

Trends for Admission and Mortality in Peptic Ulcers at a Tertiary Referral Hospital During the 2017-2021 Period

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Abbreviations:

PUD: peptic ulcer disease;
H. pylori: Helicobacter pylori;
OECD: Organisation for Economic Cooperation and Development;

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Rezumat

Trendul internărilor și mortalității în ulcerul peptic într-un spital terțiar în perioada 2017-2021

Introducere: Incidența ulcerului peptic a scăzut în ultimele decenii; este posibil ca pandemia COVID-19 să fi influențat spitalizările pentru ulcer peptic. Studiul și-a propus să evalueze internările și mortalitatea pentru ulcerul peptic complicat și necomplicat și influența perioadei pandemice.

Material și Metodă: Am efectuat un studiu observațional la un centru academic terțiar, incluzând toți pacienții internați pentru ulcer peptic în perioada 2017-2021. Am evaluat internările pentru ulcere complicate și necomplicate și factorii de risc pentru mortalitate.

Rezultate: 1416 pacienți cu ulcer au fost internați în perioada 2017-2021, cu o proporție egală de ulcere gastrice și duodenale; majoritatea pacienților au fost internați pentru hemoragie (66,7%) și perforație (17,3%). Am observat o tendință de scădere a ulcerului hemoragic și a internărilor pentru ulcer necomplicat în perioada 2020-2021, în timp ce pentru perforație nu s-a înregistrat o variație semnificativă; s-a observat o scădere a mortalității în ulcerul hemoragic din 2017 până în 2020. Internările pentru ulcer hemoragic au scăzut cu 36,6% în perioada pandemiei, dar rata mortalității a fost similară. Internările pentru ulcer perforat au scăzut cu 14,4%, cu o rată a mortalității mai mare în perioada pandemiei (16,83 față de 6,73%).

PUB: peptic ulcer bleeding;
PPU: perforated peptic ulcers;
GBS: Glasgow-Blatchford score;
BBS: Baylor bleeding score;
TSC: T-score;
OR: odds ratio.

Concluzii: S-a observat o tendință de scădere a internărilor pentru ulcer hemoragic, dar nu și pentru ulcerul perforat. Internările pentru ulcer hemoragic au scăzut cu mai mult de 1/3 în perioada pandemiei, cu rată de mortalitate similară. Internările pentru ulcer perforat au scăzut cu 1/7, cu rate de mortalitate semnificativ mai mari în perioada pandemiei.

Cuvinte cheie: ulcer peptic, ulcer hemoragic, ulcer perforat, ulcer stenozant, ulcer penetrant, pandemie COVID-19

Abstract

Background: The incidence of peptic ulcers has decreased during the last decades; the COVID-19 pandemic may have influenced the peptic ulcer hospitalizations. The study aimed to assess the admissions and mortality for complicated and uncomplicated peptic ulcers and the influence of the pandemic period.

Material and Methods: We performed an observational study at a tertiary academic center, including all patients admitted for peptic ulcers between 2017-2021. We evaluated the admissions for complicated and uncomplicated ulcers and risk factors for mortality.

Results: 1416 peptic ulcers were admitted, with an equal proportion of gastric and duodenal ulcers; most patients were admitted for bleeding (66.7%), and perforation (17.3%). We noted a decreasing trend for peptic bleeding ulcer (PUB) and uncomplicated ulcer admissions during 2020-2021, while for perforation no significant variation was recorded; a decreasing mortality in PUB was noted from 2017 to 2020. Admissions for bleeding peptic ulcer have decreased by 36.6% during the pandemic period; the mortality rate was similar. Admissions for perforated peptic ulcer have decreased by 14.4%, with a higher mortality rate during the pandemic period (16.83 versus 6.73%).

Conclusions: A decreasing trend for PUB admissions but not for perforated ulcers was noted. Admissions for PUB have decreased by more than 1/3 during the pandemic period, with a similar mortality rate. Admissions for perforated peptic ulcers have decreased by 1/7, with significantly higher mortality rates during the pandemic period.

Key words: peptic ulcer, bleeding peptic ulcer, perforated peptic ulcer, stenosing peptic ulcer, penetrating peptic ulcer, COVID-19 pandemic

Introduction

Peptic ulcer disease (PUD) remains a relatively common condition worldwide, a decreasing prevalence and hospitalization were noted during the last three decades, as a result of proton pump inhibitors use and *Helicobacter pylori* (*H. pylori*) eradication in developed countries (1-11); an Organisation for Economic Cooperation and Development (OECD) study in 36 countries (12) has found a decreased mortality and also a 25.8% hospitalization reduction from 2005 to 2014 (13). The incidence of duodenal ulcer decreased more while gastric ulcer remained relatively stable (14), but the prevalence of ulcer sites differs between European and Asian countries (7).

The main complications are peptic ulcer bleeding (PUB) and perforation; proton pump inhibitor treatment and *H. pylori* eradication have markedly decreased the prevalence of

peptic ulcer obstruction and penetration, but the complications still represent 10-20% of peptic ulcer cases (15). The literature data regarding the incidence of peptic ulcer complications are contradictory, with some studies showing a stable incidence (1,9,16) or a decreased incidence for all complications (8,17,18); some studies have shown an increased incidence for PUB (16) (Table 1). Bleeding remains the most frequent complication and also the main cause of non-variceal bleeding (3), with a ratio of bleeding to perforated peptic ulcers (PPU) of approximately 6-7:1 (15,18). Interestingly, a nationwide study in the USA between 2005 and 2014 found that, despite the decreasing hospitalization for PUD, the number of surgical procedures for PUD has increased (19).

The mortality rate has decreased over time; in a study from 2002 to 2016, the 30-day mortality rate for perforation was 20% in 2002

Table 1. Prevalence of peptic ulcer complications in published studies

Study	Main findings
<i>Incidence and hospitalizations PUD</i>	
Sung et al (1)	Decreased incidence of PUD in Belgium (1994/1995 to 2002/2003), Denmark (1993 to 2002), USA (1992 to 1999), Spain (1985 to 2000). Stable trend for hospitalizations in the US (1996 to 2005), decreased hospitalization in Netherlands (1980 to 2003) with stable rate of complicated ulcer hospitalizations in men and slight decrease in women.
Chan JSH et al (11)	Decreased hospitalizations for PUD in Hong Kong (2005 to 2014)
Azhari H et al (12)	Decreased hospitalization for PUD in Europe (2000 to 2019)
Guo H et al (13)	Decreased hospitalization for PUD in the USA (2005 to 2014), with lower rate of reduction after 2008.
Tarasconi A et al (15)	Marked reduction in incidence and rates of hospitalizations over the past 3 decades, complications still encountered in 10–20% of cases.
Bardhan KD et al (16)	Admission for peptic ulcers peaked in 1982-1986, declined from 1987 to 2001.
Johnson CH et al (17)	Decreased incidence of PUD over time (2002/2006 to 2012–2016) in England
Søreide K et al (18)	Stable incidence of PUD in most countries (1975 to 2000)
Howley IW et al (19)	Hospitalizations for PUD in Maryland, USA, declined (2009 to 2014).
<i>Complications</i>	
Sung et al (1)	Stable rate of complicated ulcer hospitalizations in men and slight decrease in women in the Netherlands (1980 to 2003).
Lau JY et al (5)	No significant change for the incidence of PUB (1990 to 2000). Decreased annual incidence of perforation in Denmark and UK (1990 to 2000)
Zhang X et al (7)	The use of acetyl-salicylic acid, NSAID, systemic corticosteroids is more frequent, which may increase the incidence of peptic ulcer complications (PUB, perforation).
Malmi H et al (8)	Decreased PUD complications in Finland (2000/2002 to 2006/2008)
Quan H et al (9)	Stable trend for PUB (2004 to 2010).
Bardhan KD et al (16)	Stable incidence of perforation, PUB increased, especially in elderly.
Søreide K et al (18)	Decline in the incidence of bleeding and perforations in Sweden, Spain, and the USA (1975 to 2000)
Howley IW et al (19)	Hospitalizations with procedures increased (2009 to 2014).

PUD=Peptic Ulcer Disease; PUB=Peptic Ulcer Bleeding.

and 10.8% in 2016 (17). In a systematic review published in 2011, pooled mortality in peptic ulcer bleeding was 8.6%, and for perforated peptic ulcers was 23.5% (5), while in another review the mortality rate for perforation was estimated between 10-30% (18). The mortality rate for complicated ulcers was closely related to the type of complication and the severity of comorbidities. For peptic ulcer bleeding several scores were developed, such as Rockall, Glasgow-Blatchford score (GBS), Baylor bleeding score (BBS), Cedars-Sinai, AIM65, and T-score (TSC) (20). For perforated peptic ulcers, the Boey score (onset of perforation above 24 hours, major comorbidities, and shock before surgery) is the most used but has shown significant variability in accuracy (15,21). For all complications, the Charlson comorbidity index represents a method for estimating concomitant disease scores and mortality risk by weighing associate diseases with scores of 1, 2, or 6 and also by adding supplemental points for advanced age (20,22), although the accuracy in prognosis of peptic ulcer bleeding is moderate (20).

The COVID-19 pandemic appeared in late 2019 and early 2020, it spread worldwide in a few months (23-27), and up to September 2022 was associated with 600 million proven infections and 6 million deaths. Gastrointestinal bleeding is a rare manifestation in COVID-19 patients (23-27), but because the infection was universally widespread, a significant percent of patients with upper or lower GIB may have simultaneously COVID-19 infection during hospital admission. 27% of infected COVID-19 patients have viral RNA in the stool (24) and as a result of the high expression of ACE-2 receptor in the gut, local infection and inflammation and also gastrointestinal bleeding may appear (24,26). Other possible mechanisms of bleeding and PUD in COVID-19 infected patients (23,26) may be related to the physiological stress and hypoxemia (COVID-19 pneumonia, sepsis, multiorgan failure), high occurrence of local thrombosis (with potentially secondary mucosal ischemia or necrosis), and to the effect of medication used for treating infection (nonsteroidal anti-inflammatory

drugs, anticoagulants). The pandemic also had multiple negative consequences on the healthcare system (initial lockdown, multiple restrictions, the need for dedicated personnel and circuits for COVID-19 patients, the need for patients' triage, and the impact of patient's fears regarding hospital presentations and admissions) (25-28). These factors can be associated with potential increased mortality rates among COVID-19-positive patients with PUB and PPU, although improvements in personnel training on endoscopy and medical care, better scheduling, and enhanced organizational measures may counterbalance these effects over time.

Material and Methods

The purpose of the study was to assess the trend of hospitalization for complicated and uncomplicated peptic ulcers admitted to the Craiova County Emergency Clinical Hospital during the 2017-2021 period, as well as the influence of the pandemic period on the outcomes of the patients admitted for bleeding or perforated ulcers (mortality rate for complicated ulcers, rebleeding rate, endoscopic hemostasis failure rate, and need for transfusion in bleeding peptic ulcers, and hospitalization duration). The indicators analyzed were the proportion of complicated cases and the type of complications, length of hospital stay, as well as the need for surgery, the transfusion requirement, and the rate of hemostasis failure for bleeding ulcers.

For uncomplicated and complicated ulcers, we selected patients aged 18 years and older admitted for PUB with specific ICD-10-AM codes for gastric, duodenal, peptic, or gastrojejunal ulcer with bleeding, for perforated ulcers (including also codes for acute peritonitis, excluding peritonitis not related to peptic ulcer), and for stenosing ulcers. Informed consent was obtained from all admitted patients, and the study protocol received approval from the local ethical committee (Protocol no 11977/24 March 2020).

Two groups of analyses were performed: in the first group, we evaluated the historical

trend on the 5 years of observation regarding admissions, mortality, percent of complicated and noncomplicated ulcers, and severity of the bleeding (assessed by prognostic scores). In the second analysis, two groups of patients were identified for the study: those admitted during the period from March 2020 to December 2021 period (referred to as the pandemic period) and those admitted during the period from March 2018 to December 2019 (matched pre-pandemic period). The analysis was conducted by stratifying the patients based on risk factors for mortality, utilizing pre-endoscopic and post-endoscopic scores (such as the original and modified Glasgow-Blatchford score, Rockall and Baylor bleeding scores, AIMS65, Cedar-Sinai, and T-score) (20). The date and time of admission and endoscopy, as well as the date of discharge, and the time between onset and admission and between admission and endoscopy were recorded.

Statistical Analysis

Statistical data were analyzed and provided using MedCalc 29.0.0. Continuous variables were compared using the Mann-Whitney test, while the Chi-square test was used for categorical variables. Descriptive data were generated to describe patient characteristics, including percentages for categorical variables and means with standard deviations, as well as medians with interquartile range for continuous variables. The association between mortality and various factors was quantified with odds ratio (OR).

Results

General Characteristics of the Patients

During 2017-2021, 1416 patients with ulcer were hospitalized (*Table 2*); the mean age was 60.8 ± 14.9 years (18-93 years) and 70% were males. There was a relatively equal proportion of gastric and duodenal ulcers (45.6 and 49.9%, respectively); 2.9% of patients have both gastric and duodenal ulcers, and anastomotic ulcers were rarely encountered (1.6%).

Most patients were admitted for bleeding (66.7%), followed by perforation (17.3%); stenosing and penetrating ulcers were rarely noted (5.3 and 1.3%, respectively). Uncomplicated ulcers were noted in 14.3% of cases.

Trend Incidence in Hospitalizations for Complicated and Non-Complicated Ulcers

We noted a decreasing trend for bleeding ulcer admissions during 2020-2021 (in the pandemic period), and also for uncomplicated ulcer admissions, while for perforation there was no significant variation during that time (*Fig. 1*).

Bleeding Peptic Ulcer

A decreasing mortality was noted from 2017 to 2020 (7.23-4.83-5.17-2.13), with a significant increase in 2021 (10.00) - *Fig. 2*.

We analyzed the temporal trend for prognostic scores in bleeding peptic ulcers to see if there was an increased severity of bleeding during 2021. We noted a slight increase for GBS, modified GBS (with no statistical significance), and a significant increase for Cedars-

Table 2. The main characteristics of patients admitted for peptic ulcer

Characteristics	Value
Age (years), mean \pm SD, range	60.8 \pm 15, 18-93
<60/60-79/>80 (%)	45.8/44.3/9.9
Gender, Male (%)	70.3
Etiology (%)	
Gastric ulcer	45.7
Duodenal ulcer	49.8
Both	2.9
Anastomotic ulcers	1.7
Mortality: Bleeding	5.85
Perforated	11.2
Complications No (%)	
Bleeding	921 (64.3)
Perforation	258 (18.0)
Stenosis	75 (5.2)
Penetrating ulcer	18 (1.3)
Uncomplicated ulcer	206 (14.4)
Bleeding ulcer	
Rebleeding rate (%)	6.6
Emergency surgery (%)	2.5
Mean hospital stays (days)	7.7 \pm 7

SD=standard deviation

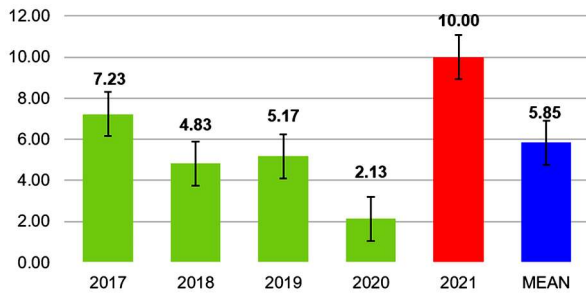


Figure 1. Trend of mortality in PUB

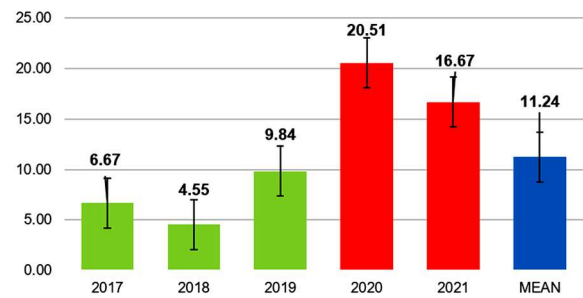


Figure 2. Trend of mortality in perforated peptic ulcers

Sinai, pre-endoscopic and full Baylor bleeding score, while for Rockall (pre-endoscopic and full score), AIM65, and T-score the difference was not significant. The most used scores for prognostic in PUB are Glasgow-Blatchford and Rockall scores, and the result suggests that no more severe cases were admitted during 2021, as compared with the 2017-2020 period.

The proportion of patients with cirrhosis was similar in 2017-2020 and 2021 (10.4 and 8.84%, $P=0.6169$). Rebleeding rate and emergency surgery had both a decreasing trend from 2017 to 2019, and increased significantly during 2021 (12.5% rebleeding rate) - *Figs. 3 and 4*. The mortality rate for PUB with emergency surgery was 37.5% during the 2017-2021 period. Time from admission to endoscopy has decreased from 2017 to 2019 and increased during 2020 and 2021 (but with no statistical significance);

mean admission to endoscopy time during 2020-2021 was below 24 hours. The mean time from onset to emergency department presentation was similar.

By comparing the proportions of active bleeding (Forrest Ia and B) and high-risk stigmata (Forrest IIA and IIB) during 2017-2021, we noted a significant increase in Forrest I+II lesions during 2021 versus 2017 (OR=1.9160, $P=0.0038$), 2019 (OR=1.5296, $P=0.03$) and 2020 (OR=1.6421, $P=0.0294$), but outside statistical significance compared with 2018 (OR=1.4750, $P=0.0521$). It is possible that a higher proportion of ulcers with a risk of rebleeding and surgery in 2021 may explain an increased mortality compared to the 2017-2020 period (*Table 3*).

Perforated Ulcer

Admissions during 2017-2019 (mean number

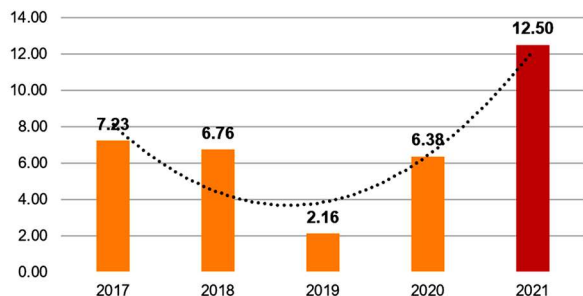


Figure 3. Trend of rebleeding rate in PUB

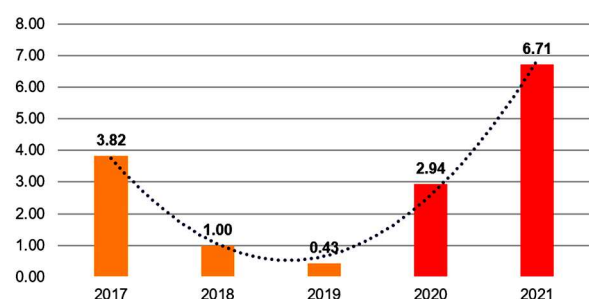


Figure 4. Trend of emergency surgery in PUB

Table 3. Trend for bleeding peptic ulcer during the 2017-2021 period

	2017	2018	2019	2020	2021
Mortality	7.23	4.83	5.17	2.13	10.00
Rebleeding	7.23	6.76	2.16	6.38	12.50
Surgery	5.42	2.42	0.86	3.55	6.25
Forrest (%)					
IA	1.20	2.42	0.43	0.71	1.25
IB	8.43	8.21	9.05	5.67	12.50
IIA	4.82	7.25	12.07	11.35	14.38
IIB	7.80	10.14	5.60	7.80	10.63
During hospitalization (%)	7.23	2.90	5.60	9.22	8.75
Hour's admission to endoscopy	20.4	16.2	10.5	17.0	18.4
Hour's onset to admission	48.2	40.9	47.6	51.5	37.9
Scores					
GBS	9.65	9.85	10.18	10.33	10.54
Modified GBS	7.99	8.49	8.77	8.88	9.08
Rockall pre-endoscopic	1.85	2.38	2.83	2.24	2.46
Rockall full	3.48	3.86	4.46	3.83	3.97
CS score	2.31	2.70	2.93	2.95	3.68
BBS pre-endoscopic	6.45	6.88	6.99	7.47	9.17
BBS full	8.02	8.27	8.29	8.45	10.73
AIM65	1.08	0.79	0.98	1.03	1.04
T-score	11.65	11.45	11.18	11.20	11.46

GBS=Glasgow-Blatchford score, CS=Cedars-Sinai, BBS=Baylor-Bleeding Score

55 cases/year) were higher than in 2020 (46.5 cases/year-15.5% reduction), but in 2021 the admissions for perforated ulcer returned to the mean value. The mortality rate was 6.7% in 2017, 4.6% in 2018, 9.8% in 2019, and increased to 20.5% in 2020 and 16.7% in 2021. Mean Boey index was higher in 2020-2021 than in 2017-2019 but no statistical difference was recorded (1.09 versus 0.79, $P=0.0861$). The mean value of the Charlson comorbidity index was higher in 2020 than in 2017-2019, and the mean CCI for 2020-2021 was 1.84 versus 1.51 for 2017-2019 but no statistically significant difference was recorded ($P=0.1276$) (Table 4). The mortality in Boey 0-1 score was 1.8% in 2017-2019 and 2.8% in 2020-2021; the

mortality in Boey 2-3 score was 53.3 in 2017-2019 and 61.1% in 2020-2021 (statistically similar between the two periods).

Stenosing and Penetrating Ulcers

75 cases of stenosing ulcers were recorded, with a higher incidence during the 2018-2020 period (53 cases); 54.7% were pre-pyloric ulcers, 40% were duodenal ulcers and 5.3% had both gastric and duodenal ulcers. 18 penetrating ulcers were found, all diagnosed during surgical procedures; all except for one case were associated with other complications (3 with bleeding, one with bleeding and perforation, 6 with perforation, 7 with stenosis).

Table 4. Trend for perforated peptic ulcers during the 2017-2021 period

	2017 No=60	2018 No=44	2019 No=61	2020 No=39	2021 No=54
Mortality	6.67	4.55	9.84	20.51	16.7
Boey score (mean)	0.95	0.59	0.79	1.17	1.03
Charlson comorbidity index (mean)	1.43	1.55	1.56	1.85	1.83
Hour's onset to surgery	30.1	19.2	29.0	35.9	23.2

Most stenosing ulcers (70.7%) were managed conservatively; surgical procedures were performed in case of older stenosis with local significant fibrosis and included gastro-entero-anastomosis in 12% (4 gastric ulcers and 5 duodenal ulcers), gastric ulcer excision in 4% (3 cases), gastrectomy in 9.3% (3 gastric ulcers and 4 duodenal ulcers), and selective vagotomy with gastric resection in one case (1.3%); two cases with concomitant perforation were managed by perforation suture. Surgery was performed in 17 cases of penetrating ulcer (gastrectomy in 9 cases, ulcer excision, and gastro-entero-anastomosis in 3 cases each, one case with concomitant perforation was treated by suture and one case with concomitant

bleeding was treated by in situ suture of the bleeding site).

Pandemic versus Pre-Pandemic Period

The admissions for bleeding peptic ulcers have decreased by 36.6% during the pandemic period. Age, gender, type of ulcer (gastric, duodenal, both, peptic), the proportion of bleeding ulcer during hospitalization for other diseases, and Forrest type of lesions were similar (*Table 5*). Although the mortality rate was similar (5.3% during the pre-pandemic period and 7.22% during the pandemic period; $P=0.3078$), the rebleeding rate was higher in the pandemic period (9.89 versus 4.58%) and

Table 5. Bleeding peptic ulcers in the pandemic period compared to the pre-pandemic period

	PRE-PANDEMIC N=415	PANDEMIC N=263	P-value
Age	63.31 ± 14.42	62.31 ± 14.64	0.3818
Gender (%M)	66.51	70.34	0.2970
Mortality	5.30	7.22	0.3078
Rebleeding	4.58	9.89	0.0082
- mortality for rebleeding	15.79	38.46	0.1071
Surgery	1.69	4.56	0.0336
- mortality for surgery	28.57	33.33	0.8296
Blood transfusions	49.64	60.46	0.006
- No. of transfused units	3.29 ± 2.83	3.66 ± 2.50	0.1889
Hospitalization days	6.85	7.33	0.3450
Type of ulcer			0.0629
- gastric ulcer	42.41	45.25	
- duodenal ulcer	53.25	46.77	
- both	2.41	6.08	
- anastomotic	1.93	1.90	
Forrest (%)			0.8421
IA	1.45	1.14	
IB	8.43	9.89	
IIA	10.12	14.45	
IIB	7.47	9.51	
During the hospitalization (%)	5.54	5.70	0.9291
Hour's onset to admission	44.48	41.87	0.4968
Endoscopy			
- admission to endoscopy (hours)	13.1	17.9	0.0377
- <24h (%)	90.72	87.06	0.1865
Scores			
GBS	10.06	10.46	0.1259
Modified GBS	8.66	9.08	0.0782
Rockall pre-endoscopic	2.64	2.38	0.0588
Rockall full	3.94	4.21	0.0873
CS score	2.87	3.39	0.0032
BBS pre-endoscopic	6.93	8.63	<0.0001
BBS full	8.29	10.03	<0.0001
AIM65	0.90	1.04	0.0773
T-score	11.30	11.46	0.3464
Charlson comorbidity index	3.01	3.14	0.4214

GBS=Glasgow-Blatchford score, CS=Cedars-Sinai, BBS=Baylor-Bleeding Score

the proportion of emergency surgery for bleeding peptic ulcer was also higher (4.56 versus 1.69%, $P=0.0082$). The mortality rate for patients with PUB who performed emergency surgery was similar during the pandemic (33.3%) and pre-pandemic period (28.6%, $P=0.8296$). The proportion of patients who needed blood transfusions was higher during the pandemic period (60.46 versus 49.64%, $P=0.006$), but the mean number of units transfused was similar. The number of hospitalization days, the interval between onset and admission, and the proportion of patients who performed endoscopy during the first 24 hours after admission were similar. The mean interval between admission and endoscopy was higher with 4.8 hours during the pandemic period ($P=0.0377$). The mean value of prognostic scores was similar, except for Cedars-Sinai and Baylor bleeding (pre-endoscopic and post-endoscopic) scores which were higher during the pandemic; the Baylor score was initially designated for the prediction of rebleeding risk.

The admissions for perforated peptic ulcers were lower in the pandemic period as compared with similar pre-pandemic period (89 cases during the pandemic period and 104 cases during the pre-pandemic period). Age,

gender, and the proportion of ulcer types (gastric, duodenal, both, peptic) were similar. The time interval between onset and intervention was similar, and the severity risk, estimated by Boey score, was also similar. The mortality, however, was much higher during the pandemic period compared with the pre-pandemic period (17.98 versus 6.73%, $OR=3.04$, 95%CI 1.1880 to 7.7649, $P=0.0204$), and the hospitalization was shorter during the pandemic period (8.6 versus 10.6, $P=0.0351$) (Table 6).

Discussions

Most admissions during the analyzed period had complicated ulcers (85.7% of cases), because of the symptom severity. The main complication was bleeding, followed by perforation, while stenosis was rarely noted, and penetrating ulcers were diagnosed in almost all cases only during surgical interventions for other complications of peptic ulcer. We noted a decreasing trend for bleeding peptic ulcers and uncomplicated ulcer admissions during 2020-2021, while for perforated ulcers a decreased admission was noted during 2020, with a return to the previous values in 2021. The rate of complications is higher in hospitalized PUD

Table 6. Perforated peptic ulcers in the pandemic period compared to the pre-pandemic period

	PRE-PANDEMIC N=104	PANDEMIC N=89	P-value
Age	52.39 ± 15.69	53.65 ± 15.69	0.5723
Gender (%M)	79.8	84.3	0.4236
Ulcer type			0.9743
gastric ulcer	39.4	40.5	
duodenal ulcer	58.7	57.3	
peptic	1.9	2.2	
Onset to admission time	29.1	24.4	0.4281
Boey score (mean±stdev)	0.78±1	1.04±0.96	0.1856
Boey score (%)			0.1928
0	52	35.3	
1	28	33.3	
2	10	23.5	
3	10	7.9	
Charlson comorbidity index (mean±stdev)	1.58±1.4	1.75±1.87	0.4578
COVID-19 % of cases (mortality)		3.37 (33.33)	
Mortality	6.73	17.98	0.0204
Hospitalization days	10.6	8.6	0.0472

cases because hospitalized cases represent more severe cases than those managed in outpatient setting; in a nationwide analysis in China, 61% of 2015 PUD admissions were complicated ulcers (29), and in another nationwide study in USA during 2012-2013, 80.25% of admitted PUD were complicated (30). In the literature geographic differences were noted (18); a study in South Korea between 2006 and 2015 showed a stable trend for PUB from 2006 to 2008 and a decrease from 2008 to 2015, more significant in men than in women, and another study in China found a reduced proportion of PUB in 2012-2013 as compared to 1997-1998 period, mainly because of the reduction of duodenal ulcer bleeding (31).

The trend for mortality for bleeding peptic ulcers has shown a decreasing value from 2017-2020 followed by an increase in 2021, associated with higher rebleeding and surgical rates during 2021, with an elevated proportion of high-risk lesions (Forrest I, IIa, IIB ulcers) in 2021 compared to the previous years; data were comparable with other published studies, in a study in Atlanta including 7079 patients with PUB over 8 years, the overall in-hospital mortality was 8.5% and the rate of surgery was 4.3% (9). 8 cases of bleeding peptic ulcer and COVID-19 infection were noted; mortality rate was 62.5% for COVID-19 positive cases compared with 7.74% for COVID-19 negative cases (OR 7.94, 95%CI 1.21-52.26, $P=0.0311$).

For perforated peptic ulcers, the mortality rate increased significantly during 2020-2021. The interval between onset symptoms and surgery was similar; the Boey score and Charlson comorbidity index were also similar. The mortality rate for emergency surgery in bleeding and perforated peptic ulcers remains high; in a study, the rate was 17.8% for operated bleeding peptic ulcers (30), while in our study was 37.5%. for perforated peptic ulcer, and the mean mortality rate was 11-20% in our study, while in several studies the mortality rate was between 10-20% (32-34).

By comparing the pandemic period with a similar pre-pandemic period, we noted a significantly decreased admission for bleeding

peptic ulcer (36.6%) and for perforated peptic ulcer (14.4%) during the pandemic period. We may presume that some patients with non-severe UGIB chose not to come to the hospital during the pandemic because of the fear effect (25), and therefore the admissions were reduced. A similar reduced UGIB was noted in several studies (26,35-37), especially during lockdown (38,39). For perforated ulcers, the fear effect may be less significant during the pandemic period, because of the severity and progression of the symptoms and lower probability of spontaneous recovery for the patients. Some studies analyzed the hospitalization rate of peptic ulcer during the pandemic; a study in 2 emergency centers in China found that in May-November 2020 the admissions declined in one hospital but the severity of cases increased (38), and some studies found decreased surgery admissions during the pandemic, although the admissions for PUB surgical emergencies were similar to the pre-pandemic period (27,34).

The mortality rate for bleeding peptic ulcers, although slightly higher during the pandemic period (7.22 versus 5.30%) was not statistically different ($P=0.3078$). Higher rates of rebleeding and emergency surgery were noted, and also a higher percentage of patients who needed blood transfusions. A longer mean time between admission and endoscopy was also recorded, but the percentage of endoscopies performed during the first 24 hours after admission was similar. The severity of the bleeding was similar. A possible explanation for the higher rebleeding rate during the pandemic period may include the delay of endoscopy and a decreased efficacy of therapeutic endoscopy, partially related to the use of protective gear. Only 8 cases of bleeding peptic ulcers were COVID-19 positive during the pandemic, and the mortality was higher for COVID-19 positive patients (62.5%); by excluding positive patients, the rebleeding rate decreased from 9.9 to 9.4% (still higher than the rate in pre-pandemic period), but mortality rate decreased from 7.22 to 5.5% (compared to 5.3% during the pandemic period). Mortality rates of UGIB in patients

with COVID-19 infections were very heterogeneous, in several studies patients admitted for UGIB mortality for UGIB and COVID-19 infection was between 21.7-59% (23,24,26,27, 38-40), mostly because of respiratory failure (26,39,40).

For perforated peptic ulcers, significantly higher mortality rates were recorded during the pandemic period (17.98 versus 6.73%), with a shorter hospitalization period. The mean time interval between symptoms and surgery, the Boey score, and the Charlson comorbidity index were similar. Although the delay of hospital presentation because of the patients (fear effect) may be suggested as a possible cause for higher mortality, our data does not sustain this possible explanation. Indirect factors related to the pandemic effect on healthcare systems (triage, reallocation of personnel, delays of proper care because of protocols, and use of protective gear may impact the efficiency of medical care) may explain the difference in mortality. Only 3 cases of patients with perforated peptic ulcer were COVID-19 positive, with a mortality rate of 33.3%. In COVID-19 negative patients with perforated ulcers, the mortality rate was 15.1% during the pandemic, slightly higher than in the pre-pandemic period, but with no statistical significance ($P=0.1000$); indirect factors similar to bleeding peptic ulcers may decrease the efficacy of perforated ulcer management.

No significant variation of stenosing and penetrating ulcers was noted in the pandemic period; both complications were rarely encountered today (41-44). In our study, 5.2% of all admitted ulcers were stenosing ulcers (6.3% of gastric ulcers and 4.3% of duodenal ulcers); two deaths were noted, both in case of concomitant perforation. 6 penetrating gastric ulcers and 12 penetrating duodenal ulcers were recorded; pancreatic penetration was noted in 83.3% (27.8% having also penetration into the hepatic hilum), and biliary duct penetration was noted in 13.7%. Mortality was related to associated ulcer complications; it was 62.5% in 8 cases associated with perfora-

tion and 50% in 4 cases associated with bleeding. Penetrating peptic ulcers are rarely encountered today because of proton pump inhibitors treatment (41); pancreas penetration is more frequent in duodenal than in gastric ulcers, and some cases of severe pancreatitis or even gastro-pancreatic fistulas were communicated (41,42). The most frequent organ involved is the pancreas, rarely gastro-hepatic omentum, biliary tract, and liver (43). Stenosing ulcers represent currently less than 5% of complicated DU and less than 1-2% of complicated GU) (44); in a study between 2005-2014, 2.4% of patients admitted with PUD have stenosis, compared with 87% PUB and 10.6% with PPU (45).

Conclusions

We noted a decreasing trend for bleeding peptic ulcer admissions during 2020-2021, while for perforated ulcers there were no significant variations, and for stenosing ulcers, a Gaussian trend was noted; admission for uncomplicated ulcers also decreased during 2020-2021.

Admissions during the pandemic period have decreased by more than 1/3 for bleeding peptic ulcers, while for perforated peptic ulcers have decreased by 1/7. For bleeding peptic ulcers, higher rates of rebleeding and emergency surgery and also a higher percentage of blood transfusions were noted, with a longer mean time between admission and endoscopy, but a similar percentage of endoscopies performed during the first 24 hours after admission. The mortality rate for bleeding peptic ulcer was similar during the pandemic period to the pre-pandemic period (7.22 versus 5.30%); 8 cases were COVID-19 positive, with 62.5% mortality rate, and by excluding positive patients, the mortality rate decreased from 7.22 to 5.5% (similar to a pre-pandemic period). For perforated peptic ulcers, significantly higher mortality rates were recorded during the pandemic period (17.98 versus 6.73%).

Author's Contributions

Conceptualization, SM.C., I.R., and D.C.; methodology, SM.C., V.F.I., and D.C.; software, SM.C., and AM.V.; validation, M.P., E.M., and VM.S.; formal analysis, I.R., and AL.G.; investigation, A.G., AL.G., and AM.V.; resources, SM.C., V.F.I., and AM.V.; data curation, V.F.I., and D.C.; writing-original draft preparation, AL.G., AM.V., and D.C.; writing-review and editing, SM.C. and I.R.; visualization, AM.V., and V.F.I.; supervision, I.R. and D.C.; project administration, SM.C., I.R., and V.F.I. All authors had read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of the Emergency Hospital of Craiova (protocol code 11977/24.03.2020).

Conflict of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

References

- Sung JJ, Kuipers EJ, El-Serag HB. Systematic review: the global incidence and prevalence of peptic ulcer disease. *Aliment Pharmacol Ther.* 2009; 29(9):938-46.
- Narayanan M, Reddy KM, Marsicano E. Peptic Ulcer Disease and *Helicobacter pylori* infection. *Mo Med.* 2018;115(3):219-224.
- Gralnek IM, Stanley AJ, Morris AJ, Camus M, Lau J, Lanas, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy.* 2015;47(10): a1-46.
- Zhang W, Liang X, Chen X, Ge Z, Lu H. Time trends in the prevalence of *Helicobacter pylori* infection in patients with peptic ulcer disease: a single-center retrospective study in Shanghai. *J Int Med Res.* 2021;49(10): 3000605211051167.
- Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. *Digestion.* 2011;84(2):102-113.
- Malmi H, Kautiainen H, Virta LJ, Färkkilä MA. Increased short- and long-term mortality in 8146 hospitalised peptic ulcer patients. *Aliment Pharmacol Ther.* 2016;44(3):234-45.
- Zhang XY, Mo HY, Huang Y. Letter: risk factor and mortality of peptic ulcer disease. *Aliment Pharmacol Ther.* 2016;44(4):424-5.
- Malmi H, Kautiainen H, Virta LJ, Färkkilä N, Koskenpato J, Färkkilä MA. Incidence and complications of peptic ulcer disease requiring hospitalisation have markedly decreased in Finland. *Aliment Pharmacol Ther.* 2014; 39(5):496-506.
- Quan S, Frolkis A, Milne K, Molodecky N, Yang H, Dixon E, et al. Upper-gastrointestinal bleeding secondary to peptic ulcer disease: incidence and outcomes. *World J Gastroenterol.* 2014;20(46):17568-77.
- Chen TH, Cheng HT, Yeh CT. Epidemiology changes in peptic ulcer diseases 18 years apart explored from the genetic aspects of *Helicobacter pylori*. *Transl Res.* 2021;232:115-120.
- Chan JSH, Chao ACW, Cheung VCH, Wong SSK, Tang W, Wu JCY, et al. Gastrointestinal disease burden and mortality: A public hospital-based study from 2005 to 2014. *J Gastroenterol Hepatol.* 2019;34(1):124-131.
- Azhari H, King JA, Coward S, Windsor JW, Ma C, Shah SC, et al. The Global Incidence of Peptic Ulcer Disease Is Decreasing Since the Turn of the 21st Century: A Study of the Organisation for Economic Co-Operation and Development (OECD). *Am J Gastroenterol.* 2022;117(9): 1419-1427.
- Guo H, Lam AY, Shaheen AA, Forbes N, Kaplan GG, Andrews CN, et al. (2021). Urban-Rural Disparities and Temporal Trends in Peptic Ulcer Disease Epidemiology, Treatment, and Outcomes in the United States. *Am J Gastroenterol.* 2021;116(2):296-305.
- Zogovic S, Bojesen AB, Andos S, Mortensen FV. Laparoscopic repair of perforated peptic ulcer is not prognostic factor for 30-day mortality (a nationwide prospective cohort study). *Int J Surg.* 2019;72:47-54.
- Tarasconi A, Coccolini F, Biffl WL, Tomasoni M, Ansaloni L, Picetti E, et al. Perforated and bleeding peptic ulcer: WSES guidelines. *World J Emerg Surg.* 2020;15:3.
- Bardhan KD, Royston C. Time, change and peptic ulcer disease in Rotherham, UK. *Dig Liver Dis.* 2008;40(7):540-6.
- Johnson CH, McLean RC, McCallum I, Perren D, Phillips AW. An evaluation of the epidemiology, management and outcomes for perforated peptic ulcers across the North of England over 15 years: A retrospective cohort study. *Int J Surg.* 2019;64:24-32.
- Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, et al. Perforated peptic ulcer. *Lancet.* 2015;386(10000):1288-1298.
- Howley IW, Bruns BR, Tesoriero RB, Vesselinov R, Kufera JA, Feliciano DV, et al. Statewide analysis of peptic ulcer disease: as hospitalizations decrease, procedural volume remains steady. *Am Surg.* 2019;85(9):1028-1032.
- Cazacu SM, Alexandru DO, Stătie RC, Iordache S, Ungureanu BS, Iovanescu VF, et al. The accuracy of pre-endoscopic scores for mortality prediction in patients with upper GI bleeding and no endoscopy performed. *Diagnostics (Basel).* 2023;13(6):1188.
- Rivai MI, Suchitra A, Janer A. Evaluation of clinical factors and three scoring systems for predicting mortality in perforated peptic ulcer patients, a retrospective study. *Ann Med Surg (Lond).* 2021;69:102735.
- Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol.* 2011;173(6):676-82.
- Marasco G, Maida M, Morreale GC, Licata M, Renzulli M, Cremon C, et al. Gastrointestinal bleeding in COVID-19 patients: a systematic review with meta-analysis. *Can J Gastroenterol Hepatol.* 2021;2021:2534975.
- Cappell MS, Friedel DM. Gastrointestinal bleeding in COVID-19-infected patients. *Gastroenterol Clin North Am.* 2023;52(1):77-102.
- Marginean CM, Popescu M, Vasile CM, Cioboata R, Mitrut P, Popescu IAS, et al. Challenges in the differential diagnosis of COVID-19 pneumonia: a pictorial review. *Diagnostics (Basel).* 2022;12(11):2823.
- Cazacu SM, Burtea DE, Iovanescu VF, Florescu DN, Iordache S, Turcu-Stolicea A, et al. Outcomes in patients admitted for upper gastrointestinal bleeding and COVID-19 infection: a study of two years of the pandemic. *Life (Basel).* 2023;13(4):890.
- Martin TA, Wan DW, Hajifathalian K, Tewani S, Shah SL, Mehta A, et al. Gastrointestinal bleeding in patients with coronavirus disease 2019: a matched case-control study. *Am J Gastroenterol.* 2020;115(10):1609-1616.
- Dong CT, Liveris A, Lewis ER, Mascharak S, Chao E, Reddy SH, et al. Do surgical emergencies stay at home? Observations from the first United States Coronavirus epicenter. *J Trauma Acute Care Surg.* 2021;91(1): 241-246.
- Zheng Y, Xue M, Cai Y, Liao S, Yang H, Wang Z, et al. Hospitalizations for

- peptic ulcer disease in China: current features and outcomes. *J Gastroenterol Hepatol.* 2020;35(12):2122-2130.
30. Havens JM, Castillo-Angeles M, Nitzschke SL, Salim A. Disparities in peptic ulcer disease: a nationwide study. *Am J Surg.* 2018;216(6):1127-1128.
 31. Wang J, Cui Y, Wang J, Chen B, He Y, Chen M. Clinical epidemiological characteristics and change trend of upper gastrointestinal bleeding over the past 15 years. *Zhonghua Wei Chang Wai Ke Za Zhi.* 2017;20(4):425-431 (Abstract).
 32. Byrne BE, Bassett M, Rogers CA, Anderson ID, Beckingham I, Blazeby JM, et al. Short-term outcomes after emergency surgery for complicated peptic ulcer disease from the UK National Emergency Laparotomy Audit: a cohort study. *BMJ Open.* 2018;8(8):e023721.
 33. Hasadia R, Kopelman Y, Olisha O, Alfici R, Ashkenazi I. Short- and long-term outcomes of surgical management of peptic ulcer complications in the era of proton pump inhibitors. *Eur J Trauma Emerg Surg.* 2018;44(5):795-801.
 34. Jian C, Zhou Z, Yang C, Zhao N, Bao H, Han S, et al. Increasing rate of hospitalization for severe peptic ulcer in digestive disease emergencies after the pandemic. *Medicine (Baltimore).* 2022;101(48):e31716.
 35. Mauro A, De Grazia F, Lenti MV, Penagini R, Frego R, Ardizzone S, et al. Upper gastrointestinal bleeding in COVID-19 inpatients: Incidence and management in a multicenter experience from Northern Italy. *Clin Res Hepatol Gastroenterol.* 2021;45(3):101521.
 36. Luu MN, Dang TP, Vo MH, Quach DT. Prevalence, causes, medical interventions, and mortality outcome of acute gastrointestinal bleeding among COVID-19 inpatients. *Curr Med Res Opin.* 2023;39(5):731-737.
 37. Duan Z, Duan Q, Liu K, Zhang X, Zhou S, On Behalf Of Xingtai Society Of Digestive Endoscopy. Impact of the COVID-19 Pandemic on Acute Upper Gastrointestinal Bleeding in Xingtai City. *Gastroenterol Res Pract.* 2021; 2021:5586030.
 38. Schmiederer A, Schwaighofer H, Niederreiter L, Profanter C, Steinle H, Ziachehabi A, et al. Decline in acute upper gastrointestinal bleeding during COVID-19 pandemic after initiation of lockdown in Austria. *Endoscopy.* 2020;52(11):1036-1038.
 39. Lui TKL, Tsui VWM, Leung WK. Impact of first wave of COVID-19 on outcomes of hospitalization for upper gastrointestinal bleeding in Hong Kong: a population-based study. *Endosc Int Open.* 2021;9(3):E284-E288.
 40. Alakuş Ü, Kara U, Taşçı C, Eryılmaz M. Upper gastrointestinal system bleedings in COVID-19 patients: Risk factors and management/a retrospective cohort study. *Ulus Travma Acil Cerrahi Derg.* 2022;28(6):762-768.
 41. Tana C, Silingardi M, Giamberardino MA, Cipollone F, Meschi T, Schiavone C. Emphysematous pancreatitis associated with penetrating duodenal ulcer. *World J Gastroenterol.* 2017;23(48):8666-8670.
 42. Dhruv S, Gurala D, Philipose J, Gumaste V. Gastropancreatic fistula: a rare complication of peptic ulcer disease. *ACG Case Rep J.* 2021;8(7):e00622.
 43. Jiao J, Zhang L. Liver involvement by perforated peptic ulcer: a systematic review. *J Clin Transl Pathol.* 2021;1(1):2-8.
 44. Jeong SJ, Lee J. Management of gastric outlet obstruction: focusing on endoscopic approach. *World J Gastrointest Pharmacol Ther.* 2020;11(2):8-16.
 45. Olufajo OA, Wilson A, Yehayes B, Zeineddin A, Cornwell EE, Williams M. Trends in the surgical management and outcomes of complicated peptic ulcer disease. *Am Surg.* 2020;86(7):856-864.