrence, it is often associated with high mortality and morbidity risk due to comorbidities; therefore it should be spared for cases for whom endoscopic and interventional radiologic treatment modalities is unsuccessful.

Keywords: Gastrointestinal, bleeding, upper, surgical treatment, urgent.

ÖZET

Tedavi modalitelerindeki gelişmelere rağmen üst gastrointestinal (GI) kanamalar hala önemli bir sağlık sorunudur. Üst gastrointestinal sistemden varis dışı ve malign olmayan kanama nedeniyle ameliyat edilen hastalarda mortalite ve morbidite oranları etkileyen risk faktörlerini değerlendirmeyi amaçladık.

Üniversite Hastanemiz Genel Cerrahi Kliniğinde varis dışı, malign olmayan akut üst GİS kanaması olan 127 olgunun kayıtları geriye dönük olarak incelendi.

Medyan yaş 60 (16-88) idi. Üst gastrointestinal kanamanın en sık nedeni 93 (%73.23) hastada görülen duodenum ülseri idi. En sık başvuru şikayeti 66 (%52) hastada görülen melena ve hematemez idi. 79 (%62.20) hastada en sık uygulanan cerrahi işlem primer sütür, bilateral trunkal vagotomi ve piloroplasti idi. 23 (%27.71) hastada exitus gelişdi. İstatistiksel olarak, mortalite ve morbidite oranlarının kadın cinsiyet (OR 6.517, %95 CI 1.559 ila 27.238, p=0.010), başvuru sırasındaki hematemez (OR 10.378, %95 CI 1.889 ila 57.005, p=0.007), komorbidite varlığı (OR 14.131, %95 CI 2.197 ila 90.904, p=0.005) ve operasyondan önceki yüksek üre seviyeleri (OR 0.937, %95 CI 0.952 ila 0.994, p=0.013) ile anlamlı şekilde ilişkili olduğu bulundu.

Cerrahi tedavi, ülserden aktif kanamayı kontrol altına almak ve nüks kanamayı önlemek için en etkili yöntem olmasına karşın, sıklıkla eşlik eden komorbiditeler nedeniyle yüksek mortalite ve morbidite riski ile ilişkilidir; bu nedenle endoskopik ve girişimsel radyolojik tedavi yöntemlerinin başarısız olduğu olgularda tercih edilmelidir.

Anahtar kelimeler: Gastrointestinal, kanama, üst, cerrahi tedavi, acil.

INTRODUCTION

Upper gastrointestinal (GI) bleeding is characterized as bleeding proximal to the ligament of Treitz. The clinical presentation varies according to the intensity of bleeding; occult bleeding, profuse melena or hematemesis, and hemorrhagic shock (1). Fifty to seventy percent of all gastrointestinal bleedings occur in the upper gastrointestinal tract, and over half of all cases are caused by ulcers that develop because of peptic activity (2,3). Approximately 70% of acute non-variceal bleedings stop spontaneously, 10% bleeds persistently, and up to 20% rebleeds in the initial 24-72 hours (3).

Although most authors suggest that upper GI bleeding ceases spontaneously in 80% of the cases, the remaining 20% of the cases face high mortality risk due to ongoing bleeding (4). Mortality rates of the surgery performed in emergencies is 10 to 50% (5). Botianu et al. express that most deaths do not result from failure of hemostasis, either medical or surgical, but mainly from comorbidities, poorly tolerated blood loss and resultant complications (6).

Over the most recent decade, the requirement for emergent surgery in upper GI bleeding has diminished significantly, yet mortality has stayed unchanged (6). The reasons responsible for this are speculated as longer lifespan of patients owing to advances in medical facilities, higher rate of comorbidities and widespread use of nonsteroidal anti-inflammatory drugs (NSAID) (7). Despite the advances in treatment modalities, upper GI bleeding is still a significant life-threatening health issue. In this study, we analyzed the risk factors leading to mortality and morbidity in patients not responding to endoscopic management and who underwent surgery for non-variceal and non-malignant bleeding from upper gastrointestinal tract.

MATERIAL and METHOD

In this study, we retrospectively examined records of 127 cases with non-variceal, non-malignant acute upper GI bleeding in cases where bleeding could not be controlled with endoscopic methods and who underwent emergent operation in the xxxxx Hospital General Surgery Clinic between January 1996 and December 2014.

The study was performed in accordance with the Declaration of Helsinki for Human Research, and was approved by the institutional ethics committee (26.11.2015-231).

Patients' files were examined for age, sex, location of bleeding, etiology, use of drugs that predispose to bleeding disorders (aspirin, NSAID), signs of previous bleeding and operation, comorbidity, hematocrit and urea levels, endoscopic findings, number of blood transfusions, performed surgical procedures, postoperative complications, hospital length of stay and mortality.

For each patient, Rockall risk scoring system which aims to predict mortality and recurrent bleeding risk and consists of three non-endoscopic (age, shock, comorbidity) and two endoscopic parameters (endoscopic diagnosis and presence of endoscopic findings suggestive of recent bleeding) was calculated using preoperative findings (8). Patients with a Rockall risk score lower than 5 were categorized as the low-risk group, and those with score at or above 5 were categorized as the high-risk group. Cardiovascular diseases, respiratory system diseases, diabetes mellitus, renal failure and other miscellaneous diseases were recorded as comorbidities.

Patients presented to the emergency department of our hospital with upper GI bleeding were admitted initially to the gastroenterology unit and were monitored for hemodynamic parameters. Fluid-electrolyte administration and acid-suppressive therapy were carried out, and blood transfusion (preferably erythrocyte suspension) was administered as required. Nasogastric and Foley catheters were placed.

In the first years of the study, as soon as all patients started medical treatment, intravenous H2 receptor blockers were used as acid-suppressing therapy, followed by proton pump inhibitors (PPI). Patients with systolic blood pressure <90 mmHg, heart rate above 120/min, urine output below 30cc/hour, and cold and pale skin were considered to be in shock.

Diagnostic and therapeutic upper GI endoscopic interventions were applied to each patient presenting with GI bleeding within the first 12 or 24 hours, depending on their clinical condition at the time of admission. Endoscopists have at least three years of training and are experienced in endoscopic interventions. They work on-call basis.

Endoscopic findings were recorded based on Forrest classification, which is used for follow up and in selecting patients for endoscopic treatment. In our study, adrenaline injections were used in the endoscopic treatment of upper GI bleeding between 1996 and 2002. Whereas, between 2002 and 2014, adrenaline injection, clips and combined treatments were used.

In instances where there was no response to supportive treatment before endoscopy, or if endoscopic intervention was insufficient in terms of bleeding control, or if bleeding continued despite two consequent endoscopic interventions in low-risk patients, or if bleeding recurred after the initial endoscopic intervention in high-risk patients, patients were taken into emergent operation. Antibiotic prophylaxis was administered to all patients in the study. Laparotomy was performed using upper midline incision. Surgical procedure was determined based on the present pathology, general status of the patient and preference of the surgeon. When we finalized our study, the interventional radiology clinic had not been fully established in our hospital yet. Therefore, it did not play a role at this stage of treatment.

Statistical analysis

Statistical analysis of the data was carried out on SPSS (Statistical Package for Social Sciences) Windows 20.0 package software. Quantitative data were expressed as mean ± standard deviation. To compare categorical data across groups, cross tables were constructed, and Chi-square/Fischer exact test was performed. For numerical variables, the normality assessment was first performed using Shapiro-Wilk test. Student-t test was used for numerical data that demonstrated normal distribution, and the Mann Whitney U test was used for numerical data that did not fit into normal distribution. Logistic regression analysis was performed to determine risk factors that affect mortality and morbidity and to determine odds ratio. Statistical significance threshold was accepted as 0.05.

RESULTS

Of 127 patients included in the study, 100 (78.8%) were men and 27 (21.2%) were women. Median age was 60 (16-88) years. The most frequent cause of upper GI bleeding was duodenal ulcer observed in 93 (73.23%) patients. Table 1 shows pathologies that caused bleeding. Aspirin or NSAID use was present in 37 (29.13%) patients. Fifty-seven (44.88%) patients had a history of GI bleeding previously at least one time prior. Eighty-six (67.71%) patients had a comorbid disease and 25 (19.68%) of them had more than one comorbid disease. Respectively, 26 patients (20.4%) had hypertension, 14 (11%) diabetes mellitus, 13 (10.2%) coronary artery disease, 11 (8.6%) chronic obstructive pulmonary disease, 6 (4.7%) heart failure, 5 (3.9%) chronic renal failure, 5 (3.9%) arthritis, 4 (3.2%) cerebrovascular disease, one (0.8%) epilepsy, one Burger's disease (0.8%). The most frequent presenting complaint was melena and hematemesis observed in 66 (52%) patients. Twenty-nine (23%) patients had signs of shock. Eight of the patients did not have endoscopy reports in their files. In 7 (5.5%) patients, the bleeding site could not be detected due to blood that filled the stomach and pyloric obstruction. As of the remaining patients, 40 (31.49%) patients had Forrest 1a, 50 (39.37%) patients had Forrest 1b, 18 (14.17%) patients had Forrest 2a, 3 (2.36%) patients had Forrest 2b, and 1 (0.78%) patient had Forrest 2c endoscopic ulcer signs. Primary suturing, bilateral truncal vagotomy and pyloroplasty were the most frequent operation procedure performed in 79 (62.20%) patients. Sixty-five patients (51.2%) developed various complications during the postoperative period, and the most frequent complication were pulmonary complications and surgical site infections (Table 2).

Table 1: Patients' pathologies in etiology.

Pathologies in etiopatogenesis	**n**	**(%)**
Duodenal ulcer	93	73.23
Gastric ulcer	25	19.68
Duodenal + gastric ulcer	1	0.79
Marginal (anastomosis) ulcer	2	1.57
Erosive gastritis	1	0.79
Pancreatic cystogastrostomy bleeding	1	0.79
Dieulafoy lesion	2	1.57
Vasculer malformation	1	0.79
Papiller bleeding after ERCP	1	0.79

ERCP: Endoscopic Retrograde Cholangiopancreatography

Table 2: Postoperative complications.		
Complication	**n**	**%**
Lung complications	25	19.68
Surgical Site Infections	16	12.60
Cardiac complications	9	7.08
Anastomosis-duodenal stumph leak	5	3.94
Evisceration	4	3.14
Recurrence of Bleeding	3	2.36
Thromboembolism	2	1.58
Urinary complications	1	0.79

The mean Rockall score of the patients was 5.82 ± 1.61 (Table 3). When those patients who did not undergo endoscopy were excluded, 36 (30.26%) of the remaining 119 patients were in the low-risk group and 83 (69.74%) patients were in the high-risk group according to the Rockall scoring system. There was no mortality in the low-risk group; however, there were 23 (27.71%) mortalities in the high-risk group. 66 (51.96%) of the patients had both hematemesis and melena, 52 (40.9%) had melena, and 9 (7.08%) had hematemesis alone. The mortality rate in these groups was 25.8%, 3.8%, and 44.4%, respectively. There was a statistically significant difference between these three groups in terms of mortality rates (p<0.00).

Table 3: Univariate analysis of clinical parameters of patient with upper gastrointestinal system bleeding					
Parameters	n (%)	**Mortality** n (%)	**P-value**	**Morbidity** n (%)	**P-value**
Age			<0.78		<0.24
≤ 59	63 (49.6)	12 (19)		29 (46)	
≥60	64 (50.4)	11 (17.2)		36 (56.2)	
Gender			<0.00		<0.00
Male	100 (63.7)	13 (13)		45 (45)	
Female	27 (36.3)	10 (37)		20 (74.1)	
Comorbidities			<0.00		<0.00
No	55 (43.3)	3 (5.5)		19 (34.5)	
Yes	72 (56.7)	20 (27.8)		46 (63.9)	
Presence of			<0.00		<0.61
Melena (M)	52 (40.9)	2 (3.8)		21 (40.4)	
M + Hematemesis	66 (52)	17 (25.8)		37 (56.1)	
Hematemesis	9 (7.1)	4 (44.4)		7 (77.8)	
Blood transfusion			<0.04		<0.01
≤4 unit	24 (18.9)	1 (4.2)		7 (29.2)	
≥4 unit	103 (81.1)	22 (21.4)		58 (56.3)	
Location			<0.37		<0.60
Stomach	31 (24.4)	4 (12.9)		17 (54.8)	
Duodenum	95 (74.8)	19 (20)		47 (49.5)	
Etiology			<0.58		<0.67
Ulcer	122 (96.1)	23 (18.9)		63 (51.6)	
Other	5 (3.9)	0 (0)		2 (40)	
Drug use			<0.51		<0.71
No	90 (70.9)	15 (16.7)		47 (52.2)	
Yes	37 (29.1)	8 (21.6)		18 (48.6)	
Bleeding history			<0.43		<0.31
No	70 (55.1)	11 (15.7)		33 (47.1)	
Yes	57 (44.9)	12 (21.1)		32 (56.1)	
Shock			<0.00		<0.00
No	97 (76.4)	5 (5.2)		39 (40.2)	
Yes	29 (22.8)	18 (62.1)		25 (86.2)	
Rockall score			<0.00		<0.00
≤4	40 (31.5)	0 (0)		12 (30)	
>4	87 (68.5)	23 (26.4)		53 (60.9)	

On univariable analysis, mortality and morbidity rates were found to be significantly associated with female sex, presence of comorbidity, presence of shock signs prior to operation, Rockall score at or above 5, blood transfusions more than 4 units, low hematocrit and high urea levels prior to operation (Table 3). In the multivariant analysis, when hematemesis symptom is evaluated in the foreground 9 patients in the hematemesis group and 66 patients in the melana + hematemesis group were combined and compared with the patients in the melana group. On multivariable analysis, female sex, hematemesis at presentation, presence of comorbidity, high urea levels prior to operation emerged as significant independent predictors of mortality (Table 4).

Table 4: Multivariate analysis showing independent factors associated with upper GI bleeding.

Clinical parameters	Odd's ratio	95% Confidence interval		p value
		Lower	Upper	
Gender				
Male	-			<0.01
Female	6.517	1.559	27.238	
Age				
≤59	-			<0.06
>60	4.122	0.943	18.017	
Transfusion (unit)				
≤4	-			<0.23
>4	5.306	0.345	81.558	
Melena (M)	-			
M+ Hematemesis	10.378	1.889	57.005	<0.00
Hematocrit	1.195	0.997	1.434	<0.05
Urea	0.937	0.952	0.994	<0.01
Comorbidities				
No	-			
Yes	14.131	2.197	90.904	<0.00
*P < 0.05				

DISCUSSION

Etiology of non-variceal and non-malignant upper GI bleeding shows diversity across different countries. While the most common cause reported in western studies is gastric ulcer, the most frequent cause that we determined in our study was duodenal ulcer, which is consistent with the results of other related studies from Turkey (7,9,10). We observed 93 (73.22%) of 127 operated cases had duodenal ulcer. Enormous gastrointestinal arterial bleeding is hard to stop endoscopically, particularly from a duodenal ulcer, due to the anatomically narrow lumen and because the bleeding site is located on the posterior wall of the duodenal bulb (11,12). Wilkins et al. stated that duodenal ulcers are more likely to erode into large vessels, causing more severe bleeding (13).

Skok et al. found that among 2905 patients with upper GI bleeding, 47.7% had peptic ulcer disease, and 94.5% were receiving NSAID and salicylates (5). In our series 37 (29.13%) patients were operated after use of aspirin and NSAID; drug use was not found to be significant for morbidity ($p<0.71$) and mortality ($p< 0.51$).

Rebleeding after initial hemostasis in peptic ulcer bleeding can be life-threatening. Lu et al. stated that rebleeding was associated with increased mortality (14). Among our patients, history of previous bleeding did not have a statistically significant effect on mortality and morbidity ($p< 0.43$), ($p< 0.31$).

Comorbid disease at an advanced age is the leading cause of mortality in upper GI bleeding. Kaplan et al. reported that upper GI bleeding had a more serious course, mortality was higher in elderly patients, and even in asymptomatic patients with comorbid disease (15). Önder et al. reported that, 47.3% of the patients had comorbid disease, mainly cardiovascular system disease and faced increased mortality risk (9). In our study, 67.71% of our patients had comorbid disease, while 19.68% had more than one comorbid disease. Statistically, presence of comorbid disease was significant in increased mortality and morbidity rates ($p< 0.00$).

Mortality and morbidity are known to be high in patients with upper GI bleeding who are taken into emergent operation while in shock (9). Gralnek et al. reported that early intensive hemodynamic resuscitation of patients with acute upper GI bleeding has been shown to decrease mortality significantly (16). In our study, 29 (23%) patients were taken into surgery with signs of shock. We observed that these patients had significantly higher rates of mortality and morbidity and a longer length of hospital stay ($p< 0.00$).

The Rockall risk score, which aims to predict mortality and recurrent bleeding risk, was calculated using preoperative findings (8). Cipolletta et al.

in their series with acute upper GI bleeding reported that 21% of the patients were in low-risk group according to the Rockall risk scoring system. These patients were discharged without serious complications or mortality and with short hospital stay and minimal cost (17). In another study, no mortality was observed in the low-risk group, whereas mortality rate was 25.4% in the high-risk group (9). Similarly in our study, there was no mortality among 36 (30.26%) patients whose Rockall score was <5, whereas mortality was observed in 23 (27.71%) of 83 patients with Rockall score 5 or above. This rate was evaluated as statistically significant ($p< 0.00$).

In our study, 40 (31.49%) cases were in Forrest 1a group and 50 (39.37%) patients were in Forrest 1b group. Presence of Forrest 1a and 1b ulcers endoscopically has been found to be an independent risk factor for persistent and recurrent bleeding in many studies. The European Society of Gastrointestinal Endoscopy recommends that in patients with persistent bleeding refractory to all modalities of endoscopic hemostasis, transcatheter angiographic embolization (TAE) should be considered. Surgery is indicated when TAE is not locally available or after failed TAE (18).

Several studies stated that the risk of mortality may be higher in patients with upper GI bleeding who require numerous blood transfusions. Akıncı et al. found that number of blood transfusion was positively correlated with both the need for surgical intervention and mortality (19). The average number of blood transfusions used in our cases was 7.96 units, and mortality and morbidity increased remarkably in whom exceeded 4 units ($p< 0.04$, $p<0.01$).

Tomizawa et al. reported that blood urea nitrogen (BUN) is an important indicator of blood loss from upper gastrointestinal system, and higher serum levels of BUN was associated with severe upper gastrointestinal bleeding (20). We found that mortality and morbidity rates increased significantly as hematocrit values decreased and as urea levels increased at the time of presentation, prior to operation ($p< 0.00$, $p< 0.00$, $p< 0.00$, $p< 0.00$).

The ideal surgical procedure for bleeding gastric ulcer is distal gastric resection including the ulcered area. Thus, both the bleeding focus and the gastric lesion with the unidentified diagnosis are removed (21). The recommended routine operation for treatment of bleeding duodenal ulcer is vagotomy, pyloroplasty and suturing the bleeding site; or vagotomy, gastric resection including Billroth I and II procedures, and suturing the bleeding lesion. If these two methods fail, the gastroduodenal artery is ligated above and below the duodenum (22). Lee et al. in their review stated that, after the primary control of bleeding focus, addition of vagotomy is debatable in surgical reduction of acid secretion since 2011, and achieving cure is possible with medical treatment of H. pylori, prevention of NSAID use and administration of PPI that eliminate gastric acid production without having the side effects of vagotomy. Based on the studies conducted by general surgeons in England and the national database of United States, authors reported that despite lack of level 1 evidence, most surgeons did not perform vagotomy as part of surgery for bleeding duodenal ulcer (23). The most frequently performed surgical procedure in our study was bilateral truncal vagotomy, pyloroplasty and control of bleeding with sutures, and this procedure was performed in 79 (62.20%) of our cases.

Our study is limited by its single-center, retrospective nature. At the same time, although it is a large series in the surgical treatment of non-variceal, non-malignant upper GI bleeding, the dates of the study are past due to the fact that it included patients before TAE. On the other hand, considering the available local resources of the hospitals, we think that the results obtained in our study will contribute to the planning of the surgical treatment.

Conclusion

In conclusion, female sex, hematemesis at presentation, presence of comorbidity, high urea levels prior to operation are significant risk factors for mortality in surgical treatment of non-variceal and non-malignant bleeding from upper gastrointestinal tract. Although surgical treatment is the most effective method to control active bleeding from the ulcer and to prevent recurrence, it is often associated with high mortality and morbidity risk due to comorbidities; therefore it should be spared for cases for whom endoscopic and interventional radiologic treatment modalities is unsuccessful.

Conflict of interest: No conflict of interest and no funding source to declare

Financial Disclosure: The authors declared that they have no financial support.

Acknowledgement: We would like to thank Selin Cin M.D for her contribution and support to this manuscript.

Author Contributions: Study concept and design – N.C., Y.P., F.T.; Acquisition of data – H.K., H.B., C.T., F.C.; Analysis and/or Interpretation – F.T., E.T.; Drafting of manuscript – N.C., E.D.; Critical Reviews – N.C., Y.P.

REFERENCES

1. Biecker E. Diagnosis and therapy of non-variceal upper gastrointestinal bleeding. World J Gastrointest Pharmacol Ther 2015;6:172-182.
2. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. BMJ 2019;364: l536.
3. Telaku S, Kraja B, Qirjako G, Prifti S, Fejza H. Clinical outcomes of nonvariceal upper gastrointestinal bleeding in Kosova. Turk J Gastroenterol 2014;25:110-115.

4. Skok P, Sinkovic A. Upper gastrointestinal haemorrhage: predictive factors of in-hospital mortality in patients treated in the medical ıntensive care unit. J Int Med Res 2011;39:1016-1027.
5. Szura M, Pasternak A. Upper gastrointestinal bleeding - state of the art. Folia Med Cracov 2014;54:59-78.
6. Botianu A, Matei D, Tantau M, Acalovschi M. Mortality and need of surgical treatment in acute upper gastrointestinal bleeding: a one year study in a tertiary center with a 24 hours/day - 7 days/week endoscopy call. Has anything changed? Chirurgia (Bucur) 2013;108:312-318.
7. Özen E, Tekin F, Oruç N, Özütemiz Ö, Aydın A, Günşar F, et al. Varis dışı üst gastrointestinal sistem kanamalı 412 olgunun irdelenmesi. Akademik Gastroenteroloji Dergisi 2007;6:62-67.
8. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996;38:316-321.
9. Önder A, Kapan M, Taşkesen F, Aliosmanoğlu İ, Arıkanoğlu Z, Gül M. Cerrahi tedavi uygulanan varis-dışı ve malignite-dışı üst gastrointestinal sistem kanamalarında mortaliteyi etkileyen faktörler. Ulusal Cerrahi Dergisi 2011;27:216-221.
10. Yalçın M, Kara B, Öztürk NA, Ölmez Ş, Taşdoğan BE, Taş A. Epidemiology and Endoscopic Findings of the Patients Suffering from Upper Gastrointestinal System Bleeding. Dicle Tıp Dergisi 2016;43:73-76.
11. Higashiyama M, Suzuki H, Watanabe C, Tomita K, Komoto S, Nagao S, et al. Lethal haemorrhage from duodenal ulcer due to small pancreatic cancer. Clin J Gastroenterol 2015;8:236-239.
12. Mille M, Engelhardt T, Stier A. Bleeding Duodenal Ulcer: Strategies in High-Risk Ulcers. Visc Med 2021;37:52-62.
13. Wilkins T, Khan N, Nabh A, Schade RR. Diagnosis and management of upper gastrointestinal bleeding. Am Fam Physician 2012;85:469-476.
14. Lu M, Sun G, Zhang XL, Zhang XM, Liu QS, Huang QY, et al. Risk factors associated with mortality and increaseddrug costs in nonvariceal upper gastrointestinal bleeding. Hepatogastroenterology 2015;62:907-912.
15. Kaplan RC, Hecbert SR, Psaty BM. Risk factors for hospitalized upper or lower gastrointestinal tract bleeding in treated hypertensives. Prev Med 2002;34:455-462.
16. Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47:a1.
17. Cipolletta L, Bianco MA, Rotondano G, Marmo R, Piscopo R. Outpatient management for low-risk nonvariceal upper gastrointestinal bleeding: a randomized controlled trial. Gastrointest Endosc 2002;55:1-5.
18. Gralnek IM, Stanley AJ, Morris AJ, Camus M, Lau J, Lanas A, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. Endoscopy 2021;53:300-332.
19. Akıncı H, Yücel T, Kuroğlu E, Özkan-Gürdal S. Varis dışı üst gastrointestinal sistem kanamalarında cerrahi ve konservatif tedavi için hasta seçiminde dikkate alınacak noktalar. Ulusal Travma ve Acil Cerrahi Dergisi 2004;10:226-231.
20. Tomizawa M, Shinozaki F, Hasegawa R, Shirai Y, Motoyoshi Y, Sugiyama T, et al. Patient characteristics with high or low blood urea nitrogen in upper gastrointestinal bleeding. World J Gastroenterol 2015;21:7500-7505.
21. Samuel R, Bilal M, Tayyem O, Guturu P. Evaluation and management of non-variceal upper gastrointestinal bleeding. Dis Mon 2018;64:333-343.
22. Dango S, Beißbarth T, Weiss E, Seif Amir Hosseini A, Raddatz D, Ellenrieder V, et al. Relevance of surgery in patients with non-variceal upper gastrointestinal bleeding. Langenbecks Arch Surg 2017;402:509-519.
23. Lee CW, Sarosi GA. Emergency ulcer surgery. Surg Clin North Am 2011;91:1-12.