

Acute upper gastrointestinal bleeding in octogenarians: Clinical outcome and factors related to mortality

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Abstract

AIM: To evaluate the aetiology, clinical outcome and factors related to mortality of acute upper gastrointestinal bleeding (AUGIB) in octogenarians.

METHODS: We reviewed the records of all patients over 65 years old who were hospitalised with AUGIB in two hospitals from January 2006 to December of 2006. Patients were divided into two groups: Group A (65-80 years old) and Group B (> 80 years old).

RESULTS: Four hundred and sixteen patients over 65 years of age were hospitalized because of AUGIB. Group A included 269 patients and Group B 147 patients. Co-morbidity was more common in octogenarians ($P = 0.04$). The main cause of bleeding was peptic ulcer in both groups. Rebleeding and emergency surgery were uncommon in octogenarians and not different from those in younger patients. In-hospital complications were more common in octogenarians ($P = 0.05$) and more patients died in the group of octogenarians compared to the younger age group ($P = 0.02$). Inability to perform endoscopic examination ($P = 0.002$), presence of high risk for rebleeding stigmata ($P = 0.004$), urea on admission ($P = 0.036$), rebleeding ($P = 0.004$) and presence

of severe co-morbidity ($P < 0.0001$) were related to mortality. In multivariate analysis, only the presence of severe co-morbidity was independently related to mortality ($P = 0.032$).

CONCLUSION: While rebleeding and emergency surgery rates are relatively low in octogenarians with AUGIB, the presence of severe co-morbidity is the main factor of adverse outcome.

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Key words: Acute upper gastrointestinal bleeding; Octogenarians; Elderly; Co-morbidity; Mortality

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INTRODUCTION

Despite considerable advances during the last decades, acute upper gastrointestinal bleeding (AUGIB) remains one of the most serious and potentially life-threatening medical cases that require hospitalization and careful monitoring of the patients. Bleeding may be caused by many different lesions of variable prognostic importance. Peptic ulcers and varices are the main and more significant causes of AUGIB. Approximately 45%-60% of the admissions for AUGIB worldwide are due to peptic ulcers^[1-5].

The percentage of older patients suffering from AUGIB has been increasing rapidly over the last years

in the Western World; the main reasons are the increase in life expectancy and the increased consumption of many drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) in this subgroup of patients. These drugs have characteristic side effects. They provoke ulcerogenesis and simultaneously increase the risk of peptic ulcer complications, mainly bleeding, in patients with a peptic ulcer history^[6,7].

Elderly patients constitute a subgroup with special characteristics who need careful handling during their hospitalization, because it is a population with considerable co-morbidity, higher medication use and greater risk for further complications. Age has been established as an independent significant risk factor for poor clinical outcome in patients with AUGIB. Mortality rates ranging from 12% to 35% for those aged over 60 years, compared with less than 10% for patients younger than 60 years of age, have been reported in previous studies^[2,8,9].

There has been limited information on the clinical outcome of the very elderly patients with AUGIB. The aim of this study was to evaluate the clinical outcome of very elderly patients being presented with AUGIB (those over 80 years old), and also to determine if there were differences in causes and clinical outcome of AUGIB in octogenarians in comparison with those younger than 80 years old. Finally, we aimed at examining factors related to mortality in octogenarians with AUGIB.

MATERIALS AND METHODS

We retrospectively reviewed the records of all patients older than 65 years of age with AUGIB hospitalized in two hospitals from January to December of 2006. The patients were divided by age into two groups: Group A patients between 65 and 80 years old and Group B patients older than 80 years of age. We included both outpatients and bleeding episodes of the upper gastrointestinal (GI) tract that occurred in already hospitalized patients (inpatients). AUGIB was diagnosed when hematemesis, bloody nasogastric aspiration, or melena as well as other clinical or laboratory evidence of acute blood loss from the upper GI tract were present.

Bleeding patients were treated according to well established guidelines of the British Society of Gastroenterology Endoscopy Committee^[10]. Management was in general the same and similar to that in the younger patients. The first steps, which are required, are clinical evaluation and resuscitation. According to the general practice, emergency endoscopy was performed in the 1st 24-hour of admission in the majority of patients, or immediately after resuscitation in patients with massive bleeding. In the majority of patients supplemental oxygen was provided during endoscopy. All patients were given topical pharyngeal anesthesia with 10% lidocaine spray. In most cases, sedation was avoided because of the risk of complications. When sedation was needed, titration of the doses was usually necessary.

Injection hemostasis with adrenaline diluted at 1:10.000 in saline 0.9% was the first line treatment in

patients with active peptic ulcer bleeding or ulcers with stigmata of recent bleeding. The use of endoclips and the application of thermal contact treatment, such as argon plasma coagulation (APC) were added to adrenaline injection in selected cases. In patients with esophageal variceal bleeding band ligation was widely used. Sclerotherapy with histoacryl injection was used for hemostasis in cases of fundic variceal bleeding. Medical treatment was the same for all patients, consisting of Proton Pump Inhibitors (PPIs) given intravenously in usual doses. Vasoactive drugs (somatostatin iv 250 mg bolus injection followed by 24-hour infusion of 250 µg/h for 5 d) were added to endoscopic treatment in patients with variceal bleeding.

Demographic and clinical characteristics of octogenarian patients were recorded and compared with those of younger patients. Each patient's age, gender, recent consumption of non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants and antiplatelet drugs, routine laboratory tests (hematocrit, urea, creatinine) and the presence of shock during admission, co-existing illnesses, the history of admissions in the past for gastric surgery or peptic ulcer complications, endoscopic diagnoses and clinical outcome have been registered in standardized database categories. Shock or hemodynamic instability was defined as systolic blood pressure less than 100 mmHg and a pulse rate of more than 100 beats/min.

Medical history of co-existing illnesses has been encountered as follows. The patients were separated into three categories, depending on the condition of the patient in the admittance. We categorized as stage 1 patients with no serious illnesses (hypertension, endocrine, orthopaedic diseases, etc.), in a rather good condition. As stage 2, we categorized patients with illnesses that need more careful monitoring than those in stage 1, as they ran the risk of destabilization (diabetes mellitus, cardiac problems, compensated cirrhosis, cancer in a stabilized condition), and finally we referred to stage 3 patients as those suffering from major health problems (such as recent myocardial infarction, decompensated cirrhosis, cancer with metastases)^[11].

Stigmata of active or recent bleeding were classified according to the Forrest Classification: Forrest Ia: active spurting bleeding; I b: active oozing bleeding; II a: non-bleeding visible vessel (NBVV); II b: adherent clot; II c: spots, a NBVV was defined as a raised red spot resistant to washing, III: no spots, ulcer with a clean base. Then we differentiated into two subgroups, depending on the need to administer endoscopic therapy or not: as high risk stigmata we named the peptic ulcers with Forrest Ia-Forrest II a, which are at greatest risk of rebleeding in comparison with the peptic ulcers with low risk stigmata Forrest II b-III.

The clinical outcome was analyzed according to the duration of hospitalization, the complications during hospitalization, the number of transfused blood units per patient, the rate of rebleeding, the need for emergency surgical hemostasis and mortality, defined as death within the hospitalization period and encountered

Table 1 Clinicoepidemiological characteristics of patients with acute upper gastrointestinal bleeding

	Group A (65-80 yr)	Group B (> 80 yr)	P (95% CI)
Female, <i>n</i> (%)	83/269 (30.8)	65/147 (44.2)	0.009 (0.37-0.85)
Inpatients with AUGIB, <i>n</i> (%)	20/269 (7.4)	9/147 (6.1)	NS
History of ulcer disease/bleeding, <i>n</i> (%)	81/269 (30.1)	48/147 (32.6)	NS
Heart rate (on admission), (mean ± SD)	86.8 ± 19.5	87.4 ± 15.7	NS
Blood Pressure(on admission), (mean ± SD)	122.6 ± 21.1	124.3 ± 25	NS
Presence of hematemesis, <i>n</i> (%)	68/269 (25.3)	21/147 (14.3)	0.012 (1.18-3.47)
Presence of shock on admission, <i>n</i> (%)	24 (4.9)	10 (2.8)	NS
Hematocrit (on admission), (mean ± SD)	30 ± 7.3	28.5 ± 7.2	0.047
Creatinine (on admission), (mean ± SD)	1.3 ± 0.8	1.5 ± 0.9	0.006
Urea (on admission), (mean ± SD)	85.0 ± 55	105.0 ± 66.0	0.001
Recent NSAIDs use, <i>n</i> (%)	152/269 (56.5)	79/147 (53.7)	NS
Recent aspirin use, <i>n</i> (%)	101/269 (37.5)	58/147 (39.4)	NS
Oral-anticoagulants use, <i>n</i> (%)	34/269 (12.6)	10/147 (6.8)	NS
Antiplatelet drugs use, <i>n</i> (%)	53/269 (19.7)	23/147 (15.6)	NS
Combined use of NSAIDs and antiplatelet drugs, <i>n</i> (%)	28/269 (10.4)	3/147 (2.0)	0.004 (1.7-18.7)
Combined use of NSAIDs and oral anticoagulants, <i>n</i> (%)	10/269 (3.7)	1/147 (0.6)	NS

AUGIB: Acute upper gastrointestinal bleeding; NSAIDs: Non-steroidal anti-inflammatory drugs; NS: No significance.

the causes of death in these patients.

Continuous variables were expressed as mean ± SD and were compared by using Student's *t* test. Categorical variables were expressed as percentages and the differences between the groups were tested for significance by using the chi-squared test. Clinical, biochemical and endoscopic factors that might have contributed to the mortality were evaluated. All these parameters were correlated with in hospital mortality initially by using univariate analysis. Variables found to be significant in the univariate analysis ($P < 0.05$) were included in a multivariate stepwise logistic regression model. All analyses were conducted by using statistical software (SPSS, version 10.0).

RESULTS

From the total number of 638 patients with acute upper gastrointestinal bleeding hospitalized during the year 2006 in both hospitals, 416 patients (268 males and 148 females) were over 65 years (65.2%). Among these patients 269 (64.7%) were between 65 and 80 years of age (Group A) and 147 (35.3%) were over 80 years (Group B, Table 1). Endoscopy was performed in the majority of patients in both groups. In only 17 patients endoscopy was impossible (15/147 in Group B and 2/269 in Group A, $P < 0.0001$, Table 2). Endoscopy was not performed in these patients due to the presence of concomitant severe disease (12/15 in Group B and 1/2 in Group A), their personal or family disagreement (3/15 in Group B and 1/2 in Group A).

Demographic-clinical characteristics of patients

The percentage of female patients in the octogenarians' group (Group B) was significantly higher than that in Group A (44.2% *vs* 30.8%, $P = 0.009$). There was no statistically significant difference in the history of previous ulcer between the two groups (Table 1).

The presence of hematemesis before admission was less common in older than in younger patients (14.3% *vs* 25.3%, $P = 0.012$). Mean hematocrit during admission was less in octogenarians ($P = 0.047$), while mean creatinine and urea levels were higher in comparison with those in Group A ($P < 0.01$, Table 1).

The percentage of patients taking NSAIDs and antiplatelet drugs before the bleeding episode wasn't different between the two groups, but the combined use of both drugs was less common in octogenarians (2.0% in Group B *vs* 10.4% in Group A, $P = 0.004$, Table 1).

The percentage of patients with coexisting diseases was higher in octogenarians (Group B) in comparison with Group A, reaching a statistically significant level (94.6% *vs* 87.7%, $P = 0.04$, Table 3). The proportions of patients having hypertension (42.8% *vs* 32.3%, $P = 0.04$) and cardiovascular diseases (59.2% *vs* 46.8%, $P = 0.02$) were higher in Group B than in Group A, while that of cirrhotic patients was less frequent (2.0% in Group B *vs* 7.0% in Group A, $P = 0.05$, Table 3).

Causes of bleeding-endoscopic findings

The main cause of bleeding in both groups was peptic ulcer (51.5% in Group B *vs* 52.8% in Group A, $P > 0.05$, Table 2). Variceal bleeding was statistically less frequent in octogenarians than in younger patients (0.7% *vs* 7.4%, respectively, $P = 0.0094$) but esophagitis (6.8% *vs* 1.8%, $P = 0.025$) and vascular diseases such as angiodysplasia (9.0% *vs* 2.2%, $P = 0.005$) were more common in the octogenarians group. High risk of active stigmata or recent bleeding in peptic ulcer bleeding patients were less common in Group B (17.6%) as compared to younger patients (25.5%), but this difference did not reach statistical significance. Endoscopic hemostasis was administered to 78 patients in the octogenarians' group and was helpful in stopping bleeding and/or preventing rebleeding. There was no complication directly related to diagnostic or therapeutic endoscopy.

Table 2 Causes of acute upper gastrointestinal bleeding (AUGIB)-endoscopic findings according to age *n* (%)

	Group A (65-80 yr)	Group B (> 80 yr)	<i>P</i> (odds ratio)
No endoscopy	2/269 (0.7)	15/147 (10.2)	< 0.0001 (0.015-0.29)
No findings	10/267 (3.7)	6/132 (4.5)	NS
Peptic ulcer	141/267 (52.8)	68/132 (51.5)	NS
Gastric ulcer	68/141 (48.2)	37/68 (54.4)	NS
Duodenal ulcer	73/141 (51.7)	33/68 (48.5)	NS
Varices	20/267 (7.4)	1/132 (0.7)	0.0094 (1.4-79.92)
Erosive gastroduodenitis	61/267 (22.8)	25/132 (18.9)	NS
Angiodysplasia	6/267 (2.2)	12/132 (9.0)	0.005 (0.08-0.62)
Mallory-Weiss	3/267 (1.1)	0/132 (0.0)	NS
Polyps	6/267 (2.2)	1/132 (0.7)	NS
Esophagitis	5/267 (1.8)	9/132 (6.8)	0.025 (0.08-0.79)
Neoplasia	15/267 (5.6)	10/132 (7.5)	NS
Stigmata of bleeding in peptic ulcer bleeding patients			
High risk stigmata	36/141 (25.5)	12/68 (17.6)	NS
Low risk stigmata	105/141 (74.4)	56/68 (82.3)	NS
F1a	7/141 (4.9)	3/68 (4.4)	NS
F1b	13/141 (9.2)	5/68 (7.3)	NS
F2a	16/141 (11.3)	4/68 (5.8)	NS
F2b	32/141 (22.6)	13/68 (19.1)	NS
F2c	8/141 (5.6)	7/68 (10.2)	NS
F3	65/141 (46.0)	37/68 (54.4)	NS
Ulcer diameter < 1 cm	117/141 (82.9)	57/68 (83.8)	NS
Ulcer diameter > 1 cm	24/141 (17.0)	11/68 (16.1)	NS
Endoscopic therapy	78/267 (29.2)	28/132 (21.2)	NS

NSAIDs: Non-steroidal anti-inflammatory drugs; F: Forrest; NS: No significance.

Table 3 Co-morbidity of patients with acute upper gastrointestinal bleeding *n* (%)

	Group A (65-80 yr)	Group B (> 80 yr)	<i>P</i> (95% CI)
No co-morbidity (Stage 0)	33/269 (12.3)	8/147 (5.4)	0.04 (1.09-5.4)
Presence of co-morbidity	236/269 (87.7)	139/147 (94.6)	0.04 (1.09-5.4)
Stage 1	56/269 (20.8)	34/147 (23.1)	NS
Stage 2	146/269 (54.3)	84/147 (57.1)	NS
Stage 3	34/269 (12.6)	21/147 (14.3)	NS
Hypertension	87/269 (32.3)	63/147 (42.8)	0.04 (0.42-0.96)
Cardiovascular diseases	126/269 (46.8)	87/147 (59.2)	0.02 (0.4-0.91)
Malignancy	30/269 (11.1)	14/147 (9.5)	NS
Pulmonary disease	26/269 (9.6)	12/147 (8.1)	NS
Neurologic diseases	21/269 (7.8)	14/147 (9.5)	NS
Cirrhosis	19/269 (7.0)	3/147 (2.0)	0.05 (1.06-12.54)
Diabetes mellitus	65/269 (24.1)	28/147 (19.0)	NS
Renal disease	12/269 (4.4)	11/147 (7.5)	NS

NS: No significance.

Clinical outcome

Blood transfusion requirements (red blood cell units per patient) were not significantly different between the two groups (2.9 ± 3.2 in Group B *vs* 2.6 ± 3.2 in Group A, $P > 0.05$), while octogenarians required more hospitalization days (8.1 ± 5.5 d *vs* 6.9 ± 4.1 d, $P = 0.013$).

Rebleeding rates after endoscopic hemostasis in octogenarians were low and not different from those in younger patients (7.5% *vs* 6.7%). Eleven patients rebled in the octogenarians' group and a second course of endoscopic hemostasis was successful in 5 out of 6 patients. Emergency surgical hemostasis for continuing or recurrent bleeding was rare in bleeding patients and was not different between the two groups (2.7% in Group B *vs* 2.6% in Group A).

In-hospital complications were more common in octogenarians (38.1% *vs* 28.3%, $P = 0.05$), whilst there were no significant differences between octogenarians and younger patients in the proportions of the main complications observed; infection (27.9% *vs* 19.7%), oligemic shock (4.1% *vs* 1.1%), ischemic episode (6.8% *vs* 8.9%) and mental status deterioration (3.4% *vs* 2.2%), for groups B and A, respectively.

More patients died in the group of octogenarians compared with the younger age group (12.2% in Group B *vs* 5.2% in Group A, $P = 0.02$). There was no significant difference in the reasons of death between the two groups; cardiovascular/cerebrovascular disease (38.9% in Group B *vs* 42.8% in Group A), malignancy (22.2% *vs* 28.6%), septic shock (22.2% *vs* 7.1%), oligemic

shock (16.7% *vs* 4.3%), whilst one patient in Group A died from hepatorenal syndrome.

In univariate analysis, factors related to mortality in octogenarians were no endoscopic examination ($P = 0.002$), presence of high risk for rebleeding stigmata ($P = 0.004$), urea on admission ($P = 0.036$), rebleeding ($P = 0.004$) and presence of severe coexisting disease ($P < 0.0001$). In multivariate analysis, only the presence of severe co-morbidity was independently related to mortality ($P = 0.032$).

DISCUSSION

Demographic features and pattern of illness in patients hospitalized with AUGIB have changed during the last decades. A fall in the incidence of AUGIB during the last years has been reported, as well as a striking increase in the proportion of older patients being presented with AUGIB^[11,12]. About 35%-45% of all patients presented with AUGIB were over 60 years old in previous studies^[13-15]. In our study this proportion is even higher. Patients over 65 years of age constitute 65.2% of the total population with AUGIB. Additionally, more than a quarter of patients were over 80 years of age. Ten years earlier in our area this percentage was 9.8%^[16]. It is clear therefore that now we have to deal with an older population with a higher risk of deterioration due to the presence of higher co-morbidities, making their management a clinical challenge.

This shift to older ages is related not only to the increased life expectancy in the western population, but also to changes in the epidemiology of peptic ulcer disease.

Over half of the cases of AUGIB are due to peptic ulcer bleeding irrespective of the patients' age. Increased use of NSAIDs in the elderly, reduced incidence of non-NSAIDs related peptic ulcers as well as better management of the chronic peptic ulcer disease, especially in younger patients, have contributed to this shift. Eradication of *H pylori*, which can be achieved in over 90% of patients with peptic ulcer, reduces ulcer recurrences as well as ulcer bleeding and rebleeding rates in young patients with idiopathic peptic ulcer disease^[17,18].

On the other side, indications of aspirin or non-aspirin non-steroidal anti-inflammatory drugs have been increasing during the last years and this has had detrimental consequences, mainly to the elderly. Age is an independent risk factor for NSAID related GI tract toxicity and ulcer formation. In older patients the risk of serious adverse events, such as peptic ulcer bleeding while taking NSAIDs, is 5.5 times that of controls, whereas in younger patients it is only 1.5 times^[19]. Moreover, concurrent use of NSAIDs and antiplatelet drugs or oral anticoagulants, often used for thromboembolic prophylaxis in the geriatric population, increases the risk of bleeding^[20]. Two thirds of our patients had taken NSAID and/or oral-anticoagulant or antiplatelet drugs. In a recently published British study, prescriptions for NSAID have been increased by about 13%, aspirin 75 mg by 460% and the prescriptions for

oral anticoagulants by 200% between 1990 and 1999 in the general population^[14]. Despite the preventive effects of proton pump inhibitors on gastrointestinal toxicity from NSAIDs, it has been found that 70%-80% of users at risk for gastroduodenal complication does not receive gastroprotection^[21,22]. The increased use of NSAIDs by the elderly explains partly the increased frequency observed in females in these ages in comparison with younger patients^[23].

Severity of bleeding does not seem to be higher in the octogenarians group. Prognostic factors of rebleeding, rates or need for emergency surgical hemostasis in our study were not more frequent in the very elderly. Variceal bleeding, which is characterized by high rebleeding rates and high mortality rate, is rare in this group. On the other hand, angiodysplasia and esophagitis, which were more frequent causes of bleeding in the very elderly, rarely produce life threatening bleeding and currently they are easily controlled endoscopically^[24,25].

In our study, endoscopy was performed on approximately 90% of patients over 80 years of age, endoscopic hemostasis was successfully applied to our patients without complications and the majority of rebleeding cases were treated with a second endoscopic hemostasis. Except for the endoscopy itself, endoscopic treatment seems also to be an effective and generally safe treatment even when it is performed in the elderly^[26,27]. In a previous study in elderly patients with peptic ulcer bleeding, no rebleeding or morbidity occurred when endoscopic treatment was performed early but there was a significantly greater risk of further bleeding and treatment related morbidity when treatment was performed after the onset of rebleeding^[28]. On the other side, from the existing data, there is no evidence that peptic ulcer bleeding is more resistant to endoscopic therapy due to possible atherosclerosis of the underlying artery. In contrast, vessels eroded by NSAIDs-related ulcers may be more amenable to endoscopic hemostasis than those eroded by chronic duodenal ulcers. Chronic duodenal ulcers, in contrast to acute ulcers, produce destruction of the duodenal bulb and erode deeper and larger vessels that bleed more severely and make endoscopic hemostasis difficult or even impossible^[29]. Moreover, in a recently published study, mild to moderate anticoagulation did not increase the rebleeding rates after endoscopic hemostasis, meaning that endoscopic hemostasis is effective in anticoagulated patients admitted to hospital with AUGIB^[30].

Blood loss and emergency surgery is poorly tolerated by elderly patients with increased co-morbidity. Successful endoscopic therapy reduces the rebleeding rates and the need for emergency surgical hemostasis, which is a known risk factor for mortality especially in the elderly, due to high rate of co-morbidity in these patients. Only 4 out of 147 patients over 80 years of age required emergency surgical intervention in our study. Despite this, overall mortality was significantly increased in octogenarians in comparison to younger patients; this is due to the higher co-morbidity in these patients. In a recent multicenter study from France, no difference in

overall mortality was found among patients over and less than 75 years old, but in this study only patients with AUGIB subjected to endoscopy were included^[31]. The percentage of deaths related directly to bleeding was generally low even in the very elderly, and the majority of elderly patients with AUGIB died of unpreventable causes. Stable elderly patients with AUGIB and no significant co-morbid illnesses and low risk endoscopic findings can even be managed safely as outpatients, as reported in a previous study^[32].

In conclusion, currently more than half of the patients hospitalized with AUGIB are over 65 years old and a quarter more than 80 years. Severity of bleeding in octogenarians is not different in comparison with younger patients, rebleeding is uncommon and the need for emergency surgical hemostasis rare. Mortality is higher than in the younger population and the presence of severe co-morbidity is the main adverse factor of clinical outcome.

COMMENTS

Background

The increase in life expectancy and increased consumption of many drugs by older people, such as non-steroidal anti-inflammatory drugs, have resulted in a rapidly increasing incidence of acute upper gastrointestinal bleeding (AUGIB) in older patients in recent years in the Western World.

Research frontiers

Elderly patients constitute a subgroup with special characteristics, such as considerable co-morbidity, higher medication use and greater risk for further complications, making their management a clinical challenge. There has been limited information on the clinical outcome of the very elderly patients with AUGIB.

Innovations and breakthroughs

This study shows that severity of bleeding in octogenarians is not different in comparison with younger patients, rebleeding is uncommon and the need for emergency surgical hemostasis rare. Mortality is higher than the younger population and the presence of severe co-morbidity is the main adverse factor of clinical outcome.

Applications

Very old patients suffering from AUGIB should be managed as younger patients, but clinicians should have in mind that their patients with severe co morbidity are at increased risk of adverse outcome.

Peer review

This paper describes causes and clinical outcome of upper GI bleeding in elderly patients. More specifically, the age groups 65-80 and 80+ are compared. The numbers are quite large (269 vs 147) and some striking differences between the groups were noted.

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