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Alimentary Tract

Time trends and outcome of gastrointestinal bleeding in the Veneto Region: A retrospective population based study from 2001 to 2010

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A R T I C L E I N F O

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A B S T R A C T

Background: Gastrointestinal bleeding is the most frequent emergency for gastroenterologists. Despite advances in management, an improvement in mortality is still not evident.
Aim: Determining time trends of gastrointestinal bleeding hospitalization and outcomes from 2001 to 2010 in the Veneto Region (Italy).
Patients and methods: Data of patients admitted with gastrointestinal bleeding from Veneto regional discharge records were retrospectively evaluated. Chi-squared and multivariate logistic regression model were used.
Results: Overall, 44,343 patients (mean age 64.2 ± 8.6 years) with gastrointestinal bleeding were analysed: 23,450 (52.9%) had upper, 13,800 (31.1%) lower, and 7093 (16%) undefined gastrointestinal bleeding. Admission rate decreased from 108.0 per 100,000 in 2001 to 80.7 in 2010, mainly owing to a decrease in upper gastrointestinal bleeding (64.4 to 35.9 per 100,000, $p < 0.05$). Reductions in hospital fatality rate (from 5.3% to 3%, $p < 0.05$), length of hospital stay (from 9.3 to 8.7 days, $p < 0.05$), and need for surgery (from 5.6% to 5%, $p < 0.05$) were observed. Surgery (OR: 2.97, 95% CI: 2.59–3.41) and undefined gastrointestinal bleeding (OR: 2.89, 95% CI: 2.62–3.19) were found to be risk factors for mortality.
Conclusions: Patient admissions for gastrointestinal bleeding decreased significantly over the years, owing to a decrease in upper gastrointestinal bleeding. Improved outcomes could be related to regional dedicated clinical gastroenterological management.

1. Introduction

Gastrointestinal bleeding (GIB) is the most probable reason for emergency hospital admission for patients with a gastrointestinal disorder and still remains an important cause of both morbidity and mortality.

The incidence of upper GIB has been estimated to be about 100 out of 100,000 cases per year and its incidence is approximately five times more than that of lower GIB [1,2]. Recent studies reported a decreasing trend of upper GIB incidence along with a slightly increasing trend of lower GIB incidence [3–5].

Over the last decades, endoscopy has become the linchpin for diagnosis, treatment, and risk categorization of GIB. According to the international guidelines [6–9], in acute GIB, early endoscopy allows to deliver prompt therapy to both active bleeding and high-risk stigmata. In the years 2003–2004 and 2007–2008, two Italian multicentre prospective observational studies highlighted the importance of endoscopic treatment in improving GIB outcomes [10,11]. Furthermore, administrative data from a population-based study from the Lazio Region (Centre of Italy) reported not only the protective effect of endoscopic procedures, but also the key role of specialist care in reducing the mortality rate [12]. However, in the last two decades, despite the improvement of clinical gastroenterological bleeding management, several international studies still failed to demonstrate a significant improvement in overall mortality [3,13,14]. Conversely, an Italian single-centre study from the Veneto Region, comparing the years 1983–1985 and 2002–2004, published an observational report of patients with upper GIB that showed a significant reduction of its incidence and improved outcomes, such as a decrease in mortality, re-bleeding rates, and need for surgery (NFS) [15]. Although widely studied, there is still insufficient evidence for the proper management of GIB, as well as for the best outcome predictor of GIB. In the present investigation, we

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aimed to evaluate the time trend and outcomes of GIB in the Veneto Region during the period 2001–2010.

2. Methods

2.1. Source of data

Administrative data on the resident population of Veneto discharged from public and academic hospitals, as well as from accredited private hospitals, with a diagnosis indicative of GIB between January 2001 and December 2010, were retrospectively collected. The hospital discharge records (HDRs) database, which included demographic data, surgery or medical procedures performed during hospitalization and both admission and discharge data, was queried according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

The Veneto Region, located in the North-East of Italy, has a resident population of 4,912,438 inhabitants (1st January 2010, data from the National Institute of Statistics, ISTAT). It is divided into 21 health districts (local health units) with 55 hospitals with emergency departments and 24 with Gastroenterology Units, of which 85% with an "out-of-hours" emergency endoscopy on-call rota.

All hospital discharge records were retrieved according to the following characteristics: (1) yearly admissions to hospitals in the Veneto Region between 2001 and 2010; (2) residents with a diagnosis indicative of GIB, including those requiring surgery according to the ICD-9-CM codes (see Appendix A). Cases were also included if the diagnosis indicative of GIB followed a primary diagnosis of haematemesis (ICD-9-CM code 578.0), blood in the stools (ICD-9-CM code 578.1), or unspecified haemorrhage of the gastrointestinal tract (ICD-9-CM code 578.9). Cases were excluded if the secondary discharge diagnoses included any of the following: pregnancy, birth, puerperium (major ICD-9-CM diagnosis categories: 11 and 14), or trauma (ICD-9-CM codes 800–999).

2.2. Data analysis and statistical comparisons

Patients included in the study were arbitrarily divided according to gender and the following nine classes of age (in years): less than 1, 1–5, 6–14, 15–24, 25–44, 45–64, 65–74, 75–84, and 85 or more. In order to calculate the overall regional rate of hospitalizations for GIB, the reference population considered was the mean number of residents in Veneto between 2001 and 2010: 4,713,312 inhabitants (data from ISTAT). Conversely, the time trend of incidences (overall, upper, lower, and undefined GIB) were calculated referring to the specific resident population of each year (data from ISTAT).

Case fatality rate for GIB was defined as the proportion of in-hospital deaths among the total number of hospitalizations for GIB. Causes of death, as well as patient comorbidities, were not available in the database. Furthermore, the database distinguished surgical from medical treatment, but was not able to identify interventional radiology, which was included into the medical procedure. NFS was defined as the percentage of patients submitted to surgery among all GIB hospitalized patients.

Comparisons between GIB overall incidence and gender were calculated by using the chi square test. Similarly, outcomes (case fatality and length of hospital stay), type of treatment (surgical versus medical), and site of bleeding (upper, lower, and undefined) were compared by means of the same statistical test.

Time trend of both incidence and outcomes were analysed using the chi square test.

A multivariate logistic regression model was used to assess the impact of gender, surgery, and diagnosis (upper, lower, and undefined GIB) on intra-hospital mortality (odds ratio (OR), 95% confidence intervals (CI)).

Statistical analyses were performed with the Epi Info™ version 3.5, 2011 software. p-Values less than 0.05 were considered statistically significant.

3. Results

In the studied period, 44,343 residents (55% males, mean age 64.2 ± 8.6 years) in Veneto were admitted to the hospitals for GIB. Overall, 23,450 patients (53%) had an upper GIB, 13,800 (31%) a lower GIB, and 7093 (16%) had an undefined GIB. Gastric and/or duodenal peptic ulcer accounted for the majority (58%) of upper GIBs, gastritis or duodenitis for 16% of them, and gastro-oesophageal varices for only 6%. Colonic diverticula and anorectal diseases represented about 60% of the overall lower GIBs.

3.1. Incidence per year per 100,000 inhabitants

The overall incidence of admissions for GIB was 94 per 100,000 inhabitants. Incidence was significantly higher in men (105.7 per 100,000) than in women (83.0 per 100,000, $p < 0.05$), with the highest incidence in the oldest age group (≥85 years) for both men (930.4 per 100,000) and women (714.0 per 100,000) (Table 1). Upper, lower, and undefined GIB had the following incidence rates: 49.8 per 100,000, 29.3 per 100,000, and 15.0 per 100,000, respectively. Upper GIB incidence was higher in men than in women (60.5 vs 39.5 per 100,000, $p < 0.05$) and the opposite was observed for lower GIB incidence (29.9 per 100,000 in women vs. 28.6 per 100,000 in men, $p < 0.05$) (Table 2).

The incidence of all hospitalizations for GIB decreased over the years from 108.0 per 100,000 inhabitants in 2001 to 80.7 in 2010 (p-value for trend <0.05), with the same significant time trend in male and female patients (Fig. 1).

The incidence of upper GIB markedly decreased over the years from 64.4 per 100,000/year to 35.9 per 100,000/year ($p < 0.05$), whereas lower GIB showed a small, non significant, increase (from 27.3 per 100,000/year to 30.6 per 100,000/year) and undefined GIB remained stable (Fig. 2).

3.2. Length of hospital stay

The mean length of hospital stay (LOS) for all causes of GIB was 8.8 days (Table 1). In both men and women, LOS significantly increased with age: from 6 days in younger patients (25–44 years old), to 9.9 days in patients older than 75 years ($p < 0.05$). From 2001 to 2010, the mean LOS significantly decreased from 9.3 to 8.7 days ($p < 0.05$).

The LOS significantly increased in patients who performed a surgical procedure ($p < 0.05$) in both genders and all sites of bleeding. Furthermore, LOS was significantly higher when surgery was performed in patients with upper GIB than in those with lower GIB (18.2 vs 11.2 days, $p < 0.05$) (Table 2).

3.3. Need for surgery and case fatality

The overall NFS for GIB was 5.0% (Table 1), without differences between genders, and showed two peaks in the age classes 25–44 years (9%) and 45–64 years (8%). NFS slightly decreased from 5.6% in 2001 to 5.0% in 2010 ($p < 0.05$) (Fig. 3).

Overall case fatality rate was 4.4%. Case fatality in both genders significantly increased from 1.2 to 2.0% in younger patients (25–44 years) to 8.5–9% in patients older than 75 years ($p < 0.05$) (Table 1).

Case fatality in patients with upper GIB was significantly higher for those who performed surgical rather than medical treatment (16.9 vs 3.6%, $p < 0.05$; OR 4.49, 95% CI: 3.79–5.32). Conversely, no significant difference was observed in patients with lower GIB

Table 1
Overall (from 2001 to 2010) hospitalized incidence rates, case fatality, need for surgery and mean length of hospital stay for gastrointestinal bleeding according to age group and gender.

	Cases (n)	Incidence rate per 100,000 inhabitants	Case fatality (%)	NFS (%)	LOS (days)
Age group (years) by gender					
Male					
All cases	24,355	105.7*	4.1	5.0	8.4
<1 year	106	45.4	0	2.0	3.4
01–05	229	19.9	0	2.0	2.9
06–14	225	11.4	0	3.0	3.3
15–24	289	12.5	1.0	4.0	5.1
25–44	2110	27.6	1.2	9.0	6.2
45–64	6302	103.0	3.1	8.0	7.7
65–74	6045	277.3	3.8	6.0	8.8
75–84	6455	547.9	5.0	5.0	9.6
≥ 85	2594	930.4	8.5	3.0	9.5
Female					
All cases	19,988	83.0*	4.8	4.9	9.2
<1 year	109	49.5	0	1.8	3.2
01–05	133	12.5	1.0	2.3	3.5
06–14	213	11.5	0	3.3	2.9
15–24	128	5.8	0	3.9	4.4
25–44	764	10.6	2.0	9.0	5.9
45–64	2624	42.6	3.0	7.6	7.8
65–74	3571	138.5	3.0	5.9	9.2
75–84	6847	348.9	4.0	4.5	10.1
≥85	5599	714.0	9.0	2.9	9.8
Overall cases	44,343	94.1	4.4	5.0	8.8

* $p < 0.05$.
NFS, need for surgery; LOS, mean length of hospital stay.

Table 2
Overall (from 2001 to 2010) hospitalized incidence rates, case fatality and mean length of hospital stay according to the site of gastrointestinal bleeding, gender and medical or surgical discharge.

	Upper GIB				Lower GIB				Undefined GIB			
	Cases[a]	Incid[b]	LOS[c]	Fatality[d]	Cases[a]	Incid[b]	LOS[c]	Fatality[d]	Cases[a]	Incid[b]	LOS[c]	Fatality[d]
Male												
All cases	13,948	60.5#	8.9	3.9	6596	28.6+	7.1	1.6	3811	16.5	8.8	8.9
Medicine	13,235	57.4	8.5	3.4	6133	26.6	6.9	1.6	3642	15.8	8.5	8.6
Surgery	713	3.1	17.2	15	463	2.0	9.2	1.5	169	0.7	16.7	16.6
Female												
All cases	9502	39.5#	9.9	4.8	7204	29.9+	8.2	2.1	3282	13.6	9.4	10.8
Medicine	9044	37.6	9.4	4.0	6818	28.3	7.9	2.0	3155	13.1	9.1	10.3
Surgery	458	1.9	19.8	19.9	386	1.6	13.6	3.1	127	0.5	16.3	23.6
Overall												
All cases	23,450	49.8	9.3	4.3	13,800	29.3	7.7	1.8	7093	15.0	9.1	9.8
Medicine	22,279	47.3	8.9	3.6*	12,951	27.5	7.4	1.8	6797	14.4	8.8	9.3
Surgery	1171	2.5	18.2♦	16.9*°	849	1.8	11.2♦	2.2°	296	0.6	16.6	19.6

GIB, gastrointestinal bleeding; Incid, hospitalized incidence rates, LOS, mean length of hospital stay.
[a] Number of cases (n).
[b] Incidence rate (per 100,000 inhabitants).
[c] Mean length of hospital stay (days).
[d] Case fatality (%).
#,+,♦,°,* $p < 0.05$. Comparisons are performed between parameters with the same symbols.

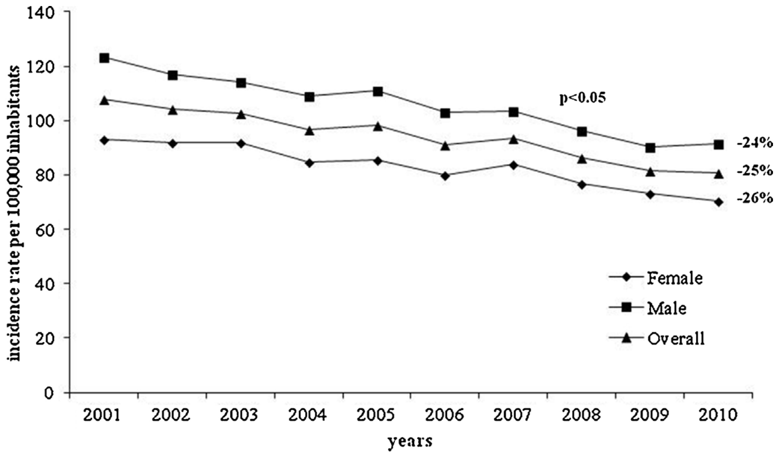
(surgery, 2.2%; medical treatment, 1.8%). Consequently, considering the patients who performed surgical treatment, case fatality was higher in patients with upper than lower GIB (16.9 vs 2.2%, $p < 0.05$; OR 8.89, 95% CI: 5.39–14.82) (Table 2).

According to a multivariate logistic model, male gender (OR: 1.27; 95% CI: 1.25–1.29), undefined GIB (OR: 2.89; 95% CI: 2.62–3.1), and surgery (OR: 2.97; 95% CI: 2.59–3.41) were identified as risk factors for mortality.

Case fatality rate for all GIBs decreased over the decade from 5.3% to 3.0% (p-value for trend <0.05) (Fig. 3).

4. Discussion

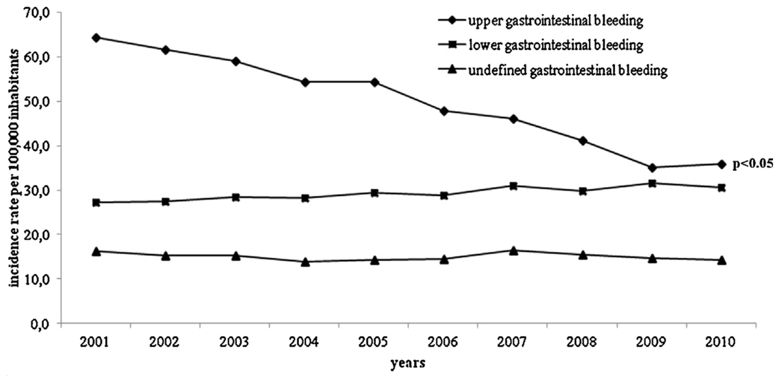
This study represents the largest Italian report on patients hospitalized for all causes of GIB. Previously published Italian studies in this field are mainly on upper GIB, and are based on analyses of a single hospital cohort [15] or multicentre registry data [10,16]. Only one study, using administrative data, presented a description of an Italian region (Lazio), but it analysed a shorter interval of time and did not compare both upper and lower GIBs' outcomes [12]. In the present study, we observed a reduced incidence of GIB by 25% over the decade 2001–2010. This was mainly related to a marked reduction of upper GIB (−45%). Conversely, lower GIB slightly increased (+11%), and undefined GIB remained stable over the years. These findings confirm recent reports from a large Spanish population-based study that described a significant decreasing time trend, from 1996 to 2005, of upper GIB, and a small but significant increase in lower GIB [3]. Last year, Laine et al. published a study from an American inpatient database that confirmed the drop of hospitalizations for upper GIB events and the marginal, non-significant increased



Cases

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Female	2166	2139	2155	2014	2055	1928	2046	1896	1824	1765
Male	2739	2583	2551	2472	2557	2391	2418	2281	2162	2201
Overall	4905	4722	4706	4486	4612	4319	4464	4177	3986	3966

Fig. 1. Hospitalized incidence rates for gastrointestinal bleeding (per 100,000 inhabitants) from 2001 to 2010 according to the gender (*p*-value for trend <0.05 for overall, male and female).



Cases

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Female	2166	2139	2155	2014	2055	1928	2046	1896	1824	1765
Male	2739	2583	2551	2472	2557	2391	2418	2281	2162	2201
Overall	4905	4722	4706	4486	4612	4319	4464	4177	3986	3966

Fig. 2. Hospitalized incidence rates for gastrointestinal bleeding (per 100,000 inhabitants) according to the bleeding source from 2001 to 2010 (*p*-value for trend <0.05 for upper gastrointestinal bleeding).

incidence of lower GIB in the decade 2001–2009 [5]. These changes in GIB epidemiology are probably due to the wide spread of both educational and prevention programmes, such as the eradication of *Helicobacter pylori* infection and the use of proton pump inhibitors (PPIs) in non-steroidal anti-inflammatory drugs (NSAIDs). Since these factors have no therapeutic effect beyond the duodenum, this could justify the stable rate of lower GIB.

The value of prevention strategies could also be limited by population-related factors (such as age, comorbidities, social conditions, and habits) [17–19]. The present study confirmed the impact of age on the incidence of GIB, with an approximately ninefold higher incidence of GIB in the population of 85-year-olds or older.

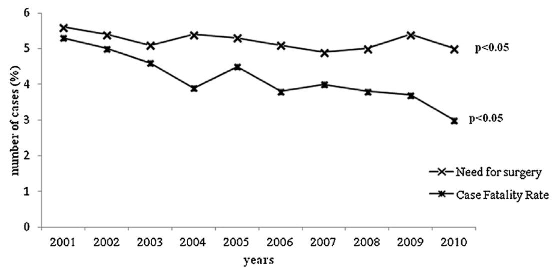


Fig. 3. Case fatality rate and need for surgery for gastrointestinal bleeding from 2001 to 2010 (*p*-value for trend <0.05).

Outcomes of GIB (length of hospital stay, NFS, and mortality) are linked to patient-related factors, GIB severity index, and quality of the health care system. In spite of the advances in clinical gastroenterological bleeding management, several large observational studies published in the last two decades failed to show a decrease in mortality [3,13,14]. Increasing age and comorbidities, in fact, could limit the effect of the improvements in health care [20]. A large case-control study of all patients admitted for upper GI haemorrhage to the NHS hospitals in England during the period 1999–2007 (about 500,000 cases) reported a decrease in the overall 28-day mortality. This decreasing trend was maintained even when results were adjusted for age and comorbidities [21]. The controversial literature data [3,13–15,19,21–23] could be related to the different number of enrolled cases as well as to the different population characteristics over the years in terms of age, gender, social conditions, and comorbidities. Our results report a significant improvement in GIB outcomes over the years, such as reduced in-hospital case fatality rate (from 5.3% to 3%), NFS (from 5.6% to 5%), and length of hospital stay (from 9.3 to 8.7 days). Assuming that our population did not considerably change over the study period, one could suppose that the improved results reflect the health organization in Veneto. In fact, in Veneto the health organization provides a dedicated management of GI bleeders ensuring an early endoscopy (within 24 h of admission) to 85% of the population, thanks to a capillary distribution of endoscopy units with an out-of-hours service.

Improved outcomes were also reported in a study from a single hospital cohort located in Veneto, which compared patients with upper GIB between the years 1983–1984 and 2002–2004 [15]. In this study, the early endoscopy rate increased significantly between the two periods analysed, reaching 88% in 2002–2004. Recently, a British survey based on hospitalized patients with upper GIB in 2007 showed that only 52% of British hospitals provided an emergency out-of-hours endoscopy service, underling the difficulties to promote the diffusion of on-call rota gastroenterological bleeding teams in a “real-life” context [22].

The present study showed that need of surgery and undefined source of bleeding are significant risk factors for mortality in GIB events. These factors are strictly related to the limitations of diagnostic and therapeutic endoscopy, as demonstrated by an Italian prospective multicentre study [11]. Particularly, we observed that the impact of surgical treatment on mortality was significant in patients with upper and undefined GIB, but not in lower GIB. One can hypothesize that an easier surgical approach, as well as a better identified source of bleeding, in colonic rather than gastrointestinal sites could improve the outcomes.

Despite the extensive number of cases collected during the ten years considered, our study has some limitations. The study refers to in-hospital mortality, whereas the 30-day mortality after discharge was not included. Furthermore, our database did not take into account patients’ comorbidities. In spite of these limitations, the analysis of administrative clinical data remains a powerful tool for supporting regional clinical gastroenterological management in the effort to improve the quality of medical care and assess the appropriateness of both diagnostic and therapeutic approaches according to practical guidelines.

In summary, the present study described GIB hospitalizations in a whole Italian region (Veneto Region) over the first decade of the new millennium, showing a decreasing incidence in overall GIB, which is mainly determined by a drop of upper GIB hospitalizations. Similarly, over the years, the NFS and in-hospital mortality rate decreased, demonstrating that the costs of maintaining a complex health organization, including an out-of-hours endoscopy service, is beneficial.

Conflict of interest statement

All the authors have no conflict of interest to disclose.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dld.2013.11.005.

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