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Endoscopic Findings and Clinical Outcomes in Ventricular Assist Device Recipients with Gastrointestinal Bleeding

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Abstract

Background—Gastrointestinal bleeding (GIB) is an important clinical problem in recipients of ventricular assist devices (VAD), although data pertaining to the endoscopic evaluation and management of this complication are limited in the medical literature.

Aims—We sought to identify the most common endoscopic findings in VAD recipients with GIB, and to better define the diagnostic and therapeutic utility of endoscopy for this patient population.

Methods—Twenty-six subjects with VAD and overt GIB were retrospectively identified. Clinical and endoscopic data were abstracted for each subject on to standardized forms in duplicate and independent fashion. Raw data and descriptive statistics were reported.

Results—Non-peptic vascular lesions were the most common cause of GIB. A definitive cause of bleeding was identified by endoscopy in almost 60% of subjects. Endoscopic hemostasis was achieved in 14/15 patients in whom bleeding did not stop spontaneously. Rebleeding occurred in 50% of subjects and was successfully retreated or stopped spontaneously in all cases. Colonoscopy did not establish a definitive diagnosis or deliver hemostatic therapy in any case.

Conclusions—Vascular malformations account for the overwhelming majority of bleeding lesions in VAD patients with GIB. Endoscopy seems to be a safe and effective tool for diagnosing, risk stratifying, and treating this patient population, although multiple endoscopies may be necessary before therapeutic success, and the incidence of rebleeding is high. A prospective multi-center registry is necessary to establish evidence-based management algorithms for VAD recipients with GIB.

Keywords

Ventricular assist device; Gastrointestinal hemorrhage; Endoscopic evaluation; Endoscopic hemostasis

Introduction

Ventricular assist devices (VADs) are surgically implanted pumps that provide mechanical circulatory support (MCS) to patients with severe systolic heart failure refractory to medical therapy. These devices, which have been shown to increase survival and improve quality of life [1, 2], can be used as a bridge to heart transplantation or serve as destination therapy for patients who are not appropriate transplant candidates [3–5]. MCS therapy utilizing VADs has revolutionized the management of end-stage heart failure and provides life-saving therapy to many patients awaiting heart transplantation or those who are suboptimum candidates.

Despite the demonstrated survival benefit, morbidity after VAD placement remains substantial [2, 4, 5]. Complications such as stroke, infection, and right heart failure occur for a substantial number of patients. Additionally, acute gastrointestinal bleeding (GIB), particularly for patients with continuous flow (non-pulsatile) devices, seems to be an important clinical problem for this patient population [6–9]. Data pertaining to the endoscopic evaluation and management of this complication are limited in the medical

literature, and evidence-based algorithms to approach this problem are not currently available.

The objectives of this study were to determine endoscopic findings in VAD recipients with GIB, and to better define the diagnostic and therapeutic utility of endoscopy for this patient population. We also sought to characterize the pattern of endoscopic test utilization in order to begin developing evidence-based algorithms for this patient population.

Methods

This study was conducted after approval from the University of Michigan institutional review board. The University of Michigan Hospital electronic medical record system was retrospectively queried for all patients hospitalized between January 2002 and December 2009 with concurrent diagnoses of VAD and any form of gastrointestinal hemorrhage. Criteria for inclusion in the study were:

1. presence of a VAD for at least one month (excluding intra-aortic balloon pump or other extracorporeal and paracorporeal device intended to provide temporary support);
2. GIB, defined as a clinical history of overt blood loss (hematemesis, melena, or maroon stools, or bright red blood per rectum) *and* a concomitant acute decline in hemoglobin of at least 2 g/dl; and
3. availability of sufficient information within the medical record to enable complete abstraction of the a priori defined data points.

After subjects meeting inclusion criteria were identified, the electronic medical record for each patient was reviewed and clinical data were abstracted on to standardized forms in duplicate and independent fashion by two investigators (KP and JL). A third investigator consolidated these data and oversaw the process of discrepancy resolution (AR). The variables for which data were abstracted are summarized in Table 1.

Statistical Analysis

Descriptive statistics (mean and median) are presented in the results section. In addition, data for each patient with confirmed GIB, including:

1. etiology of bleeding;
2. diagnostic modality;
3. therapeutic modality; and
4. clinical outcomes

were presented in raw tabular form.

Results

Over the eight-year retrospective study period, 237 patients underwent VAD placement at the University of Michigan (134 continuous flow; 103 pulsatile). Sixty-five patients had

concurrent diagnoses of VAD and some form of GIB. Of these, 26 subjects met inclusion criteria and were deemed appropriate for this analysis of patients with a ventricular assist device and clinically relevant overt gastrointestinal hemorrhage. The remaining subjects were excluded because either MCS was temporary in nature or the GIB was not substantial enough to meet inclusion criteria. For all reported percentages in this study, the denominator is 26. Most of the reported gastrointestinal bleeding data pertain to the subject's index bleeding event.

Demographics

The mean age of subjects in this study was 60.4 years (range 31–78). Seventeen subjects (65%) were men. All subjects had a diagnosis of systolic heart failure. Fifteen of the subjects (58%) developed heart failure as a result of coronary artery disease. Seven (27%) developed heart failure as a result of valvular heart disease; only one subject had aortic stenosis. Eleven subjects (42%) had renal failure (defined as creatinine ≥ 1.4 mg/dl) at the time of their index post-VAD bleed. The mean Charlson comorbidity index was 4.3 (range 2–7). Twenty-two subjects (85%) had a Heartmate II (continuous flow) VAD. Three subjects (12%) had a Heartmate XVE (pulsatile) device. One subject (4%) had a Heartware HVAD (continuous flow) device. One of the subjects with a Heartmate II had a concurrent Abiomed extracorporeal right ventricular assist device.

Twenty-two subjects (85%) were taking daily aspirin at the time of hemorrhage. Sixteen subjects (62%) were taking warfarin. Twelve subjects (46%) were taking dipyridamole. Five subjects (19%) were taking pentoxifylline and 3 (12%) were taking clopidogrel. One subject (4%) was on argatroban. Twenty subjects (77%) were on more than one anticoagulant or antiplatelet agent.

History of Pre-VAD Gastrointestinal Bleeding and Endoscopy

Four subjects (15%) had experienced clinically significant GIB before VAD placement. Of these, two had an endoscopically identified cause; one bled from gastric antral erosions and the other from a gastric ulcer. Eight subjects (31%) had undergone some form of endoscopic evaluation before VAD placement, including the four subjects with a previous history of GI hemorrhage. Three subjects had an esophagogastroduodenoscopy (EGD) and colonoscopy, two had undergone colonoscopy only, and two had undergone EGD only; one had undergone a flexible sigmoidoscopy. The indications for endoscopic evaluation were GIB (four subjects), colorectal cancer screening (two subjects), small-volume bright red blood per rectum (one subject), iron-deficiency anemia (one subject), diverticulitis (one subject), and nausea (one subject). The endoscopic diagnoses for those undergoing pre-VAD evaluation were: diverticulosis (two subjects), gastric ulcer (one subject), gastric erosions (one subject). No subjects were found to have arteriovenous malformations (AVMs).

Bleeding Presentation

The median time between VAD placement and GI hemorrhage was 32 days, with a mean time to hemorrhage of 118 days (6–704 days). Fifteen (58%) subjects presented with melena. One presented with a combination of melena and maroon stools. Six (23%) presented with maroon stools. Three presented with bright red blood per rectum. The mean

hemoglobin nadir for patients with GIB was 7.7 g/dl (range 4.9–12). Eleven subjects (42%) had an INR > 1.5 at presentation, with four patients (15%) having an INR > 3.0. Nineteen subjects (73%) required blood transfusion with an average of three units of packed red blood cells transfused (range 2–15 units).

Endoscopic Evaluation

All 26 subjects underwent some form of endoscopic evaluation. Twenty-four (92%) subjects underwent upper endoscopy. Sixteen (67%) underwent colonoscopy. Thirteen (50%) underwent video capsule endoscopy (VCE). Four patients (15%) underwent balloon-assisted enteroscopy. Eight subjects (33%) underwent a radionuclide tagged red blood cell scan. Four (15%) of these underwent angiography for a positive tagged red cell result.

Nineteen of the 26 subjects (73%) were found to have evidence of recent hemorrhage (fresh or digested blood) on endoscopic evaluation. Of these, a secure diagnosis was eventually achieved for 17 subjects, 16 endoscopically and one surgically. Suspected, but not confirmed, diagnosis for the other two subjects was achieved on the basis of endoscopy (19%). Seven subjects had no evidence of recent hemorrhage during endoscopic evaluation. Suspected, but not confirmed, sources of bleeding were identified endoscopically for four of these. For the remaining three no potential sources were identified despite endoscopic evaluation of the UGI tract, small bowel, and colon.

Causes of Bleeding and Treatment

The reported causes of bleeding for all 17 subjects with a confirmed source are listed in Table 2. The most common etiology was vascular lesions, AVMs accounting for 38% of subjects and Dieulafoy lesions accounting for 15%. Peptic ulcers accounted for 8%. Of the 17 patients with a confirmed diagnosis, the cause of the index bleed was determined by upper endoscopy for nine subjects. Four patients were diagnosed by video capsule endoscopy (VCE) and three were diagnosed by small-bowel enteroscopy. For one patient diagnosis was achieved by right hemicolectomy. A definitive diagnosis was not achieved for any subject by colonoscopy. In cases where a definitive diagnosis was made, a median of 3.3 endoscopic procedures were necessary to identify the source (range 1–9 endoscopies). Of the six subjects with suspected (but not confirmed) sources of bleeding, the presumed cause was determined by colonoscopy for three patients, upper endoscopy for two patients, and VCE for one patient.

Initial endoscopic hemostasis was achieved in 14/17 (83%) subjects with a definitive source of bleeding, and in 14/15 (93%) patients for whom bleeding did not stop spontaneously. Hemostasis was achieved with upper endoscopy for nine subjects, balloon-assisted enteroscopy for four patients, small-bowel enteroscopy for one subject. For two subjects, bleeding stopped spontaneously before endoscopic hemostasis could be attempted, and for one subject hemostasis was achieved by right hemicolectomy.

Outcomes

Of the 14 patients for whom initial hemostasis was achieved endoscopically, seven had clinically relevant recurrent hemorrhage. Of these, four bled from the same source and all

four were successfully re-treated. Three bled from different sources and two of these three were successfully treated endoscopically. One of these subjects bled from an ulcer that developed as a result of electrocautery used to treat a small bowel AVM one week previously; this lesion stopped bleeding spontaneously with cessation of anticoagulation. One patient with a gastric Dieulafoy lesion and another with a duodenal AVM had second episodes of rebleeding and were endoscopically treated, again with sustained response. On average, rebleeding occurred a median of 18 days after the index event (range 7–29 days).

Seven of the 26 patients did not have evidence of recent hemorrhage on initial endoscopic evaluation. Of these, only one patient developed clinically relevant rebleeding.

None of the subjects in this study died within 30 days of their index bleeding event. Two subjects died within six months of their index bleeding event, neither from a direct complication of gastrointestinal hemorrhage.

Complications

The 26 subjects in this study underwent a total of 97 endoscopic procedures in the evaluation and management of their initial bleeding event. None of these procedures was associated with complications.

Discussion

Gastrointestinal bleeding after VAD placement is an important clinical problem, occurring in 15–40% of recipients [2, 6–8]. Although this complication is well described, little is known about the use of endoscopy in the evaluation and management of this patient population. This study is the largest and most comprehensive to systematically investigate the diagnostic yield and therapeutic efficacy of endoscopy in VAD recipients who experienced overt gastrointestinal hemorrhage.

Our data indicate that vascular lesions (AVMs and Dieulafoy lesions) account for the overwhelming majority of bleeding sources in VAD recipients. This finding is in agreement with previously proposed mechanisms suggesting that, akin to aortic stenosis, VAD recipients may develop altered neurovascular physiology that could potentiate the development of AVMs [10, 11]. Patients with continuous flow VADs experience a consistently narrow pulse pressure that induces increased sympathetic tone and subsequent smooth muscle relaxation, promoting arteriovenous dilation [12].

This higher predisposition to bleeding from vascular malformations is exacerbated by the proteolysis and depletion of the von Willebrand factor (vWF) that occurs as blood crosses the impeller mechanism of continuous flow VADs. vWF multimers are thought to be particularly important in maintaining platelet-mediated hemostasis as blood flows through AVMs [8, 13–15]. Indeed, in the University of Michigan experience, 17% of subjects with continuous-flow devices developed bleeding, compared with only 3% of those with pulsatile devices, congruent with previously published data revealing a much higher risk of bleeding for patients with continuous flow VADs [8].

Our study contradicts the suggestion of the second largest study on this topic proposing that aggressive gastrointestinal evaluation may be of limited utility in identifying and addressing GIB in VAD recipients [7]. Our experience suggests that endoscopy is a safe and essential tool in the evaluation, risk-stratification, and management of this patient population. A fundamental difference in these studies is that >50% of subjects in our cohort underwent endoscopic evaluation of the small bowel, compared to only one subject in the previous study. Indeed, almost 30% of our patients had vascular malformations beyond the ligament of Treitz. The advent of deep bowel endoscopy enables therapy of AVMs throughout the small intestine, as evidenced by the four patients in our study who experienced sustained hemostasis after ablation therapy at the time of balloon-assisted enteroscopy.

A definitive diagnosis was established by endoscopy for 58% of subjects. With the exception of one case, endoscopy was successful in establishing a diagnosis in all subjects with sustained hemorrhage that eventually required some form of intervention for hemostasis. In contrast, angiography was ineffective in establishing a diagnosis or achieving hemostasis for the four patients who underwent this intervention.

From a risk-stratification standpoint, evidence of recent hemorrhage within the GI tract on endoscopic evaluation predicted sustained or recurrent bleeding in 18/19 subjects (95%). Conversely, the absence of fresh or recent blood on endoscopic evaluation predicted the lack of clinically relevant rebleeding for six of seven such patients.

Therapeutically, endoscopic hemostasis seemed critical in the management of this patient population. Endoscopy provided initial therapy in all but one patient with sustained bleeding. This patient had undergone a complete endoluminal evaluation with evidence of active colonic hemorrhage, but inadequate visualization of the bleeding source. He eventually underwent a right hemicolectomy, providing definitive therapy for a colonic AVM. On average, however, 3.3 endoscopic procedures were necessary for each patient before the cause of bleeding was established, and several subjects underwent an additional procedure for hemostasis. The incidence of rebleeding after initial endoscopic hemostasis was 50% within 30 days, although recurrent hemorrhage was successfully treated by endoscopy in all cases of sustained rebleeding.

In this limited cohort of patients, a relative lack of diagnostic and therapeutic utility was observed for colonoscopy. A definitive diagnosis was not provided by colonoscopy in any case, nor was colonoscopic hemostatic therapy delivered. All but one subject with sustained hemorrhage bled from an upper GI or small-bowel source. Those patients for whom endoscopic hemostatic therapy was successful underwent an average of 2.2 unnecessary colonoscopies, suggesting overutilization of this test for VAD recipients. Although colonoscopy is likely to be important in some VAD patients with GIB, particularly those presenting with bright red blood per rectum, prospective studies are necessary to establish the cost and clinical effectiveness of an algorithm preferentially concentrating on EGD and capsule endoscopy (+ balloon-assisted enteroscopy if necessary) for those presenting with any form of bleeding other than bright red blood per rectum.

Although this study serves as the first comprehensive endoscopic characterization of GIB in VAD recipients, the results should be interpreted with caution, because this was a retrospective analysis of a small cohort of patients. These results may provide an initial basis for establishing evidence-based practice, but mostly underscore the need for a prospective multi-center registry of bleeding events in VAD recipients.

In summary

- a. The most common cause of GIB in VAD recipients is vascular lesions.
- b. Endoscopy seems to be a safe and effective tool for diagnosing, risk stratifying, and treating VAD patients with GIB, although multiple endoscopies may be necessary before therapeutic success, and the incidence of rebleeding is high.
- c. Evaluation of the small bowel appears important for this patient population and diagnostic and therapeutic success is reasonable for patients with a negative EGD.
- d. On the basis of this small cohort, colonoscopy seems to be of limited utility and is overutilized for VAD patients with bleeding; further studies are necessary to establish whether a strategy of preferential upper GI tract and small bowel evaluation will dominate standard bleeding algorithms that include early colonoscopy.
- e. A prospective multi-center registry is necessary to establish evidence-based algorithms for management of VAD patients with GIB.

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Table 1

Synopsis of the data abstraction form used in this study

General clinical factors	
1. Demographics	
2. Comorbid conditions and Charlson comorbidity index	
3. Cardiac diagnoses, including pre-VAD echocardiographic information	
4. Assist device information	
5. Medications, including antiplatelet therapy, anticoagulants, proton-pump inhibitors, and non-steroidal anti-inflammatory drugs	
Preoperative gastrointestinal history	
1. History and course of GI bleeding before VAD placement	
2. History of preoperative endoscopic evaluation	
Clinical characteristics of bleeding	
1. Time from VAD implantation to index bleeding event	
2. Type of hemorrhage: hematemesis, melena, maroon stools, BRBPR	
3. Hemoglobin nadir during bleeding	
4. Coagulation data	
5. Transfusion requirements	
Diagnostic evaluation of index bleeding event	
1. Upper endoscopy	
2. Colonoscopy	
3. Video capsule endoscopy	
4. Balloon-assisted enteroscopy	
5. Tagged red cell study	
6. Angiography	
Source of bleeding identified (y/n)	
Concrete diagnosis (y/n)	
Modality of diagnosis	
Etiology of bleeding (final diagnosis)	
Method of hemostasis	
Rebleeding, cause, and method of hemostasis	
1. 3 days	
2. 1 month	
3. 6 months	
Death and cause	
1. 3 days	
2. 1 month	
3. 6 months	

Table 2

Causes, evaluation, therapy, and outcomes of bleeding in the 16 study subjects with confirmed causes of GIB

#	Cause	Diagnosis	Therapy	Rebleed	Repeat therapy
1	Jejunal AVM	VCE	BAE	No	None
2	Jejunal AVM	SBE	BAE	No	None
3	Jejunal AVM	VCE	BAE	20 days, same lesion	BAE
4	Jejunal AVM	VCE	None, stopped spontaneously	No	None
5	Jejunal AVM	SBE	BAE	7 days, post-therapy ulcer	None, stopped spontaneously
6	Gastric and duodenal AVMs	EGD	EGD	12 days, same lesions	EGD
7	Gastric, duodenal, and jejunal AVMs	SBE	SBE	8 days, same lesions	SBE
8	Gastric ulcer	EGD	EGD	23 days, separate ulcer	None, no therapy for low risk stigmata
9	Duodenal AVM	EGD	EGD	32 days, same lesion	EGD
10	Duodenal Dieulafoy	VCE	None, stopped spontaneously	No	None
11	Duodenal Dieulafoy	EGD	EGD	No	None
12	Duodenal Dieulafoy	EGD	EGD	No	None
13	Duodenal ulcer	EGD	EGD	No	None
14	Gastric Dieulafoy	EGD	EGD	29 days, separate Dieulafoy	EGD
15	Gastric AVM	EGD	EGD	No	None
16	Cameron's ulcer	EGD	EGD	No	None
17	Colon AVM	Right hemicolectomy	Right hemicolectomy	114 days, duodenal AVM	EGD

AVM, arteriovenous malformation; EGD, esophagogastroduodenoscopy; VCE, video capsule endoscopy; BAE, balloon-assisted enteroscopy; SBE, small-bowel enteroscopy