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Research Article

In-Hospital Nonvariceal Upper Gastrointestinal Bleeding following Cardiac Surgery: Patient Characteristics, Endoscopic Lesions and Prognosis

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Background. Nonvariceal upper gastrointestinal bleeding (NVUGIB) can occur following cardiac surgery, with sparse contemporary data on patient characteristics and predictors of outcome in this setting. *Aim*. To describe the clinical and endoscopic characteristics of patients with NVUGIB following cardiac surgery and characterize predictors of outcome. *Methods*. Retrospective review of 131 consecutive patients with NVUGIB following cardiac surgery from 2002 to 2005. Demographic characteristics, therapeutic management, and predictors of outcomes were determined. *Results*. 69.5% were male, mean age: 68.8 ± 10.2 yrs, mean Parsonnet score: 24.6 ± 14.2. Commonest symptoms included melena (59.4%) or coffee ground emesis (25.8%). In-hospital medications included ASA (88.5%), heparin (95.4%, low molecular weight 6.9%), coumadin (48.1%), clopidogrel (22.9%), and NSAIDS (42%). 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. Endoscopic evaluation (122 patients) yielded ulcers (85.5%) with high-risk lesions in 45.5%. Ulcers were located principally in the stomach (22.5%) or duodenum (45.9%). Many patients had more than one lesion, including esophagitis (28.7%) or erosions (26.8%). 48.8% received endoscopic therapy. Mean lengths of intensive care unit and overall stays were 10.4 ± 18.4 and 39.4 ± 46.9 days, respectively. Overall mortality was 19.1%. Only mechanical ventilation under 48 hours predicted mortality (O.R = 0.11; 95% CI = 0.04−0.34). *Conclusions*. This contemporary cohort of consecutive patients with NVUGIB following cardiac surgery bled most often 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.

1. Introduction

Upper gastrointestinal bleeding (UGIB) remains an important complication following cardiac surgery since, 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].

The primary objective of this study was thus to report on the clinical and endoscopic presentations of patients undergoing cardiac surgery while identifying the impact of modern-day supportive care, including endoscopic therapy. Additionally, we attempted to determine independent

Table 1: Patient characteristics.

	No mortality, $N = 106$	Mortality, $N = 25$	P values
Age	68.7 ± 9.7	69.1 ± 12.3	$P = 0.5800$
Gender (male)	71.7% (63.0%–80.4%)	60.0% (39.4%–80.6%)	$P = 0.2533$
Parsonnet score	24.0% (21.1%–26.8%)	27.6% (21.4%–33.7%)	$P = 0.2717$
Documented history of:			
Liver failure	1.9% (0.0%–4.5%)	0.0%	$P = 0.4889$
Chronic renal failure	13.3% (6.7%–19.9%)	36.0% (15.8%–56.2%)	$P = 0.0076$
Heart failure	13.2% (6.7%–19.8%)	32.0% (12.3%–51.7%)	$P = 0.0238$
Ischemic heart disease	76.4% (68.2%–84.6%)	68.0% (48.3%–87.7%)	$P = 0.3833$
Other heart disease	16.0% (8.9%–23.1%)	12.0% (0.0%–25.7%)	$P = 0.6136$
Asthma	5.6% (1.2%–10.1%)	12.0% (0.0%–25.7%)	$P = 0.2596$
COPD	9.4% (3.8%–15.1%)	20.0% (3.2%–36.9%)	$P = 0.1356$
Diabetes mellitus	26.4% (17.9%–35.0%)	28.0% (9.1%–46.9%)	$P = 0.8720$
Major recent operation	0.9% (0.0%–2.8%)	0.0% (0.0%-0.0%)	$P = 0.6259$
Major sepsis	0.0%	0.0%	
Disseminated malignancy	0.0%	0.0%	
Other solid malignancy	8.5% (3.1%–13.9%)	0.0% (0.0%-0.0%)	$P = 0.1311$
Hematological malignancy	1.0% (0.0%–2.8%)	0.0% (0.0%-0.0%)	$P = 0.6242$
Dementia	0.0%	0.0%	
CVA/TIA	10.4% (4.5%–16.3%)	16.0% (0.6%–31.4%)	$P = 0.4271$
Hypertension	67.9% (58.9%–77.0%)	72.0% (53.1%–90.9%)	$P = 0.6926$
Trauma	1.9% (0.0%–4.5%)	4.0% (0.0%–12.3%)	$P = 0.5252$
Symptoms on presentation:			
Melena	59.2% (49.6%–68.9%)	60.0% (39.4%–80.6%)	$P = 0.9435$
Coffee ground emesis	25.0% (16.5%–33.5%)	68.0% (9.1%–46.9%)	$P = 0.7576$
Hematochezia	13.5% (6.8%–20.1%)	12.0% (0.00%–25.7%)	$P = 0.8462$
Hematemesis	11.5% (5.3%–17.8%)	12.0% (0.00%–25.7%)	$P = 0.9485$
Initial hemodynamic instability	45.8% (35.7%–56.0%)	52.2% (30.1%–74.3%)	$P = 0.5842$
Medication during hospitalization:			
PPI	10.9% (4.7%–17.1%)	13.0% (0.0%–27.9%)	$P = 0.7685$
H2RA	29.7% (20.6%–38.8%)	13.0% (0.0%–27.9%)	$P = 0.1028$
Steroids	15.1% (8.2%–22.0%)	28.0% (9.1%–46.9%)	$P = 0.1271$
Aprotinin	0.0%	0.0%	
ASA	88.6% (82.4%–94.8%)	88.0% (74.3%–100.0%)	$P = 0.9359$
Heparin	95.3% (91.2%–99.4%)	96.0% (87.7%–100.0%)	$P = 0.8774$
Coumadin	45.3% (35.7%–54.9%)	60.0% (39.4%–80.6%)	$P = 0.1852$
Clopidogrel	22.6% (14.5%–30.7%)	24.0% (6.0%–42.0%)	$P = 0.884$
LMWH	6.6% (1.8%–11.4%)	8.0% (0.0%–19.4%)	$P = 0.8039$
NSAIDS	42.5% (32.9%–52.0%)	40.0% (19.4%–60.6%)	$P = 0.8231$
Steroids	15.1% (8.2%–22.0%)	28.0% (9.1%–46.9%)	$P = 0.1271$

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.

2. Methods

2.1. Study Design and Selection of Participants. We reviewed the care and outcomes of patients who presented with an episode of nonvariceal upper gastrointestinal bleeding (NVUGIB) complicating cardiac surgery between January 2002 and July 2005. Patients were identified through an institutional database maintained by the Department of Cardiovascular Surgery in which all admissions are entered prospectively. In addition, patient information was also abstracted from a retrospective review of medical charts. We collected pre-, intra-, and postoperative variables, including postoperative complications. Three trained experienced research staff and a clinical monitor used a standardized glossary of terms that included definitions of all variables entered into the study.

2.2. Study Population. We included patients presenting with NVUGIB within 30 days following cardiac surgery between

January 2002 and July 2005. NVUGIB 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]. We excluded patients initially assessed at another institution for the present episode of bleeding and subsequently transferred to the participating site, patients who were not already in hospital at the time of bleeding, and patients not undergoing cardiac surgery. Approval was obtained from our institutional research ethics board.

2.3. Data Collection. Recorded data included the following variables: immediate prehospitalization 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.

2.4. 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 ± 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 (SAS Institute, Cary, NC, USA).

3. Results

3.1. 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. An exhaustive list of overall population characteristics is available upon request and is listed in Tables 1 and 2 according to the outcome of survival or mortality.

3.2. Types of Cardiac Surgeries Performed. The types of cardiac surgeries included coronary artery bypass grafting (CABG) (57.9%), with aortic valve replacement (7.3%), off-pump CABG (5%), complex procedures (more than one surgical procedure) (3.6%), CABG with mitral valve (MV) repair (3.28%), MV repair (2.90%), MV replacement (1.93%), CABG with MV replacement (1.54%), and heart transplant (1.16%).

Table 2: Laboratory data at presentation.

	No mortality $N = 106$	Mortality $N = 25$	P values
WBC (10^9/L)	12.5 ± 6.6	13.8 ± 4.6	$P = 0.1167$
Creatinine (mmol/L)	136.2 ± 87.8	165.4 ± 104.0	$P = 0.1640$
Urea (mmol/L)	16.3 ± 33.4	20.5 ± 16.3	$P = 0.0367$
INR	1.6 ± 0.8	2.3 ± 3.2	$P = 0.0888$
PT (sec)	19.0 ± 7.4	23.0 ± 17.5	$P = 0.1067$
PTT (sec)	50.9 ± 32.2	63.1 ± 46.6	$P = 0.1020$
HCT	26 ± 6	25 ± 4	$P = 0.6522$
Platelets (10^9/L)	253.0 ± 133.8	203.4 ± 123.9	$P = 0.0584$

3.3. 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).

3.4. Outcomes and Multivariable Analysis. The mean length of stay was 39.7 ± 46.9 days, with a mean duration of ICU admission of 10.4 ± 18.4 days. 19.1% of patients died. The other outcomes broken down by survival or not are listed in Table 3.

The results of univariable analysis are presented in Tables 1 and 2 for presenting demographics in the form of historical and laboratory characteristics on presentation as well as outcomes amongst patients who survived and died. 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. The sole significant

Table 3: Outcomes.

	No mortality, $N = 106$	Mortality, $N = 25$	P values
Transfusions related to bleeding:			
Packed red blood cells	91.1% (85.4%–96.7%)	91.7% (79.7%–100.0%)	$P = 0.9285$
Fresh frozen plasma	47.5% (37.6%–57.4%)	45.8% (24.3%–67.3%)	$P = 0.8814$
Platelets	20.4% (12.5%–28.3%)	24.0% (6.0%–42.0%)	$P = 0.6913$
Mechanical ventilation up to 48 hours	74.3% (65.6%–82.9%)	24.0% (6.0%–42.0%)	$P < 0.0001$
Complications:			
C. Difficile colitis	9.4% (3.8%–15.1%)	28.0% (9.1%–46.9%)	$P = 0.0130$
Acute tubular necrosis requiring hemofiltration/dialysis	10.4% (4.5%–16.3%)	44.0% (23.1%–64.9%)	$P < 0.0001$
Ischemic bowel/bowel obstruction/	4.7% (0.6%–8.8%)	24.0% (6.0%–42.0%)	$P = 0.0018$
Mediastinitis/sternal dehiscence requiring flap	5.7% (1.2%–10.1%)	12.0% (0.0%–25.7%)	$P = 0.2596$

independent predictor of lowered mortality was mechanical ventilation <48 hours (OR = 0.11; 95% CI: 0.04–0.34).

4. 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 bleeding in this contemporary setting was also associated with a significant mortality rate (19.1%).

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 19.1% 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 ± 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 mortality may 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 duodenal ulcers in postoperative vascular patients [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 presenting 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 coprescription of antisecretory agents is in part

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.

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References

[1] R. A. Perugini, R. K. Orr, D. Porter, E. M. Dumas, and B. S. Maini, "Gastrointestinal complications following cardiac surgery: an analysis of 1477 cardiac surgery patients," *Archives of Surgery*, vol. 132, no. 4, pp. 352–357, 1997.

[2] M. Hata, M. Shiono, H. Sekino et al., "Prospective randomized trial for optimal prophylactic treatment of the upper gastrointestinal complications after open heart surgery," *Circulation Journal*, vol. 69, no. 3, pp. 331–334, 2005.

[3] F. Filsoufi, P. B. Rahmanian, J. G. Castillo, C. Scurlock, P. E. Legnani, and D. H. Adams, "Predictors and outcome of gastrointestinal complications in patients undergoing cardiac surgery," *Annals of Surgery*, vol. 246, no. 2, pp. 323–329, 2007.

[4] A. N. Barkun, M. Bardou, E. J. Kuipers et al., "International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding," *Annals of Internal Medicine*, vol. 152, no. 2, pp. 101–113, 2010.

[5] A. Barkun, S. Sabbah, R. Enns et al., "The Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy (RUGBE): endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting," *American Journal of Gastroenterology*, vol. 99, no. 7, pp. 1238–1246, 2004.

[6] V. Parsonnet, D. Dean, and A. D. Bernstein, "A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease," *Circulation*, vol. 79, no. 6, part 2, pp. I3–I12, 1989.

[7] A. A. Mangi, E. R. Christison-Lagay, D. F. Torchiana et al., "Gastrointestinal complications in patients undergoing heart operation: an analysis of 8709 consecutive cardiac surgical patients," *Annals of Surgery*, vol. 241, no. 6, pp. 895–904, 2005.

[8] B. Andersson, R. Andersson, J. Brandt, P. Höglund, L. Algotsson, and J. Nilsson, "Gastrointestinal complications after cardiac surgery—improved risk stratification using a new scoring model," *Interactive Cardiovascular and Thoracic Surgery*, vol. 10, no. 3, pp. 366–370, 2010.

[9] G. L. Moneta, G. A. Misbach, and T. D. Ivey, "Hypoperfusion as a possible factor in the development of gastrointestinal complications after cardiac surgery," *American Journal of Surgery*, vol. 149, no. 5, pp. 648–650, 1985.

[10] T. Müller, A. N. Barkun, M. Martel et al., "Non-variceal upper GI bleeding in patients already hospitalized for another condition," *American Journal of Gastroenterology*, vol. 104, no. 2, pp. 330–339, 2009.

[11] A. T. Yilmaz, M. Arslan, U. Demirkilc, E. Ozal, E. Kuralay, H. Bingol et al., "Gastrointestinal complications after cardiac surgery," *European Association for Cardio-Thoracic Surgery*, vol. 10, no. 9, pp. 763–767, 1996.

[12] I. D. Norton, C. S. Pokorny, D. K. Baird, and W. S. Selby, "Upper gastrointestinal haemorrhage following coronary artery bypass grafting," *Australian and New Zealand Journal of Medicine*, vol. 25, no. 4, pp. 297–301, 1995.

[13] E. Lebovics, S. S. Lee, B. M. Dworkin et al., "Upper gastrointestinal bleeding following open heart surgery. Predominant finding of aggressive duodenal ulcer disease," *Digestive Diseases and Sciences*, vol. 36, no. 6, pp. 757–760, 1991.

[14] U. Halm, F. Halm, D. Thein, F. W. Mohr, and J. Mössner, "Helicobacter pylori infection: a risk factor for upper gastrointestinal bleeding after cardiac surgery?" *Critical Care Medicine*, vol. 28, no. 1, pp. 110–113, 2000.

[15] G. S. Musleh, N. C. Patel, A. D. Grayson et al., "Off-pump coronary artery bypass surgery does not reduce gastrointestinal complications," *European Journal of Cardio-thoracic Surgery*, vol. 23, no. 2, pp. 170–174, 2003.

[16] K. P. Croome, B. Kiaii, S. Fox, M. Quantz, N. McKenzie, and R. J. Novick, "Comparison of gastrointestinal complications in on-pump versus off-pump coronary artery bypass grafting," *Canadian Journal of Surgery*, vol. 52, no. 2, pp. 125–128, 2009.

[17] I. Sanisoglu, M. Guden, Z. Bayramoglu et al., "Does off-pump CABG reduce gastrointestinal complications?" *Annals of Thoracic Surgery*, vol. 77, no. 2, pp. 619–625, 2004.

[18] D. J. Cook, H. D. Fuller, G. H. Guyatt et al., "Risk factors for gastrointestinal bleeding in critically ill patients," *The New England Journal of Medicine*, vol. 330, no. 6, pp. 377–381, 1994.

[19] A. Jayaprakash, C. McGrath, E. McCullagh, F. Smith, G. Angelini, and C. Probert, "Upper gastrointestinal haemorrhage following cardiac surgery: a comparative study with vascular surgery patients from a single centre," *European Journal of Gastroenterology and Hepatology*, vol. 16, no. 2, pp. 191–194, 2004.

[20] C. V. Egleston, T. F. Gorey, A. E. Wood, and E. M. McGovern, "Gastrointestinal complications after cardiac surgery," *Annals of the Royal College of Surgeons of England*, vol. 75, no. 1, pp. 52–56, 1993.

[21] G. D'Ancona, R. Baillot, B. Poirier et al., "Determinants of gastrointestinal complications in cardiac surgery," *Texas Heart Institute Journal*, vol. 30, no. 4, pp. 280–285, 2003.

[22] M. Ait houssa, C. Selkane, Y. Moutaki Allah et al., "Upper digestive bleedings after cardiac surgery," *Annales de Cardiologie et d'Angeiologie*, vol. 56, no. 3, pp. 126–129, 2007.

[23] M. Bhat, M. Larocque, M. Amorim et al., "Prediction and prevention of upper gastrointestinal bleeding after cardiac surgery: A case control study," *Canadian Journal of Gastroenterology*, vol. 26, no. 6, pp. 340–344, 2012.

[24] J. Leonard, J. K. Marshall, and P. Moayyedi, "Systematic review of the risk of enteric infection in patients taking acid suppression," *American Journal of Gastroenterology*, vol. 102, no. 9, pp. 2047–2056, 2007.