Visceral Medicine

Research Article

Visc Med 2024;40:30–37
DOI: 10.1159/000535061

Received: June 8, 2023
Accepted: November 5, 2023
Published online: January 2, 2024

Long-Term Outcomes following Acute Upper Gastrointestinal Bleeding Remain Poor: A Single-Center Comparison over Two Distinct Time Periods within the Last 15 Years in Finland

Juho Luomajoki[a] Laura Mattila[a] Johanna Laukkarinen[a, b] Mika Ukkonen[a, b, c]

[a]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [b]Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland; [c]Department of surgery, Kuopio University Hospital, Kuopio, Finland

Keywords
Acute upper gastrointestinal bleeding · Endoscopy · Gastroscopy · Mortality

Abstract
Introduction: Acute upper gastrointestinal bleeding (AUGIB) is a common and life-threatening condition. This study aimed to compare the causes and long-term outcomes of AUGIB over two distinct periods in the last 15 years. ***Methods:*** This population-based study included consecutive patients who underwent emergency upper endoscopy for visible bleeding in 2006 and 2016. Our primary focus was on long-term mortality up to 5 years after the endoscopy, although short-term mortality was also reported. ***Results:*** A total of 832 patients (median age 67 [12–96] years, 37% female) were included, with peptic ulcer disease (48%), esophagitis (20%), and variceal bleeding (15%) being the most common diagnoses. The incidence of AUGIB increased with age, reaching 8.31 cases per 1,000 person-years among those aged 80 years or older. Mortality rates at 30 days, 90 days, 1 year, and 5 years were 13%, 16%, 27%, and 47%, respectively. The standardized mortality ratio was high in all age groups, with particularly elevated rates observed among younger patients compared to the standard population. Variceal bleeding, liver cirrhosis, and chronic alcohol abuse were associated with the highest mortality. Only two short-term deaths were attributed to failed hemostasis. The primary causes of death were malignancies, liver failure, and cardiac failure. No improvement in outcomes was observed between the two time periods. ***Conclusion:*** Although the treatment of AUGIB may be relatively straightforward, the outcomes following treatment remain poor. High mortality can be attributed to the presence of coexisting conditions and patients' lifestyle.

Introduction

Acute upper gastrointestinal bleeding (AUGIB) is a prevalent and life-threatening condition that necessitates prompt medical attention [1]. It refers to hemorrhage originating from the gastrointestinal tract proximal to the ligament of Treitz and can be attributed to various causes such as peptic ulcer disease, varices, gastroduodenal erosions, esophagitis, Mallory-Weiss tears, and malignancy [2].

Previous studies have revealed geographical variations in the incidence rates of AUGIB, exhibiting a global decreasing trend [2–5]. Short-term mortality rates for AUGIB are significant, ranging from 1.1% to 11% according to a previous systematic review [6].

Although short-term mortality is relatively well documented, there remains a paucity of research examining the long-term outcomes associated with AUGIB [7–9].

Juho Luomajoki and Laura Mattila shared first authorship.

karger@karger.com
www.karger.com/vis

Correspondence to:
Mika Ukkonen, mika.ukkonen@fimnet.fi

Table 1. Patient and disease-specific characteristics

Variable	Years 2006 (*n* = 321)	Years 2016 (*n* = 511)	All patients (*n* = 832)
Age, median (min–max)	63 (12–95) years	69 (16–96) years	67 (12–96) years
Sex, female, *n* (%)	115 (37)	193 (38)	308 (37)
No comorbidities, *n* (%)	77 (24)	61 (12)	138 (17)
CCI, median (min–max)	3 (0–12)	4 (0–12)	4 (0–12)
Chronic alcohol use, *n* (%)	110 (34)	155 (30)	265 (32)
Anticoagulative medication, *n* (%)			
Acetylsalicylic medication	80 (25)	115 (23)	195 (23)
Warfarin medication	29 (9.0)	69 (14)	98 (12)
Heparin medication	2 (0.6)	48 (9.4)	50 (6.0)
Other anticoagulation	20 (6.2)	18 (3.5)	38 (4.6)
Corticosteroid medication, *n* (%)	16 (5.0)	43 (8.4)	59 (7.1)
SSRI medication, *n* (%)	13 (4.0)	36 (7.0)	49 (5.9)
NSAID medication, *n* (%)	39 (12)	54 (11)	93 (11)
Etiology of the bleeding, *n* (%)			
Peptic ulcer disease	157 (49)	242 (47)	399 (48)
Esophagitis	72 (22)	92 (18)	164 (20)
Variceal bleeding	55 (17)	70 (14)	125 (15)
Gastritis	31 (10)	56 (11)	87 (11)
Mallory-Weiss lesion	22 (6.9)	12 (2.3)	34 (4.1)
Malignancy	10 (3.1)	42 (8.2)	52 (6.3)
Helicobacter pylori infection, *n* (%)	64 (20)	12 (2.3)	76 (9.1)

CCI, Charlson Comorbidity Index; SSRI, selective serotonin reuptake inhibitor; NSAID, nonsteroidal anti-inflammatory drug.

Understanding the long-term prognosis and consequences of AUGIB is crucial for developing comprehensive management strategies. Therefore, the objective of this study was to investigate the long-term outcomes and associated factors in patients experiencing AUGIB.

Materials and Methods

This population-based study included consecutive patients who underwent emergency upper gastrointestinal endoscopy for AUGIB between 2006 and 2016 at Tampere University Hospital, Finland. Patients were identified by retrieving all cases associated with the Nordic Medico-Statistical Committee classification of surgical procedures (NOMESCO, version 1.13) codes UJD10 (esophagogastroduodenoscopy), UJD02 (gastroscopy), UJC12 (esophagoscopy), JFC12 (esophageal stenting). Only patients with visualized upper gastrointestinal bleeding were included. Those without available follow-up data were excluded.

Patient demographics, bleeding etiology, risk factors for AUGIB, and procedures performed for treatment were recorded. The incidence of AUGIB was calculated by comparing annual disease rates to the population census of the study hospital region (Statistics Finland, https://pxnet2.stat.fi/PXWeb/pxweb/fi/StatFin/). Survival data for all subjects were obtained from the Finnish Population Register Centre.

Study Hospital

All patients with suspected upper gastrointestinal bleeding underwent urgent endoscopy at the study's endoscopy unit. Proton-pump inhibitor therapy was initiated at the emergency department and continued daily (pantoprazole 40 mg 1x1-2 i.v.). Somatostatin infusion was administered if variceal bleeding was suspected. Warfarin therapy and new direct oral anticoagulants were interrupted unless contraindicated. Reversal agents were administered if required. Patients were admitted to the surgical ward or intensive care unit if required.

All endoscopies were performed by either consultant gastroenterologists or surgeons or by residents with a minimum of 2-year experience in emergency endoscopies. During endoscopy, standard hemostasis modalities were used, and transcatheter angiographic embolization was performed if endoscopic hemostasis failed. No patients underwent surgery. In cases of peptic ulcer disease secondary to *Helicobacter pylori* infection, *H. pylori* was eradicated. Nonsteroidal anti-inflammatory drugs were discontinued for nonsteroidal anti-inflammatory drug-associated ulcers. Repeat endoscopies were performed if required. Patients received continuous proton-pump inhibitor medication until the etiology of ulcers was determined. New direct oral anticoagulants were resumed after bleeding control. Patients with alcohol-associated etiologies received brief alcohol intervention. Motivated patients were provided information on rehabilitation programs.

Outcomes

The main outcome measure was mortality at 30 days, 90 days, 1 year, and 5 years. Standardized mortality ratio (SMR) was calculated by comparing observed mortality to expected all-cause mortality in the Finnish population during the study period. The analysis was performed for subgroups based on diagnostic groups, age, and sex. Outcomes during the two study periods were compared, and the Kaplan-Meier curve was used to illustrate mortality.

Results

A total of 832 patients (median age 67 [12–96] years, 37% female) underwent upper gastrointestinal endoscopy during the study period, with a median follow-up time of

Table 2. Etiologies of the upper gastrointestinal bleeding and associated comorbidities and medications

	Peptic ulcer (n = 399), %	Esophagitis (n = 265), %	Variceal bleeding (n = 125), %	Gastritis (n = 87), %
Alcohol abuse	24	46	67	15
HBP infection	16	5.5	0.8	12
NSAID	18	9.1	1.6	6.9
SSRI	6.3	4.3	3.2	5.7
Corticosteroids	8.3	6.1	2.4	5.7
Anticoagulative therapy	51	14	7.2	4.6

HBP infection, *Helicobacter pylori* infection; SSRI, selective serotonin reuptake inhibitor; NSAID, non-steroidal anti-inflammatory drug.

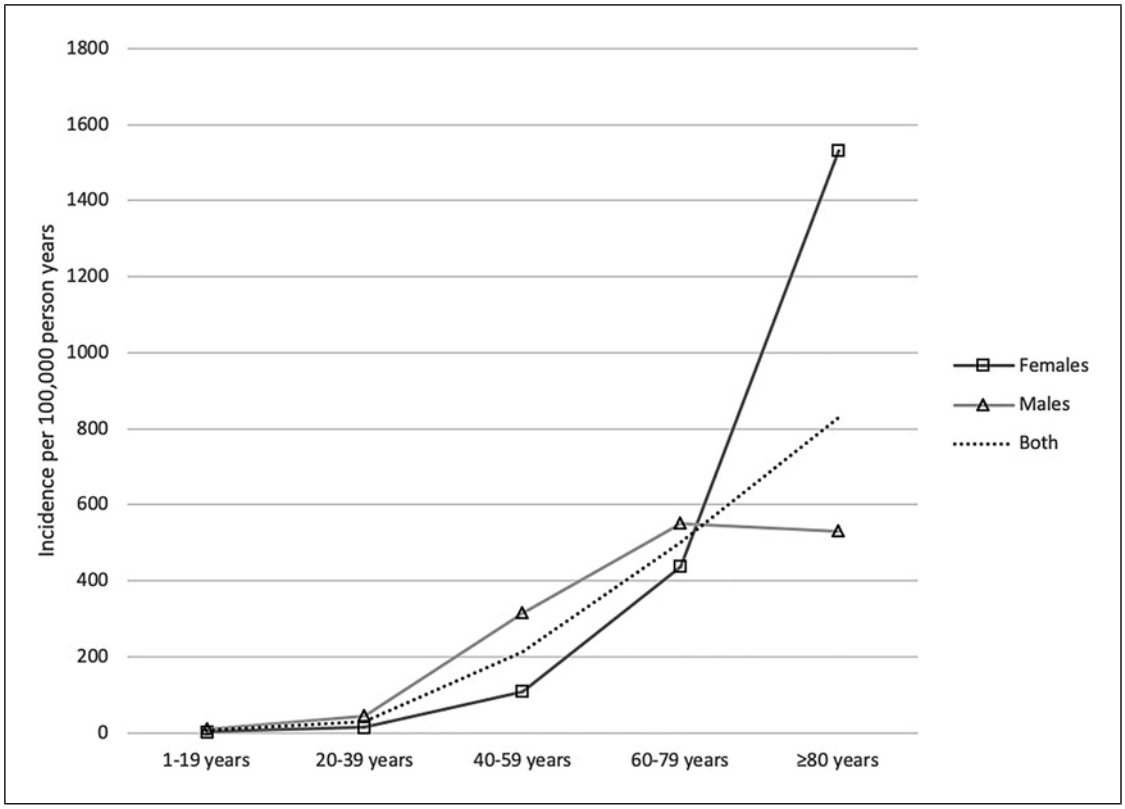

Fig. 1. Incidence of gastrointestinal bleeding in different age groups.

53 (0–170) months. The majority of patients had significant comorbidities, as indicated by a median Charlson Comorbidity Index (CCI) of 4 (0–12). Patients undergoing endoscopy in the later study period were older (median age 69 vs. 63 years, $p < 0.001$) and had a higher prevalence of significant comorbidities (median CCI 4 vs. 3, $p < 0.001$). Twenty-five percent of patients (n = 213) were on anticoagulative therapy, with acetylsalicylic (23%) and warfarin (12%) therapies being the most common. Twenty patients (2.4%) were on dual anticoagulation, and 12 (1.4%) were on triple anticoagulation. Patient demographics are described in Table 1, and different etiologies for bleeding are presented in Table 2.

Older age was associated with a higher incidence of bleeding, as depicted in Figure 1. The incidence of AUGIB increased from 0.06/1,000 person-years among those aged less than 20 years to 8.31/1,000 person-years among those aged 80 years or older. Correspondingly, mortality rates increased with age. Table 3 presents the observed mortality rates according to different etiologies of bleeding. The highest mortality was observed among those with variceal bleeding and malignancy-associated bleeding. Seventy-one percent of patients with preexisting liver cirrhosis died during the study period. While alcohol etiology and preexisting cirrhosis were associated with poor outcomes, 5-year mortality exceeded 30% even

Table 3. Survival and mortality rates according to specific subgroups

Variable	*n*	Mortality				Median survival, months
		30-day, %	90-day, %	1-year, %	5-year, %	
Sex, female	308	10*	13	26	48	18 (0–153)
Sex, male	524	15*	17	27	47	14 (0–165)
Age group						
0–49 years	128	6.3*	9.4*	11**	22**	29 (0–130)
50–79 years	558	13*	15*	27**	47**	14 (0–165)
≥80 years	146	16*	23*	38**	72**	17 (0–153)
Etiology of the bleeding						
Peptic ulcer disease	399	11*	13*	21*	40%**	19 (0–161)
Alcohol abuse	94	9.6	12	19	38	24 (0–157)
Helicobacter pylori	62	1.6*, [a]	3.2*, [a]	6.5*, [a]	21*, [a]	61 (0–161)
NSAID	73	1.4*, [a]	4.1*, [a]	11*, [a]	27*	29 (0–156)
SSRI	25	4.0	8.0	16	32	33 (0–125)
Corticosteroids	33	12	21	36*	67*, [a]	13 (0–105)
Esophagitis	164	9.8	13	23	45	21 (0–152)
Variceal bleeding	125	22*	26*	40**	63**	9 (0–132)
Gastritis	87	9.2	9.2	24	54	24 (0–163)
Mallory-Weiss tear	34	2.9	8.8	15	32	54 (0–165)
Malignancy	52	35**	40**	60**	65*	2 (0–141)
Comorbidities						
No comorbidities	138	4.3*	5.8**	15**	28**	22 (0–165)
Coronary artery disease	126	10	16	30	60*	21 (0–161)
Congestive heart failure	34	15	21	41*	77**	13 (0–72)
Peripheral vascular disease	33	18	21	27	64	19 (0–151)
Dementia	40	20	25	38	78**	18 (0–89)
COPD	51	14	16	28	51	16 (0–163)
Diabetes						
Liver failure	116	24**	30**	46**	71**	6 (0–112)
Moderate to severe	30	17**	30**	47**	77**	9 (0–112)
Overall	832	13	16	27	47	15 (0–165)

Statistical comparison: *p value 0.50–0.001; **p value <0.001. NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitor; COPD, chronic obstructive pulmonary disease. [a]Comparison between patients with peptic ulcer disease with different etiologies.

among patients with benign and nonprogressive etiologies (e.g., Mallory-Weiss tears and peptic ulcer disease). Coexisting diseases, including heart failure (77% vs. 46%, $p < 0.001$), coronary artery disease (60% vs. 45%, $p = 0.003$), dementia (78% vs. 46%, $p < 0.001$), were associated with higher 5-year mortality, while short-term mortality was not significantly increased compared to other population.

The highest standardized mortality ratio (SMR) was observed among patients aged 1–19 years, as described in Table 4. The expected risk of dying is lowest in the younger population, which partially explains the high observed SMR. Nonetheless, among those with AUGIB, SMR is high in all age groups. The SMRs for different age groups in the study were as follows: 1.176 for patients aged less than 20 years, 31 for those aged 20–39 years, 69 for those aged 40–59 years, 18 for those aged 60–79 years, and 3.8 for those aged over 80 years. Short-term deaths were typically caused by malignancies (32%), liver failure (21%), and cardiovascular failure (12%), as shown in Table 5. Continuous bleeding was responsible for only two deaths.

Mortality rates increased during the study period, as presented in Table 6. However, when excluding short-term deaths from the analysis, the overall mortality rates slighly improved. The 90-day mortality rates were 14% in 2006 versus 17% in 2016 ($p = 0.227$), 1-year mortality rates were 25% versus 28% ($p = 0.312$), and 5-year mortality rates were 46% versus 38% ($p = 0.509$).

The Kaplan-Meier survival curves are illustrated in Figures 2 and 3. Figure 2 compares mortality between the two distinct study periods, while Figure 3 compares mortality between patients with variceal and non-variceal bleeding.

Discussion

This study highlights the association of AUGIB with unfavorable outcomes, and unfortunately, no significant improvements were observed during the

Table 4. Comparison of observed and expected annual mortality rates (per 1,000 person-years)

Age group	Mortality			
	expected (E)	observed (O)	excess (O-F)	SMR
1–19 years	0.17	200	200	1.176
20–39 years	0.68	21	20	31
40–59 years	3.5	242	239	69
60–79 years	15	269	254	18
≥80 years	98	377	279	3.8

Expected mortality = observed deaths in the whole population/size of the same aged population * 1,000. Observed mortality = observed number of deaths in the study population/sample size of same aged patients * 1,000. SMR = Observed mortality/Expected Mortality. SMR, standardized mortality ratio.

Table 5. Causes of short-term deaths (<30 days)

Causes of death	Share of patients, %
Malignancy	32
Liver failure (cirrhosis patients)	21
Cardiovascular failure	12
Infection/aspiration pneumonia/sepsis	7.9
Other[1]	11
Unknown	16

[1]Including 2 patients with continuous bleeding.

Table 6. Mortality during two study periods

Variable	2006, %	2016, %	*p* value
Overall, 30-day	9.7	15	0.036
Overall, 90-day	14	17	0.227
Overall, 1-year	25	28	0.312
Overall, 5-year	46	38	0.509

study period. Patients with variceal bleeding and preexisting liver cirrhosis experienced particularly poor outcomes.

Consistent with previous studies [1, 2], the incidence of AUGIB increases with age. Bleeding episodes were relatively uncommon in individuals aged less than 39 years. However, after the age of 40, the incidence nearly doubled every 20 years. In this study, the incidence exceeded 8 per 1,000 person-years in those aged 80 years or older. Consequently, the aging population poses a significant burden on healthcare systems due to the rising number of patients requiring hospitalizations, endoscopic procedures, and even endovascular interventions for management. In addition to hospitalizations, older patients often require ongoing medical management and follow-up examinations. Moreover, caregivers may experience productivity loss while providing support during hospitalization and recovery [10]. These factors contribute to increased healthcare costs and strain already limited resources [11]. Therefore, implementing preventive measures becomes crucial.

Standardized procedures have the potential to enhance outcomes. In our study hospital, management of gastrointestinal bleeding followed European guidelines [12]. However, there are cases that require a more tailored approach, especially when dealing with specific or rare conditions and coexisting diseases lacking sufficient evidence for standardized protocols [13]. Hence, a more tailored approach should be considered for some patients based on patient and disease-specific characteristics. Collaborative efforts among multidisciplinary teams may ensure comprehensive and coordinated care. Overall, earlier studies have reported improved outcomes associated with multidisciplinary approach [14, 15]. Early identification and risk stratification using systems such as the Glasgow-Blatchford Score [16] can further improve outcomes [17]. Minimizing waiting times for higher risk patients is important, as prompt interventions like endoscopic hemostasis significantly enhance patient outcomes [12].

Once appropriately performed endoscopic hemostasis is achieved, the focus should shift to long-term outcomes. Excluding short-term deaths, only 3% of patients died within 90 days. However, 1 year after the procedure, over one-sixth of patients had died, and at 5 years after endoscopy, forty percent of patients had died. Short-term deaths were primarily caused by underlying comorbidities, with only 2 patients dying due to continuous bleeding. Surprisingly, the youngest patients had the highest standardized mortality, likely due to the severity of their existing health conditions leading to bleeding. Individuals with a history of ongoing alcohol abuse had particularly poor outcomes. The debate revolves around whether lifestyle modifications can improve survival. In our study hospital, patients with a history of alcohol abuse received alcohol mini-interventions, and motivated patients were provided information on rehabilitation programs. Earlier studies have reported promising results

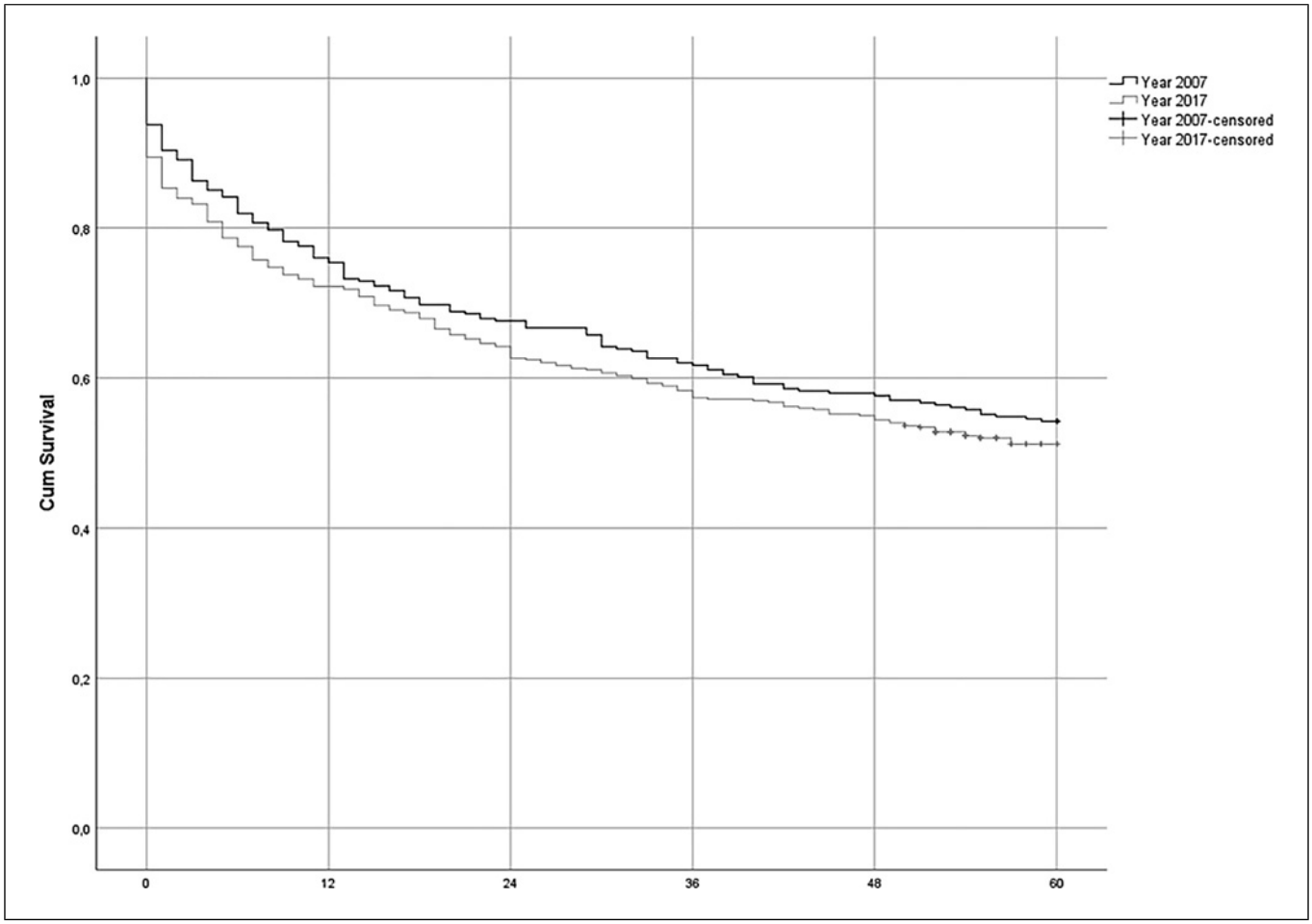

Fig. 2. Kaplan-Meier curve of survival, comparison between two study periods.

associated with lifestyle education [18–20]. However, AUGIB often manifests as a late manifestation of chronic alcohol abuse, with many of our study patients already suffering from a significant liver dysfunction before hospital admission. Consequently, the authors believe that interventions would be most beneficial if implemented before these manifestations occur. Nevertheless, patient education and lifestyle modifications may help reduce the risk of recurrence of AUGIB. Additional targets for patient education could include smoking cessation, weight management, and adopting healthy dietary practices [21]. Promoting healthy lifestyles and effectively managing comorbidities have the potential to reduce the incidence of bleeding episodes and alleviate the economic burden on healthcare systems. However, exploring improvements in later care for coexisting diseases falls beyond the scope of this study, necessitating further research on how our practices can mitigate patients' modifiable risk factors.

This study has a few limitations. First, it was a single-center retrospective study. However, all emergency endoscopies within the hospital district were performed at the study hospital, and follow-up data were available for all patients. We were unable to register exact time of the endoscopy; however, vast majority of endoscopies are performed during office hours, and only those with severe bleeding undergo endoscopy during on-call hours. Overall, the short-term mortality rate in this study was slightly worse than what was reported in earlier studies [6]. This difference could be attributed to patient selection, as our study hospital did not choose a palliative approach even for the most fragile patients. This may also explain an unexpected change in short-term mortality. A more conservative approach may have been chosen in the first cohort, which could also account for the lower number of endoscopies performed during that time period. The disparities in mortality rates were primarily observed within the first 30 days, after which the mortality rates remained largely similar. Patients undergoing endoscopy were preoperatively often assessed only by emergency physicians. Therefore, a multidisciplinary approach may help us evaluate who will benefit from endoscopy.

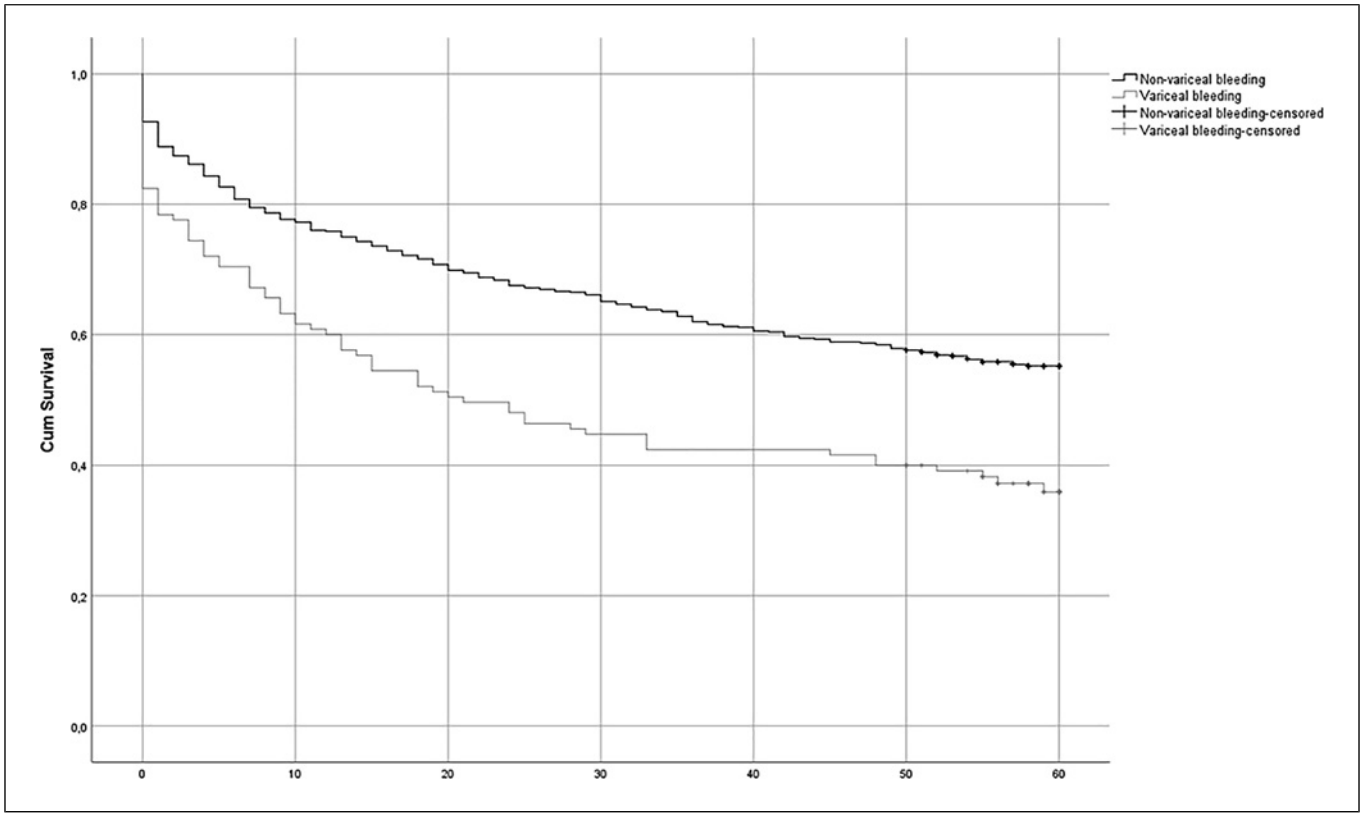

Fig. 3. Kaplan-Meier curve of survival, comparison of patients with variceal and non-variceal bleeding.

Conclusion

Long-term outcomes after AUGIB are dismal, and the majority of bleedings and deaths are associated with comorbidities and patients' lifestyle. During the two distinct study periods, the outcomes did not improve but remained practically similar.

Statement of Ethics

The study was performed according to the Helsinki Declaration. Due to retrospective nature of this study, this study did not require ethical approval in accordance with local/national guidelines. Written informed consent from participants was not required in accordance with local/national guidelines.

Conflict of Interest Statement

All the authors declare they have no conflicts of interest.

Funding Sources

This study was conducted without any external funding.

Author Contributions

Each author (Juho Luomajoki, Laura Mattila, Johanna Laukkarinen, and Mika Ukkonen) contributed in study design and writing of the final manuscript. Juho Luomajoki, Laura Mattila, and Mika Ukkonen contributed in data collection. Juho Luomajoki and Mika Ukkonen performed data analysis and contributed in writing of the initial manuscript. The study was supervised by Johanna Laukkarinen and Mika Ukkonen.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Vora P, Pietila A, Peltonen M, Brobert G, Salomaa V. Thirty-year incidence and mortality trends in upper and lower gastrointestinal bleeding in Finland. JAMA Netw Open. 2020;3(10):e2020172.

2 Hreinsson JP, Kalaitzakis E, Gudmundsson S, Björnsson ES. Upper gastrointestinal bleeding: incidence, etiology and outcomes in a population-based setting. Scand J Gastroenterol. 2013;48(4):439–47.

3 van Leerdam ME, Vreeburg EM, Rauws EA, Geraedts AA, Tijssen JG, Reitsma JB, et al. Acute upper GI bleeding: did anything change? Time trend analysis of incidence and outcome of acute upper GI bleeding between 1993/1994 and 2000. Am J Gastroenterol. 2003;98(7):1494–9.
4 Wuerth BA, Rockey DC. Changing epidemiology of upper gastrointestinal hemorrhage in the last decade: a nationwide analysis. Dig Dis Sci. 2018;63(5):1286–93.
5 Abougergi MS, Travis AC, Saltzman JR. The in-hospital mortality rate for upper GI hemorrhage has decreased over 2 decades in the United States: a nationwide analysis. Gastrointest Endosc. 2015;81(4):882–8.e1.
6 Jairath V, Martel M, Logan RF, Barkun AN. Why do mortality rates for nonvariceal upper gastrointestinal bleeding differ around the world? A systematic review of cohort studies. Can J Gastroenterol. 2012;26(8):537–43.
7 Crooks CJ, Card TR, West J. Excess long-term mortality following non-variceal upper gastrointestinal bleeding: a population-based cohort study. PLoS Med. 2013;10(4):e1001437.
8 Miilunpohja S, Jyrkkä J, Kärkkäinen JM, Kastarinen H, Heikkinen M, Paajanen H, et al. Long-term mortality and causes of death in endoscopically verified upper gastrointestinal bleeding: comparison of bleeding patients and population controls. Scand J Gastroenterol. 2017;52(11):1211–8.
9 Miilunpohja S, Kärkkäinen J, Hartikainen J, Jyrkkä J, Rantanen T, Paajanen H. Need of emergency surgery in elderly patients with upper gastrointestinal bleeding: survival analysis during 2009-2015. Dig Surg. 2019;36(1):20–6.
10 Keita Fakeye MB, Samuel LJ, Drabo EF, Bandeen-Roche K, Wolff JL. Caregiving-Related work productivity loss among employed family and other unpaid caregivers of older adults. Value Health. 2023;26(5):712–20.
11 Campbell HE, Stokes EA, Bargo D, Logan RF, Mora A, Hodge R, et al. Costs and quality of life associated with acute upper gastrointestinal bleeding in the UK: cohort analysis of patients in a cluster randomised trial. BMJ Open. 2015;5(4):e007230.
12 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(3):300–32.
13 Sung JJY, Laine L, Kuipers EJ, Barkun AN. Towards personalised management for nonvariceal upper gastrointestinal bleeding. Gut. 2021;70(5):818–24.
14 Loftus TJ, Go KL, Hughes SJ, Croft CA, Smith RS, Efron PA, et al. Improved outcomes following implementation of an acute gastrointestinal bleeding multidisciplinary protocol. J Trauma Acute Care Surg. 2017;83(1):41–6.
15 Lu Y, Loffroy R, Lau JY, Barkun A. Multidisciplinary management strategies for acute non-variceal upper gastrointestinal bleeding. Br J Surg. 2014;101(1):e34–50.
16 Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356(9238):1318–21.
17 Chen IC, Hung MS, Chiu TF, Chen JC, Hsiao CT. Risk scoring systems to predict need for clinical intervention for patients with nonvariceal upper gastrointestinal tract bleeding. Am J Emerg Med. 2007;25(7):774–9.
18 Mdege ND, Fayter D, Watson JM, Stirk L, Sowden A, Godfrey C. Interventions for reducing alcohol consumption among general hospital inpatient heavy alcohol users: a systematic review. Drug Alcohol Depend. 2013;131(1–2):1–22.
19 Havard A, Shakeshaft A, Sanson-Fisher R. Systematic review and meta-analyses of strategies targeting alcohol problems in emergency departments: interventions reduce alcohol-related injuries. Addiction. 2008;103(3):368–76; discussion 377–8.
20 Nagy R, Ocskay K, Váradi A, Papp M, Vitális Z, Izbéki F, et al. In-hospital patient education markedly reduces alcohol consumption after alcohol-induced acute pancreatitis. Nutrients. 2022;14(10):2131.
21 Kim SH, Yun JM, Chang CB, Piao H, Yu SJ, Shin DW. Prevalence of upper gastrointestinal bleeding risk factors among the general population and osteoarthritis patients. World J Gastroenterol. 2016;22(48):10643–52.