Clinical Backgrounds and Outcomes of Elderly Japanese Patients with Gastrointestinal Bleeding

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Abstract

Objective  Elderly gastrointestinal bleeding (GIB) patients sometimes cannot be discharged home. In some cases, they die after hemostasis, even following appropriate treatment. This study investigates the clinical backgrounds and outcomes of elderly Japanese GIB patients.

Methods  The medical records of 185 patients (123 men, 62 women; mean age 68.2 years; range 10-99 years) with GIB symptoms who underwent esophagogastroduodenoscopy or colonoscopy to detect or treat the source of GIB were retrospectively reviewed. We compared the outcomes between patients ≤70 (n=85) and >70 (n=100) years. The clinical backgrounds of the patients who died or changed hospitals to undergo rehabilitation or receive palliative care were evaluated, as were the association of four factors with these poor outcomes: GIB (re-bleeding or uncontrolled bleeding), endoscopic procedure-related complications, exacerbation of the pre-existing comorbidity, and any complications that were not directly related to GIB.

Results  Of the patients ≤70 and >70 years of age, three (3.5%) and 17 (17.0%), respectively, were transferred to another hospital (p=0.003). One (1.2%) and five (5.0%), respectively, died (p=0.144). All three patients ≤70 years old that changed hospitals did so because their comorbidities became worse. The reasons for changing hospitals in the 17 patients >70 years of age included exacerbation of a pre-existing comorbidity (41.1%, 7/17), other complications (35.4%, 6/17), GIB itself (17.6%, 3/17), and endoscopic procedure-related complications (5.9%, 1/17).

Conclusion  Although non-elderly and elderly GIB patients had similar mortality rates, many more elderly patients could not be discharged home for various reasons.

Key words: elderly, gastrointestinal hemorrhage, complication, treatment outcome

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Introduction

The expanding elderly population and the current incidence of gastrointestinal bleeding (GIB) are both common problems worldwide. Despite improvements in pharmacological and endoscopic hemostasis (1-8), GIB remains a serious, and at times, even a fatal clinical event in elderly patients. 90% of acute GIB deaths occur in patients over 65 years of age (9), and more than 1% of individuals over 80 years of age are hospitalized for GIB every year (10). Moreover, GIB is associated with higher rates of morbidity and mortality in elderly than in younger individuals (11-14). Morbidity and mortality due to GIB in elderly individuals have been shown to depend on the nature of the bleeding lesion (15, 16), the use of various drugs [e.g., antithrombotic drugs, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids] (17-22), and the presence of pre-existing comorbidities (23-26).

In daily clinical practice, many elderly patients cannot be discharged home after successful hemostasis for various reasons. Even following appropriate GIB treatment procedures, some elderly patients develop unexpected complications, which cause further problems. These patients’ physical func-

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tioning may worsen; many may require longer hospital stays. These patients often are transferred to another facility to undergo rehabilitation or receive palliative care. Some are later relocated to institutions that provide nursing care for elderly individuals, thereby increasing health care costs in already-expensive health care environment.

Japan has one of the most rapidly aging populations in the world, with over 20% of the current population 65 years of age or older. However, few reports have so far evaluated the effects of clinical characteristics on the GIB outcomes. As the elderly population continues to increase, clinicians, especially endoscopists, will be more likely to treat elderly patients. This study investigated the backgrounds and clinical outcomes of elderly Japanese patients with GIB in daily clinical practice.

Materials and Methods

This analysis defined patients over 70 years of age as elderly. Medical records from the Department of Gastroenterology at Tokyo Medical University were retrospectively evaluated to identify patients with GIB symptoms (e.g., hematemesis, hematochezia, tarry stool, anemia) who underwent either esophagogastroduodenoscopy (EGD) or colonoscopy (CS) between April 1, 2012, and March 10, 2014, to detect or treat the source of GIB. The decision to perform EGD or CS was based on clinical symptoms, with EGD performed in patients with upper GIB (UGIB) (e.g., hematemesis, tarry stool) and CS performed in patients with lower GIB (LGIB) (e.g., hematochezia).

In addition to evaluating the patients who underwent emergency endoscopy, this study evaluated patients who underwent scheduled endoscopy and those who developed GIB both in hospital and out of hospital. Patients who developed GIB in a hospital included those hospitalized for both gastroenterological diseases and diseases of other organ systems (e.g., cerebral infarction, ischemic heart disease, renal disease, dementia/mental conditions, malignancy). Patients whose source of bleeding was the oral cavity, small intestine, or anus, patients with undetermined lesions, and patients who underwent follow-up endoscopy of bleeding lesions detected or treated previously were excluded.

The causes of GIB vary in clinical practice. The rate of postoperative bleeding is particularly increasing, as more patients are undergoing therapeutic endoscopy [e.g., endoscopic submucosal dissection (ESD), and endoscopic mucosal resection (EMR)] for early malignant lesions in the gastrointestinal tract (27-35).

Despite variations in the bleeding rates, the post-ESD bleeding rate has been reported to be equal to or higher than the post-EMR bleeding rate (27-34). Postoperative bleeding has been reported to occur in approximately 5.3-16.5% of patients after gastric ESD (28-31) and in 4.4% after colorectal ESD (34). In most patients, postoperative bleeding can be successfully treated by endoscopic hemostasis, although one UGIB study reported no significant differences in the rates of re-bleeding and uncontrolled bleeding requiring surgical hemostasis between patients with peptic ulcer and postoperative ulcer (35). Many elderly GIB patients are treated with antithrombotic drugs; research shows that their use is an independent risk factor for delayed postoperative bleeding (30). Therefore, patients with this type of iatrogenic bleeding were included in this study.

We compared the clinical outcomes between elderly and non-elderly patients. We determined four outcome categories: (1) death, (2) changing hospitals, (3) discharge to home, (4) healing in ambulatory care, and (5) others, with the latter including patients who changed hospitals for reasons such as a lack of vacancy to receive special therapy.

All patients in this study lived independently at home before admission, though detailed data on activities of daily living (ADL) were unavailable. Thus, patients who lost the functional capacity necessary for discharge to home were classified as changing hospitals. These patients were transferred to another hospital to undergo rehabilitation, receive palliative care, or have specialized nursing care post-GIB treatment.

The causes of changing hospitals were classified into four categories: (1) GIB itself (e.g., re-bleeding, uncontrolled bleeding), (2) endoscopic procedure-related complications, (3) exacerbation of a pre-existing comorbidity, and (4) all other complications, with the latter defined as complications not directly related to bleeding or endoscopic procedures nor an exacerbation of a pre-existing comorbidity. The causes of mortality were also compared.

The following patient characteristics were evaluated: GIB causes, prescribed agents, pre-existing comorbidities, and onset (out of hospital/during hospital stay). Comorbidities investigated included congestive heart failure, osteoarthritis, connective tissue disease, renal disease, liver disease, hematologic disease, respiratory disease, dementia/mental illness, diabetes mellitus, malignancy, cerebral infarction/transient ischemic attack or carotid/intracranial large artery atherosclerosis, ischemic heart disease, arteriosclerosis obliterans, cardiogenic cerebral embolism, atrial fibrillation, and deep venous thrombosis/pulmonary embolism. Use of the following drugs was recorded: non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents (e.g., aspirin, clopidogrel, cilostazol, ticlopidine, prostaglandin preparations, sarpogrelate), anticoagulants (e.g., warfarin), and corticosteroids (e.g., cortisone, hydrocortisone, prednisone).

All characteristics were compared between elderly and non-elderly patients, as well as between elderly patients who were discharged home and those who either changed hospitals or died.

Statistical analysis

Statistical analyses were conducted using the \( \chi^2 \) test or Mann-Whitney U test. We considered a \( p \) value under 0.05 to be statistically significant.
Table 1. Characteristics of the 185 Patients.

|                      | Non-elderly (n=85) | Elderly (n=100) | p     |
|----------------------|--------------------|-----------------|-------|
| Age (years)          | 55.0±11.7          | 79.5±6.4        | <0.01 |
| Sex (M/F)            | 67/18              | 56/44           | 0.001 |
| UGIB/LGIB            | 51/34              | 59/41           | 0.890 |
| Hemoglobin level (g/dL) | 10.6±3.3          | 9.0±2.4         | 0.002 |
| Presence of pre-existing comorbidity (%) | 53 (62.4%) | 90 (90.0%) | <0.001 |
| 1                    | 27                 | 31              | 0.911 |
| 2                    | 15                 | 36              | 0.005 |
| ≥3                   | 11                 | 23              | 0.078 |
| Use of NSAIDs, antiplatelet drugs, anticoagulants, or corticosteroids (%) | 29 (34.1%) | 59 (59.0%) | <0.001 |
| 1 drug               | 25                 | 41              | 0.101 |
| 2 drugs              | 4                  | 13              | 0.052 |
| ≥3 drugs             | 0                  | 5               | 0.037 |
| Use of H2RA or PPI (%) | 33 (38.8%)       | 50 (50.0%)      | 0.128 |
| Onset                |                    |                 |       |
| Out of hospital/During hospital stay | 62/23    | 64/36           | 0.194 |

Data are shown as the mean±standard deviation. Significant p values are shown in bold.

UGIB: upper gastrointestinal bleeding, LGIB: lower gastrointestinal bleeding, H2RA: H2 receptor antagonists, PPI: proton pump inhibitor, NSAIDs: non-steroidal anti-inflammatory drugs

Results

The study cohort included a total of 185 patients (123 men and 62 women) who underwent endoscopy (mean age 68.2 years and range 10-99 years); of these, 100 (54.0%) patients were >70 years of age. A total of 112 patients (60.5%) underwent endoscopic (n=110) or angiographic (n=2) hemostasis, with none undergoing surgery for hemostasis. Sources of bleeding were UGIB in 110 patients and LGIB in 75. GIB developed in 126 outpatients, with 83 (65.9%) of these hospitalized urgently after endoscopy. The other 59 patients developed GIB during their hospital stay.

The characteristics of elderly patients and non-elderly patients are shown in Table 1, and their pre-existing comorbidities in Table 2. Comorbid diseases (p<0.001); a low hemoglobin level (p=0.002); and the use of NSAIDs, antithrombotic agents, anticoagulants, or corticosteroids (p<0.001) were significantly more frequently observed in elderly patients than non-elderly ones with GIB. Pre-existing comorbidities were common in elderly patients, but only liver disease was more common in non-elderly patients.

Figs. 1 and 2 show the sources of UGIB and LGIB, respectively, in non-elderly and elderly patients. The most frequent cause of UGIB in elderly patients was gastric ulcer (47.5%), followed by duodenal ulcer (13.6%). The most common cause of LGIB in elderly patients was rectal ulcer (41.5%), followed by diverticulosis (24.4%). In non-elderly patients, however, the most common causes of UGIB were gastric ulcer (19.6%) and duodenal ulcer (19.6%). The most common cause of LGIB in non-elderly patients was post-ESD/EMR bleeding (26.5%), followed by lower gastrointestinal malignancy (20.6%) and diverticulosis (17.6%).

Clinical outcomes

We compared the clinical outcomes of non-elderly (n=85) and elderly patients (n=100) (Fig. 3). After GIB treatment, three non-elderly and 17 elderly patients changed hospitals (3.5% vs. 17.0%; p=0.003). However, the mortality rates were similar in non-elderly and elderly patients (1.2% vs. 5.0%; p=0.144). Delayed endoscopic hemostasis can also change outcomes, but no significant difference existed between non-elderly and elderly patients in the mean time from the initial detection of GIB symptoms to endoscopic intervention (1.362±2.3 vs. 3.183±5.9 days; p=0.120).

The detailed causes of death or changing hospitals in 140 non-elderly and elderly patients who either were hospitalized for GIB or developed GIB during their hospital stay are shown in Table 3. The two patients who changed hospitals for reasons such as lack of a vacancy to receive special therapy were excluded. Comorbidity exacerbation was the most frequent cause for changing hospitals or death in both the elderly and non-elderly groups. Elderly patients changed hospitals for various reasons, the most frequent being “any other complications.”

We also compared the patient characteristics between elderly patients discharged home (n=60) and ones who changed hospitals or died post-endoscopy (n=22) (Table 4). The factors that were significantly more frequently identified in the latter group included occurrence of hemodynamic shock (p=0.008); use of NSAIDs, antiplatelet agents, anticoagulants, or corticosteroids (p=0.007); the presence of more than three pre-existing comorbidities (p=0.035); and the occurrence of GIB during hospital stay (p=0.005). However, there were no significant differences in age and multiple drug usage.

Discussion

This study details the poor outcomes of elderly patients hospitalized for GIB in daily clinical practice. Compared with younger patients, elderly patients tended to be unable to perform the ADL necessary for hospital discharge to
Table 2. Patients with Pre-existing Comorbidities (n=185).

| Pre-existing comorbidities                        | Non-elderly (53/85) | Elderly (90/100) | p     |
|--------------------------------------------------|----------------------|------------------|-------|
| 1. Congestive heart failure                       | 7                    | 7                | 0.751 |
| 2. Osteoarthritis                                | 10                   | 25               | 0.022 |
| 3. Connective tissue disease                     | 1                    | 1                | 0.907 |
| 4. Renal disease                                 | 3                    | 13               | 0.022 |
| 5. Liver disease                                 | 12                   | 5                | 0.032 |
| 6. Hematologic disease                           | 5                    | 5                | 0.791 |
| 7. Respiratory disease                           | 2                    | 10               | 0.035 |
| 8. Dementia/mental disease                       | 7                    | 19               | 0.035 |
| 9. Diabetes mellitus                             | 16                   | 36               | 0.009 |
| 10. Malignancy                                   | 11                   | 8                | 0.269 |
| Pre-existing comorbidity requiring antithrombotic agents |                      |                  |       |
| Cerebral infarction/TIA or carotid/intracranial large artery atherosclerosis | 3                    | 16               | <0.001|
| Ischemic heart disease                           | 3                    | 15               | 0.018 |
| Arteriosclerosis obliterans                      | 1                    | 7                | 0.052 |
| Cardiogenic cerebral embolism                    | 1                    | 1                | 0.702 |
| Atrial fibrillation                              | 8                    | 9                | 0.923 |
| Deep venous thrombosis/pulmonary embolism        | 1                    | 3                | 0.395 |

Significant p values are shown in bold.
TIA: transient ischemic attack

Additionally, they were more likely to change hospitals in order to undergo rehabilitation or receive palliative care after GIB treatment. However, the non-elderly and elderly mortality rates did not differ significantly. Several studies from abroad have reported that aging is a risk factor for post-GIB mortality (11-14); however, Japanese studies have reported that aging was not related to the prognosis in GIB patients (36, 37).

The lack of any effect of age on mortality in Japanese patients may be due to the high clinical level of hemostatic procedures in Japan. The rate of successful hemostasis in Japan has generally been reported to be over 95% due to improvements in hemostatic procedures (38-41). Indeed, all hemostasis treatments in this study were ultimately successful, even in patients with uncontrolled bleeding or who experienced bleeding again. This outcome may be specific to elderly patients with GIB in Japan. Ultimately, any GIB can be cured, but it may seriously affect elderly patients’ physical capability or general condition. Many patients who were treated successfully may require long-term treatment and become bedridden, resulting in a discrepancy between the hemostatic and clinical outcomes in elderly patients. Although the main goal of GIB treatment is to save lives, appropriate hospital discharge is important for both the quality of life of elderly patients and for health care economics. Preventing elderly people from becoming limited in performing ADL is essential, too.

Similar to previous studies, this study found the main cause of death to be an exacerbation of a pre-existing comorbidity (23-26). Moreover, elderly patients frequently changed hospitals for various reasons, including GIB itself, endoscopic procedure-related complications, an exacerbation of pre-existing comorbidities, and other complications, with the latter being the most common. Seven elderly patients (8.5%, 7/82) changed hospitals after developing other complications, including congestive heart failure (n=2), cytomegalovirus colitis (n=1), pneumonia (n=1), pyelonephritis (n=1), pseudomembranous colitis (n=1), and cholecystitis (n=1). Although the causes of these complications are unclear, they may be due to the generally fragile health status of elderly patients, such as weakened pulmonary and respiratory functions and immune systems. Regardless, these findings demonstrate that various unexpected complications can develop following GIB treatment in elderly patients. Clinicians should therefore be prepared to manage unpredicted complications following treatment of GIB.

Poor outcomes in elderly patients may also vary according to the cause of bleeding. This study found that a frequent cause of LGIB in elderly patients was rectal ulcers. Similarly, a previous study reported that rectal ulcers caused active LGIB in 8.2% of patients with severe hematochezia, which may be life threatening (42). The exact cause of rectal ulcers is unclear, but they may occur in part due to fecal impaction and being bedridden over a long period of time. Most patients with rectal ulcers in this study were patients with multiple comorbidities and those who tended to originally be in poor general health.

In contrast, all five elderly (four men, one woman; mean age 74.4 years, range 70-79 years) and 13 non-elderly (10 men, three women; mean age 53.6 years, range 28-69 years) patients with post EMR/ESD bleeding successfully recovered and were either in ambulatory care or had been discharged to living at home. However, two of these elderly patients experienced hemodynamic shock, two experienced bleeding again, and three had pre-existing comorbidities (and were prescribed NSAIDs or an antiplatelet drug as a result). Therefore, these patients were considered to have successfully tolerated EMR/ESD and any complications pre-
**Figure 1.** Number of patients (total 110) with various causes of UGIB among non-elderly (n=51) and elderly patients (n=59). UGIB: upper gastrointestinal bleeding, GAVE: gastric antral vascular ectasia, ESD: endoscopic submucosal dissection, EMR: endoscopic mucosal resection.

**Figure 2.** Number of patients (total 75) with various sources of LGIB among non-elderly (n=34) and elderly patients (n=41). LGIB: lower gastrointestinal bleeding, ESD: endoscopic submucosal dissection, EMR: endoscopic mucosal resection.

**Figure 3.** Clinical outcomes in non-elderly (n=85) and elderly patients (n=100). *Changing hospital to undergo rehabilitation or receive palliative care or specialized nursing care.*
Table 3. Causes of Changing Hospitals or Death Post-GBT Treatment in the 140 Non-elderly and Elderly Patients Hospitalized for GIB Or Developing GIB during Their Hospital Stay.

| Outcome                          | Non-elderly (n=58) | Elderly (n=82) | p   |
|----------------------------------|--------------------|----------------|-----|
| Changing hospitala (%)           | 3 (5.2%)           | 17 (20.7%)     | 0.010 |
| Causes                           |                    |                |     |
| GIB itself                       | 0                  | 3              |     |
| Endoscopic procedure-related complication | 0                  | 1              |     |
| Exacerbation of the comorbidity  | 3                  | 7              |     |
| Any other complicationb         | 0                  | 6              |     |
| Death (%)                        | 1 (1.7%)           | 5 (6.1%)       | 0.208 |
| Causes                           |                    |                |     |
| GIB itself                       | 0                  | 1              |     |
| Endoscopic procedure-related complication | 0                  | 0              |     |
| Exacerbation of the comorbidity  | 1                  | 3              |     |
| Any other complicationb         | 0                  | 1              |     |

Two patients who changed hospitals for reasons, such as a lack of vacancy to receive special therapy were excluded. Significant p values are shown in bold.
aChanging hospital to undergo rehabilitation or receive palliative care or specialized nursing care.
bComplications not directly related to bleeding or endoscopic procedures and not an exacerbation of the comorbidity.

Table 4. Comparison between the Elderly Patients who Were Discharged Home (n=60) and Those who Changed Hospital or Died (n=22).

|                        | Discharged (n=60) | Changed hospitala or died (n=22) | p   |
|------------------------|-------------------|---------------------------------|-----|
| Age                    | 79.4±6.9          | 80.5±5.5                        | 0.324 |
| Sex (M/)               | 36/24             | 9/13                            | 0.124 |
| UGIB/LGIB              | 40/20             | 12/10                           | 0.313 |
| Hemoglobin level (g/dL)| 8.9±2.3           | 8.0±2.2                         | 0.191 |
| Use of NSAIDs, antiplatelet drugs, anticoagulants, or corticosteroids | 29                  | 18                             | **0.007** |
| 1 drug                 | 20                | 13                              | *0.035* |
| 2 drugs                | 7                 | 3                               | *0.809* |
| ≥3 drugs               | 2                 | 2                               | 0.284 |
| Presence of pre-existing comorbidities | 53                | 22                              | 0.094 |
| 1                      | 21                | 5                               | 0.290 |
| 2                      | 21                | 8                               | 0.909 |
| ≥3                     | 11                | 9                               | **0.035** |
| Re-bleeding or uncontrolled bleeding | 7                  | 3                               | 0.809 |
| Hemodynamic shock      | 5                 | 7                               | **0.008** |
| Onset                  |                    |                                 |     |
| Out of hospital/During hospital stay | 40/20             | 7/15                            | **0.005** |

Data are shown as the mean±standard deviation. Significant p values are shown in bold.
aChanging hospital to undergo rehabilitation or receive palliative care or specialized nursing care.

This study found no significant differences in the characteristics of elderly patients discharged to home and of elderly patients who changed hospitals or died. However, the usage of many drugs has generally been associated with poorer outcomes (17-22). The lack of any association in this study may be due to the small number of patients observed.

GIB can be seen as a secondary or terminal event in some patients in poor condition or dying from their primary illness, such as disseminated intravascular coagulation or multi-organ failure. About 70% of the elderly patients who changed hospitals or died had been hospitalized for a concurrent extra-intestinal organ system disease (e.g., osteoarthritis, cerebral infarction, ischemic heart disease, renal disease, dementia/mental disease, or malignancy). This population likely included some patients with poorly-controlled concurrent or terminal illnesses. These patients were probably in poor health before having GIB, with their condition worsening after GIB treatment. For these patients, hemostasis may represent the only symptomatic therapy; if so, it
would be very difficult to achieve any substantial improvement in their clinical outcomes. It is clinically important not only to focus on bleeding control in elderly patients, but also to pay close attention to the evaluation of their clinical status.

This study investigated the outcomes in elderly GIB patients, including the incidence of various complications and the patients’ fragile physical condition affected by diverse etiology. Japan’s population has a high proportion of elderly individuals, so an increase in the number of bedridden elderly patients is a major social and health problem. Although various factors - like age, medications, comorbidities, bleeding cause, and preexisting conditions - should be regarded in treating GIB in elderly patients, current guidelines do not differentiate GIB management based on patient age. Further clinical evaluation of the etiology of GIB and contributing factors is essential for efficient, appropriate hospital discharge of these patients.

**Limitations**

The limitations associated with this study include the small number of patients at a single institution, the retrospective study design, and the short study period. The possibility of bias due to various confounding factors suggests that propensity score matching may be needed to reduce any bias. However, this may be difficult due to the small number of patients in this study. Additionally, university hospitals face pressure to shorten the length of their patients’ stay. Thus, variations between our study hospital and general hospitals in the frequency of hospital transfer and the indications for hospitalization may exist.

**The authors state that they have no Conflict of Interest (COI).**

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