Upper Gastrointestinal Bleeding In Cardiac Patients ,Clinical And Endoscopic Profile

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Abstract:

Background: Upper gastrointestinal bleeding (UGIB) can occur in cardiac patients affecting the prognosis, limited data is available on patient characteristics and predictors of outcome in this cohort.

Aim: To describe the clinical and endoscopic characteristics of patients with UGIB in cardiac patients and characterize predictors of outcome.

Methods: Prospective and Retrospective study of 655 consecutive patients with UGIB in cardiac patients from 2013 to 2016. Demographic characteristics, Therapeutic management, and predictors of outcomes were determined.

Results: 71.1% were male, mean age: 58.8 ± 9.2 yrs, mean Commonest symptoms included melena (49.4%) or coffee ground emesis (35.8%). In-hospital medications included heparin (92.4%, ASA (78.5%), low molecular weight.9%), coumadin (48.1%), clopidogrel (31%), and NSAIDS (32%). Initial hemodynamic instability was noted in 33.1%. Associated laboratory results included hematocrit 28 ± 6 ,platelets 243 ± 133 109/L, INR 1.7 ± 1.6 , and PTT 53.3 ± 35.6 s. Endoscopic evaluation (650 patients) yielded ulcers (73.5%) with high-risk lesions in 39.5%. Ulcers were located principally in the stomach (22.5%) or duodenum (45.9%). Many patients had more than one lesion, including esophagitis (30.7%) or erosions (22.8%). 37.8% received endoscopic therapy. Mean lengths of intensive care unit and overall stays were 9.4 \pm 18.4 and 30.4 \pm 46.9 days, respectively. Overall mortality was 5.1%. Only mechanical ventilation under 48 hours predicted mortality (0.R = 0.11; 95% CI = 0.04–0.34).

Conclusions: Most common cause of UGIB in cardiac patients was from ulcers or esophagitis; many had multiple lesions. ICU and total hospital stays as well as mortality were significant. Mechanical ventilation for under 48 hours was associated with improved survival. Early diagnosis and prompt treatment can improve prognosis.

I. INTRODUCTION

Upper gastrointestinal bleeding (UGIB) remains an important complication in cardiac patients although infrequent, these complications are clinically relevant because

of their associated mortality [1]. Many GI complications are reported, with only few studies addressing specifically upper GI bleeding in this context [1–3]. Moreover, the generalizability of past study findings is limited by differences between the supportive cares administered over a decade ago versus today. Indeed, data are limited on endoscopic findings, the role of modern endoscopic treatment, and the effectiveness of currently approved pharmacological approaches such modern endoscopic hemostasis and adjuvant PPI administration [4].

Hemorrhage still constitutes a major cause of morbidity and mortality in the ICU. The apparent failure of better clinical management to improve mortality rates associated with gastrointestinal bleeding may be partly due to selection bias. Patients who die of gastrointestinal hemorrhage generally have multiple chronic comorbidities and are elderly,¹⁰¹ and these factors probably largely account for the unchanged mortality rate.^{141, 169} and ¹⁷⁴

Gastrointestinal bleeding may be divided into upper and lower sources, with the ligament of Treitz constituting the anatomic dividing line. Gastrointestinal bleeding in the ICU is usually detected as *coffee grounds* in the nasogastric aspirate; fecal occult blood; or as hematemesis, melena, or hematochezia in more acute circumstances. It may be accompanied by a decrease in hemoglobin and hematocrit or might present purely with symptoms from blood loss and not only on the severity, nature, and location of the bleed, but also on patient characteristics The primary objective of this study was thus to report on the clinical and endoscopic presentations of patients. Additionally, we attempted to determine independent predictors of mortality in this highly selected patient population, that we hypothesized would be more dependent on underlying comorbidity than the actual severity and cause of bleeding ulcers

II. METHODS

All consecutive cardiac patients presenting with an episode of upper gastrointestinal bleeding UGIB between august 2013 and april 2016. Patients information was collected for all variables and analysed. UGIB was confirmed through written documentation by a health care professional of hematemesis and/or coffee ground vomiting, melena or hematochezia on rectal examination, the recovery of a bloody nasal gastric aspirate, or a combination thereof [5]. A complete history, thorough physical examination, monitoring of vital signs, establishment of an intravenous line, and resuscitation, when needed, was performed for each patient. Intravenous fluids were administered to all patients with an insufficient fluid volume status. The number of transfused blood units was indicated according to individual requirements.

Liver function and serum creatinine were assessed on admission and serially during hospitalization. Complete blood count, serum sodium, and number of units of blood received were recorded. All patients underwent upper endoscopy within 12-24 h of admission and therapy was initiated according to the endoscopic findings. For all patients, ciprofloxacin (500 mg every 12 h) was administered orally for 5 days. Patients with an actively bleeding peptic ulcer or visible vessels received an injection of adrenaline, followed by continuous omeprazole infusion at 8 mg/h for 3 days, which was then continued orally (13). Urine analysis, chest X-ray, ascitic fluid analysis, and fluid culture (if needed) were performed to detect sources of infection. All patients underwent abdominal ultrasonography and testing for the surface antigen of the hepatitis B virus (HBsAg) and hepatitis C virus antibodies (HCV Abs).

DATA COLLECTION: Recorded data included the following variables: immediate pre hospitalization characteristics such as demographic information, symptoms, signs, and laboratory data at the onset of bleeding, and the Parsonnet score [6]. We also noted information from the hospital stay, including details about the cardiac surgery, endoscopic findings (including the likely cause of bleeding) and hemostasis, supportive treatment and administered pharmacotherapy. Total and intensive care unit (ICU) lengths of stay were also abstracted. Additional outcomes of interest were the development of *Clostridium difficile-* (C. difficile-) associated diarrhea (defined as diarrhea accompanied by a positive C. difficile toxin assay), sternal infection, heart failure, and the need for mechanical ventilation and its duration. Bleeding outcomes that were recorded included the need for blood transfusions and the need for surgery related to the episode of NVUGIB. The intensity of GI bleeding (GIB) was classified as follows: moderate, requirement of <4 U of packed red blood cells (PRBCs); severe, requirement of 4-6 U of PRBC; and massive, presence of hypovolemic shock and/or the requirement of >6 U of PRBCs. Hypovolemic shock was defined as systolic blood pressure <90 mmHg or a reduction of >40 mmHg compared with the baseline, together with signs of hypoperfusion unresponsive to the administration of plasma expanders and PRBCs

STATISTICAL ANALYSIS: Descriptive data were generated for independent and dependent variables. All categorical data were expressed as proportions and 95% CI. All continuous data were expressed as means \pm standard deviations. Logistic regression modeling was carried out to identify independent predictors of mortality using possible clinically relevant variables associated with mortality on univariable analysis (adopting a threshold inclusion *P* value of 0.15). All statistical analyses were carried out using the SAS software version 9.2

STUDY POPULATION CHARACTERISTICS

The mean age was 68.8 ± 10.2 years, with 69.5% of patients being male. Presenting symptoms included melena (59.4%), coffee ground emesis (25.8%), hematochezia (13.2%), and hematemesis (11.6%). Initial hemodynamic instability was noted in 47.1%. Associated laboratory results included hematocrit 26 ± 6, platelets 243 ± 133 109/L, INR 1.7 ± 1.6, and PTT 53.3 ± 35.6 s. Most patients had some preexisting condition, or some laboratory abnormalities.

Types of Cardiac procedures dependend upon patients cardiac disease and status were Stenting, CABG, Primaryy PTCA, thrombolysis, conservative management. Endoscopic Information. Endoscopy was performed in 92.9% (95% CI 88.3–97.4%) of patients, and on average occurred 12.1±8.0 days after surgery, and 1.6±4.1 days after the onset of clinical symptoms and signs of bleeding. Overall, 85.5% of these patients had ulcers as the cause of the UGIB (45.9% duodenal, 22.5% gastric, 9.2% esophageal, multiple sites in 22.4%). Other etiologies of UGIB included esophagitis (28.7%), gastroduodenal erosions (26.8%), Dieulafoy lesions (3.5%), and Mallory-Weiss tears (2.6%), with 37.9% of patients exhibiting more than one lesion. The breakdown of the appearance of the lesions deemed the most likely source of bleeding according to Forrest classification; Ia or Ib (19.2%); IIa (11.1%), IIb (15.2%), IIc or III (50.5%), and no scope or lesions in 4.0%. Overall, 48.8% received endoscopic therapy (71% injection, 25% injection and thermal, 4% injection and clips).

Significant differences were noted for the presence of chronic renal failure (P = 0.008), heart failure (P = 0.024), and blood urea nitrogen (P = 0.037). In Table 3, differences in outcomes and complications included mechanical ventilation <48 hours (P < 0.0001), *C. difficile* colitis (P = 0.013), acute tubular necrosis requiring hemodialysis/dialysis (P < 0.0001) and ischemic bowel/ bowel (P = 0.002).

When introducing characteristics associated with death in multivariable analysis, the final model included age, platelets, and mechanical ventilation.

III. DISCUSSION

This study describes the endoscopic spectrum of lesions in patients presenting with an upper GI bleed following cardiac surgery. The vast majority (85.5%) had ulcers on endoscopy either in the esophagus, stomach, duodenum, or at multiple sites. In addition, a substantial proportion (28.7%) was found to have esophagitis. GI bleeding events were associated with prolonged ICU and overall hospital stays. GI bleedingin this contemporary setting was also associated with a significant mortality rate (5.1%). Although rare in this setting, GI complications have recently been reported in 53% of a series of 8709 consecutive patients [7]. The most common manifestation is that of UGI bleeding [8], noted in 16%. The mortality of GI complications in the postcardiac surgery patient has long been noted to be high [9]. Our findings of a 5.1% mortality confirm that this is still true today and in fact remains very elevated, even when compared to an unselected group of patients with in-hospital onset of nonvariceal UGI bleeding in the same country for whom the observed mortality rate was 11% [10]. Visceral hypoperfusion is often quoted as the main pathophysiological factor leading to GI complications, including bleeding, in this setting with additional contributing factors relating to patient comorbidities [11]. Indeed, the average age of the patients is elevated and in our study was 68.8 yrs \pm 10.2 years, which is similar to what others have reported [7]. An antecedent history of ulcer disease, although not noted in our study, has been reported to be a risk factor for the development of UGI bleeding in past analyses [12].

In a series of 4892 patients undergoing open heart surgery, 18 developed upper gastrointestinal bleeding, all of whom were receiving antiplatelet or anticoagulant medication at the time of the bleed [13], a finding approximating results from our own series. Halm et al. assessed the effect of *Helicobacter pylori* infection as a risk factor for UGI bleeding after cardiac surgery, failing to find a significant association [14]. On the other hand, patients with UGI bleeding have usually experienced a significantly longer duration of cardiopulmonary bypass and aortic cross-clamp time [14]. An analysis of 1477 cardiac surgery patients focusing on the broader issue of postoperative GI complications concluded that the use of a left internal mammary artery also seemed to be a risk factor [1].

The role of on- and off-pump surgery in the development of postoperative GI complications remains controversial with disparate findings in the literature [15-17].

Our finding of a protective association between a shortened course of ventilatory support (under 48 hours) and subsequent mortalitymay reflect lesser systemic involvement which has also been associated with a decreased incidence of associated stress related mucosal disease reported in this subgroup of patients; indeed, independent risk factors for GI bleeding in an ICU population include respiratory support for greater than 48 hours in addition to the presence of a coagulopathy [18].

Some have suggested a lesser incidence of bleeding ulcers in postoperative vascular patients duodenal [19].However, in most reports, commonly reported lesions at endoscopy have included, as in our series, gastroduodenal ulcers or erosions and esophagitis [12, 20-22]. These findings are similar to those noted for in-hospital and outpatient patients with an episode of NVUGIB [5, 10]. Subsequent management therefore utilizes similar therapeutic approaches including the performance of early endoscopy, therapeutic hemostasis, and pharmacotherapy in appropriate patients [4]. This management scheme, however, must be even more greatly individualized and guided by a cautious assessment of the cardiorespiratory status of the postcardiac surgery patient. The increased performance of endoscopic hemostasis exceeding the proportion of patients with high risk stigmata may be due to a more aggressive attitude in this group of patients that is not evidence-based, or an under reporting attributable to the retrospective nature of the data collection. A randomized trial that initially assessed patients with endoscopy and followed these with postoperative endoscopic studies suggested the benefit of PPIs in this highly selected patient group [2], a finding echoed by a recent underpowered observational study [23]. The observed low rate of prophylactic co prescription of antisecretory agents is in part Ulcers 5 explained by widely publicized fear of side effects such as the development of C. difficile-associated diarrhea [24].

In conclusion, in this contemporary large series of old and sick consecutive patients presenting with an upper GI bleed following cardiac surgery, many patients had multiple endoscopic lesions, with mostly ulcers (85.5%) and esophagitis (28.7%) noted. The ICU and total hospital stays were markedly prolonged, with significant mortality. Only duration of mechanical ventilation less than 48 hours was associated with an improved survival.

Risk factors for GICs reported in the literature are older age, increased duration of bypass, sepsis, renal failure, prolonged ventilation, low cardiac index, and emergent surgery.⁸⁻¹²) In the present study, 5 possible predictors of GICs after CABG were identified: age over 70, diabetes mellitus (particularly insulin-dependent diabetes), history of cerebrovascular disease, history of renal failure (use of hemodialysis) and postoperative LOS. In our series, no cases of single peptic ulcer were observed. However, we gave

medicine such as H2-blocker or proton-pump inhibitor to many patients who underwent cardiopulmonary bypass surgery, preventively. Therefore, H2-blocker or proton-pump inhibitor might prevent patients from single peptic ulcer. Moreover, no in-hospital deaths occurred, due to prompt treatment with blood trans- fusion and endoscopic ablation and/or clipping. Bacterial overgrowth, mucosal atrophy, loss of barrier function, and bacterial translocation are reported to occur due to intestinal changes following cardiopulmonary bypass.¹⁴⁻¹⁶ Recently, urine intestinal fatty acid binding protein has been reported to be elevated in the presence of GICs and it has also been suggested that steroids can prevent the intestinal microcirculatory alterations that occur after cardiopulmonary bypass. By performing blood transfusion and emergent endoscopic ablation and/or clipping, it appeared that mortality was avoided among the present cases. We concluded that prediction of GIC from relevant risk factors and treatment with blood transfusion and prompt endoscopic ablation and/or clipping are essential.

IV. CONCLUSIONS

Most common cause of UGIB in cardiac patients was from ulcers or esophagitis; many had multiple lesions. ICU and total hospital stays as well as mortality were significant. Mechanical ventilation for under 48 hours was associated with improved survival. Early diagnosis and prompt treatment can improve prognosis.

MANAGEMENT OF UPPER GASTROINTESTINAL BLEED IN THE SETTING OF THE USE OF DUAL ANTIPLATELET

GI bleed in these patient is a critical challenge. If the patient has high risk stigma of bleed endoscopic therapy is done apart from PPI infusion and other supportive therapy. There is no role of initiating efforts to reverse the effects of antiplatelet like platelet infusion, etc. A critical question is: when to resume antiplatelet? This case has to be individualized and certain facts have to be considered.

Aspirin has a half-life of only 20 min; however, after the stoppage of aspirin, the pharmacodynamics effect persists for the duration of platelet life span of 7-10 days as the platelet is unable to effectively synthesize new COX enzymes.

Clopidogrel is a pro-drug and hence there is a delay of 3-5 days before the onset of antiplatelet activity. Like aspirin, the antiplatelet effect is irreversible, but platelet function has been demonstrated to return to normal 7 days after the withdrawal of clopidogrel.

The other variable in this situation is the risk of thrombosis. In patients taking aspirin for primary prophylaxis (no overt CV disease), the risk of subsequent bleeding likely outweighs CV disease), the risk of subsequent bleeding likely outweighs CV benefit and it can be discontinued in acute stage without increasing risk of thrombosis. In contrast, the benefit of low dose aspirin for secondary prophylaxis in patients with established CV disease is much larger and failure to resume low dose aspirin after ulcer bleeding is associated with the increased risk of thrombosis as well as mortality. Discontinuation of antiplatelet therapy (particularly clopidogrel) is a crucial independent factor for the development of stent thrombosis. A study demonstrated that the incidence of major CV events was significantly higher if dual antiplatelet therapy was discontinued within 1 month of bare-metal stent, 3 months of sirolimus drug eluting stent, and 6 months of paclitaxel drug-eluting stent placement. The risk of stent thrombosis increases after 5 days without antiplatelet therapy. If clopidogrel need to be temporarily stopped in the context of an acute GI hemorrhage, then discontinuation of therapy should be limited to this interval.

The timing of resumption of aspirin is not clear and the date are based primarily on observational studies. While a systematic review found that thrombotic events occurred at a mean of 10.7 days after aspirin withdrawal, another review on secondary prevention stopping aspirin perioperatively reported the mean interval after discontinuation for acute cerebral events as 14.3 days and for ACS 8.5 days.

In the absence of high-risk stigmata for re-bleeding (bleeding visible vessel, nonbleeding visible vessel, or adherent clot), APAs can be resumed immediately after endoscopy. Since most peptic ulcer rebleeding occurs within the first 3 days of presentation, resuming APAs at 3-5 days after the last dosing is a reasonable strategy in the management of bleeding ulcer patients with high-risk stigmata of recent hemorrhage.

Because the risk of stent thrombosis with removal of



APAs is high within the critical periods following PCI and antiplatelet effects of aspirin and clopidogrel may last at least a few days after cessation, resuming antiplatelet therapy at 3 days after the last dosing is recommended for the bleeding ulcer patients undergoing recent coronary stenting.



Stigmata of recent hemorrhage			Forrest Classification	Prevalence in patients with UGIB Modified from RUGBE ^{PO}	Prevalence in ulcer bleeding Modified from CORI ^{53]}	Prevalence in ulcer bleeding Modified from Laine ^[90]	Rate of further bleeding Modified from Laine ^[59]
				Registry of 1869 patients 1999-2002 Canada	Database of 3874 EGDs 2000-2004 USA	Pooled data from prospective trials	
Spurting vessel Oozing vessel Non-specified active bleeding	Active bleeding	High-risk stigmata e	IA IB	3% 22% 2%	9%	18%	55%
Non-bleeding visible vessel Adherent clot	stigne No-active bleeding Low-n stigma		IIA IIB	10% 7%	6% 7%	17% 17%	43% 22%
Flat pigmented spot Clean base		Low-risk stigmata	IIC III	5% 47%	13% 52%	20% 42%	10% 5%
Unknown					12		

Table 2



Fig.2 - Algorithm for the reductoge measurement of partners with researched agence parameteristical submittance (a) parameteristical submittance (b) parameteristical











Figure 2 & 3: hemoclip being applied in bleeding lesion

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