Outcomes of gastrointestinal bleeding in patients with left ventricular assist devices: a tertiary care experience

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ABSTRACT

Background and study aims Left ventricular assist device (LVAD) placement is a therapeutic modality for patients with end-stage heart failure. Gastrointestinal bleeding is a common complication following LVAD implantation. The aim of this study was to report our experience in management and outcomes of gastrointestinal bleeding in a large cohort of patients with LVADs.

Patients and methods We performed a retrospective review of all patients who underwent LVAD implantation at the University of Rochester Medical Center from January 2008 to June 2017. Data were collected on patient characteristics, clinical aspects of gastrointestinal bleeding events, and procedural interventions. A Cox proportional hazard model was utilized to identify potential risk factors for a gastrointestinal bleeding event.

Results During the study period, 345 patients underwent LVAD implantation. Of these, 125 patients (36.2 %) experienced 297 gastrointestinal bleeding events resulting in 533 endoscopic procedures. The diagnostic yield of endoscopy in determining a bleeding source was 49.5 %. If required, therapeutic interventions were successful in achieving homeostasis in 96.2 % of procedures. Our 30-day overall post-procedure adverse event (AE) rate was 6.6 %. Procedure-related (bleeding, infection, and perforation) AEs were very minimal (2.8 %). A Cox proportional hazard model indicated that older age at implant, female sex, African-American race, diabetes mellitus, and pulmonary hypertension were statistically significant predictors of a gastrointestinal bleeding event following LVAD implantation.

Conclusions LVAD patients have a high risk of gastrointestinal bleeding. Endoscopy was able to safely locate a bleeding lesion in approximately half of our patients and was successful in treating bleeding lesions in a majority of the cases.

Introduction

Heart failure (HF) has an estimated prevalence of 2.2 % in the United States, with an expected increase of 3 % to 4 % in the next 20 years [1, 2]. Left ventricular assist device (LVAD) implantation is the standard of care in end-stage HF refractory to medical management either as a bridge to transplant or as destination therapy. Currently, nearly 50 % of LVADs are being implanted as destination therapy [3]. One of the most common adverse events (AEs) in the post-LVAD implantation period is gastrointestinal bleeding, with a reported prevalence of 14.8 % to 23.0 % [4–9].

Pathogenesis of a gastrointestinal bleeding event in the LVAD patient population is not completely understood; however, it is often reported that gastrointestinal bleeding events occur due to development of a gastrointestinal angiodysplasia (GIAD) [9–11]. The pathophysiological mechanism underlying gastrointestinal bleeding occurrence in patients with LVAD may be similar to Heyde's Syndrome, in that patients with aortic stenosis are at a higher risk of gastrointestinal bleeding [12]. In patients with an LVAD, the normal pulse pressure is dimin-

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ished and is comparable to severe aortic stenosis. A loss of pulse pressure is believed to create alterations in hemodynamics that trigger the development of angiodysplasias [12, 13]. In addition, reduction in pulse pressure creates shear forces that can contribute to occurrence of an acquired von Willebrand disease (vWD) [14]. In vivo reductions in von Willebrand factor (vWF) have been confirmed in LVAD patients, with normalization of levels post-heart transplant [15]. An acquired vWD produces a coagulopathy, which increases overall bleeding risk that is compounded by the requirement for prophylactic anticoagulation for all LVAD patients. Cohort studies examining preimplantation risk factors for development of gastrointestinal bleeding events in patients with LVADs have produced mixed results. Several studies have reported that increased age at time of LVAD placement may increase risk of a subsequent gastrointestinal bleeding [6, 16–19]. Other studies have indicated that a history of gastrointestinal bleeding, use of the LVAD as destination therapy, or right heart dysfunction are independent risk factors for gastrointestinal bleeding in LVAD patients [20–23].

Most suggested management approaches advocate for endoscopic evaluation and intervention, with a reported diagnostic yield ranging from 30 % to 71 % for gastrointestinal bleeding in the LVAD population [6, 18, 24–27]. There is a school of thought that endoscopic management may have limited utility in the LVAD population, as a majority present with an occult gastrointestinal bleeding, making diagnosis more difficult with conventional endoscopic techniques [28]. This limitation may be overcome with early use of device-assisted enteroscopy (DAE) to directly visualize more of the small bowel. A recent systematic review reported that performing DAE early in the course of assessment for suspected gastrointestinal bleeding in this population is associated with decreased transfusion requirements, decreased time to endoscopic intervention, and a high diagnostic yield [29]. In addition, use of video capsule endoscopy (VCE) may further increase diagnostic yield as VCE allows the endoscopist to narrow down the location of a gastrointestinal bleeding source prior to performing DAE. Although the literature describing the utility of endoscopy in assessment of a gastrointestinal bleeding in the LVAD patient is increasing, there is still considerable disagreement on its utility versus conventional management.

The aim of this study is to report our experience in endoscopic management and outcomes of gastrointestinal bleeding in the LVAD population at an academic tertiary care setting. To date, our cohort represents the largest single-center gastrointestinal bleeding data in the LVAD population reported in the literature. Specific areas of interest were to identify potential risk factors for gastrointestinal bleeding and describe outcomes and safety of endoscopic management of gastrointestinal bleeding in LVAD patients.

Patients and methods

Study population & data collection

We retrospectively reviewed electronic medical records of all patients who underwent implantation of an LVAD at the University of Rochester Medical Center (Rochester, NY) between January 2008 and June 2017 to identify those that were admitted with gastrointestinal bleeding (gastrointestinal bleeding). Each gastrointestinal bleeding event was considered independent, and thus analyzed separately. Data were obtained on clinical presentation at time of gastrointestinal bleeding, length of each hospitalization, relevant laboratory studies, and requirements for transfusion per gastrointestinal bleeding event. In addition, data were collected on all endoscopic and radiologic procedures performed during each hospitalization, location of gastrointestinal bleeding (if source identified), endoscopic interventions (if applicable), and post-procedural (30-day) AE rates. An identifiable source of bleeding was defined as: a lesion seen during an endoscopic exam that had evidence of active or recent bleeding that was documented by the endoscopist to be significant enough to cause the patient's clinical presentation. This study protocol was reviewed and approved by the University of Rochester Medical Center institutional review board. All patients who underwent an endoscopic procedure had proper informed consent taken in accordance with institutional policies.

Statistical methods

Baseline clinical characteristics were compared between patients with or without gastrointestinal bleeding events during follow-up. Continuous measures were expressed as mean ± SD and range while categorical data were summarized as frequencies and percentages. Statistical comparisons were performed using the Wilcoxon rank-sum test for continuous variables and chi-square test for dichotomous variables, as appropriate. Diagnostic yield was calculated as the number of endoscopic procedures that revealed a bleeding source/total number of endoscopic procedures (note: procedures performed after a source of bleeding was located were not included in this calculation).

Success rate of endoscopic intervention(s) was defined as the number of procedures wherein hemostasis was achieved/total number of procedures with endoscopic intervention (note: there were several procedures with more than one endoscopic intervention, for the purpose of this calculation, each procedure with an intervention was only counted once toward the denominator). Thirty-day AE event rate was defined as any AE occurring within 30 days of the completion of the procedure. Each procedure was considered independently. For the vast majority of subjects with complete follow-up data (n = 330), survival analysis techniques were utilized. The cumulative probability of gastrointestinal bleeding was displayed using the Kaplan-Meier method and statistical significance was determined to compare different groups with the log-rank test. Multivariate Cox proportional hazards regression models were used to model the time-to-event endpoints of index gastrointestinal bleeding and mortality. Covariates associated with predicting risk of these endpoints were determined employing the "best

subsets" regression methodology. Specifically, the best subsets method of variable reduction examines the best models containing one, two, or three variables, and so on, and makes comparisons based on the global score chi-square statistic. In addition, variables needed to be significant at $P < 0.10$ for inclusion in the model. For the mortality endpoint, gastrointestinal bleeding was modeled as a time-dependent covariate in the proportional hazards regression model. Analyses were performed using Microsoft Excel, SPSS Version 24 (IBM) and SAS 9.4.

Results

A total of 345 patients underwent LVAD implantation during the study period, with 125 (36.2%) having at least one gastrointestinal bleeding event. Each gastrointestinal bleeding event was recorded independently (n = 297). Patients experienced a median of two bleeds with a median time-to-index gastrointestinal bleeding of 0.54 years (range = 0–6.24 years). Patient characteristics are described in ▶Table 1. Statistical analyses revealed that those with a gastrointestinal bleeding were more likely to be older (60.0 vs. 54.4; $P < 0.001$), of African-American race (21.0% vs. 10.7%; $P = 0.05$), diagnosed with Type 2 diabetes mellitus (DM-II) (36.8% vs. 26.8%; $P = 0.05$), pulmonary hypertension (12.0% vs. 5.0%; $P = 0.02$), or chronic kidney disease (32.8% vs. 19.1%; $P < 0.001$); and to have ischemic cardiomyopathy as an indication for LVAD implant (46.3% vs. 31.5%; $P = 0.02$).

As demonstrated in the KM graphs (▶Fig. 1, ▶Fig. 2, ▶Fig. 3), younger patients (≤60) had cumulative probability of 24% at 3 years while older patients had a probability of 56%. Similarly, patients who were not diabetic at baseline had a 3-year cumulative probability of gastrointestinal bleeding of 32% while those who were diabetic had rate of 53%.

Results of the multivariate Cox proportional hazards models for index gastrointestinal bleeding and mortality are shown in ▶Table 2 and ▶Table 3. Predictors associated with risk of gastrointestinal bleeding were age at implant, sex, African-American race, diabetes, pulmonary hypertension, and history of acute MI. Risk of a gastrointestinal bleeding event increased by 6% for each year older at the time of implant. Male patients exhibited a 37% lower risk than females. Patients of African-American race had more than double (2.75 times) the risk of developing a gastrointestinal bleeding. Comorbidities of DM-II and pulmonary hypertension each independently elevated risk of gastrointestinal bleeding by approximate two-fold (HRs 1.8 and 2.2, respectively) while history of acute MI halved the risk. For the mortality endpoint, even after adjustment for age at implant, diabetes and NYHA class, time-dependent gastrointestinal bleeding significantly increased risk of mortality (HR 2.36, 1.58–3.53). When adjusting for baseline Hemoglobin, these results were similar (over 20% were missing this biomarker and so were included in primary analysis).

Characteristics of each independent gastrointestinal bleeding event are portrayed in ▶Table 4. In patients hospitalized for their gastrointestinal bleeding event, median length of stay (LOS) was 8 days (range 0–173 days). The majority of patients (59.2%) were readmitted for a subsequent gastrointestinal bleeding event. Median time to readmission (following prior hemostasis, if the patient had multiple readmissions for gastrointestinal bleeding events) was 118 days. Upon presentation for gastrointestinal bleeding evaluation, median hemoglobin concentration was 6.9 g/dL (Range 4.0–15.0), and a median INR of 2.0 (Range 1.0–8.6). Patients were transfused with a median of four units of packed red blood cells per admission for gastrointestinal bleeding, using standard transfusion thresholds of hemoglobin less than 7.0 g/dL.

Procedural characteristics are described in ▶Table 5. To evaluate LVAD patients with a suspected gastrointestinal bleeding, 533 endoscopic procedures were performed. At time of their gastrointestinal bleeding event, the majority of patients were on an antithrombotic regimen (97%), with the most common being a combination of warfarin plus aspirin (73%). The most common presentations of gastrointestinal bleeding were melena (n = 142; 47.8%) and symptomatic anemia, without overt signs of gastrointestinal bleeding (n = 77; 25.9%). If a source of bleeding was determined, the location was most often in the stomach (n = 113; 39.4%) or small bowel (n = 83; 28.9%). GIADs were the most frequent endoscopic finding (n = 121; 42.4%). Our overall diagnostic yield for endoscopic evaluation of gastrointestinal bleeding was 49.5%. A total of 226 interventions were performed, with the most common being argon plasma coagulation (n = 77; 34.1%) or endoclip placement (n = 67, 29.6%). The success rate in achieving hemostasis by performing endoscopic interventions was 96.2%. Procedure-related AEs were very minimal (2.8%) in our cohort. Thirteen post-procedure bleeds were noted; however, it was difficult to delineate if these were a continuation of their index bleeding event. Perforation (n = 1) occurred in the rectosigmoid, during colonoscopy and was managed successfully with endoscopic Ovesco clip closure. One case of acute phlebitis was seen following peripheral intravenous placement and was managed conservatively with a 10-day course of antibiotics. Thirty-day post-procedure AEs included LVAD pump thrombosis (0.38%), cerebrovascular accident (CVA; 0.75%), and death (2.6%). No reported deaths were associated with endoscopic procedures or interventions.
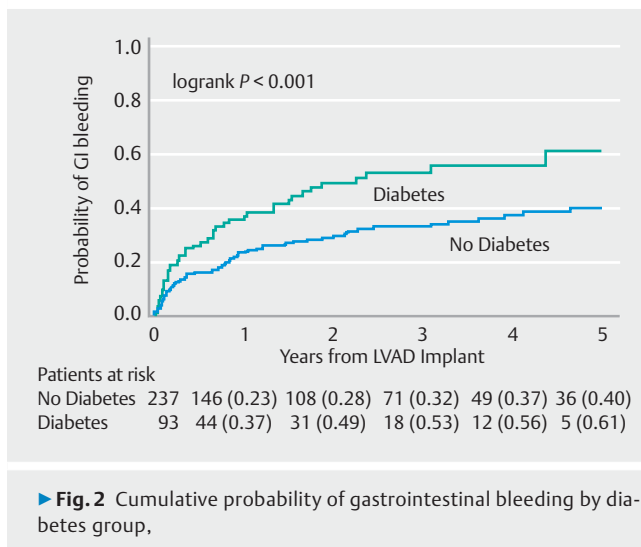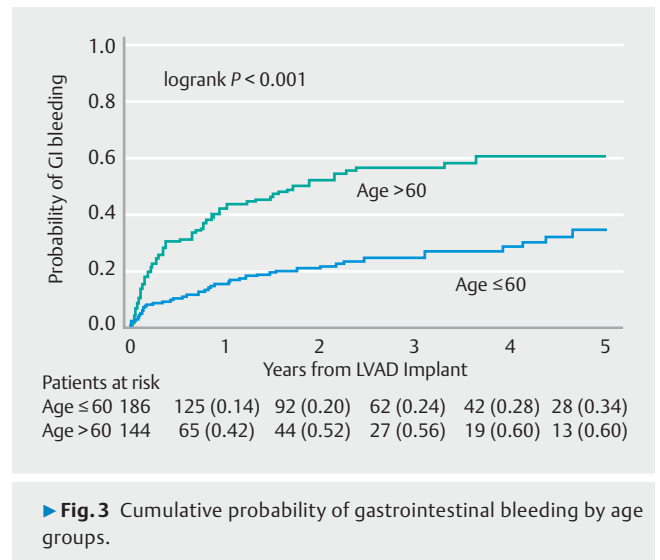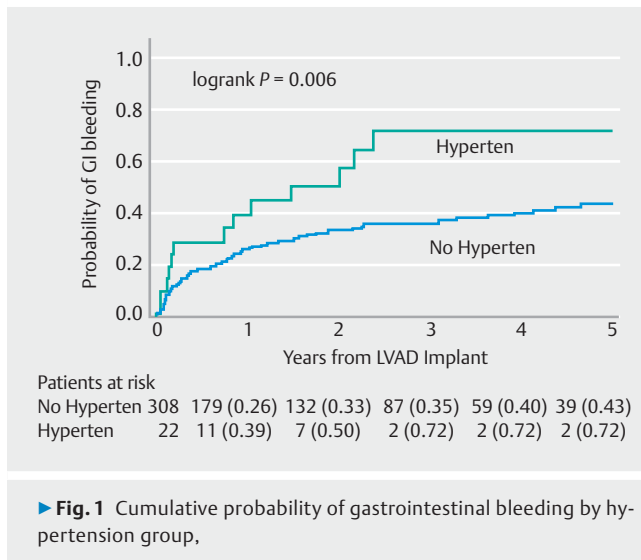
Discussion

Gastrointestinal bleeding is the most common, long-term AE post-LVAD placement and can lead to significant morbidity and need for repeated endoscopic procedures. To our knowledge, this cohort represents the largest single-center report on endoscopic management of gastrointestinal bleeding events in the LVAD population. Our study confirms that gastrointestinal bleeding is a very common AE following LVAD implantation (36.2%; n = 125/345). Interestingly, our cohort had a higher rate of bleeding in LVAD patients as compared to national averages (36.2% vs. 14.8–23.0% in prior literature, potentially related to the significantly longer time patients spend in our region waiting for heart transplantation, coupled with the increasing number of LVAD devices being implanted as destination therapy [29]. Although moderate in severity, these gastro-

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▶ **Table 1** Patient Characteristics in LVAD patients with and without gastrointestinal bleeding events.

	Total population (n = 345)	Non-gastrointestinal bleeding (n = 220)	Gastrointestinal bleeding (n = 125)	*P* value
Age at LVAD implant (mean, SD)	56.4 (12.0)	54.4 (12.6)	60.0 (9.9)	**< 0.001**
▪ Range, years	18–86	18–81	22–86	
Sex				
▪ Male	277 (80.3 %)	180 (81.8 %)	97 (77.6 %)	0.34
▪ Female	68 (19.7 %)	40 (18.2 %)	28 (22.4 %)	
Race (n = 339)				
▪ White	288 (84.9 %)	190 (88.4 %)	98 (79.0 %)	**0.05**
▪ African-American	49 (14.5 %)	23 (10.7 %)	26 (21.0 %)	
▪ Other	2 (0.59 %)	2 (0.93 %)	0 (0 %)	
BMI at LVAD implant (mean, SD)	29.5 (6.0)	29.5 (5.4)	29.4 (6.9)	0.94
▪ Range, BMI (kg/m^2)	14.2–72.7	16.9–48.0	14.2–72.7	
Comorbidities at LVAD implantation				
▪ CHF	303 (87.8 %)	190 (86.3 %)	113 (90.4 %)	0.27
▪ HTN (n = 344)	170 (49.4 %)	100 (45.7 %)	70 (56.0 %)	0.07
▪ CAD	168 (48.7 %)	101 (45.9 %)	67 (53.6 %)	0.17
▪ Hyperlipidemia	165 (47.8 %)	100 (45.4 %)	65 (52.0 %)	0.24
▪ DM-II	105 (30.4 %)	59 (26.8 %)	46 (36.8 %)	**0.05**
▪ CKD	83 (33.9 %)	42 (19.1 %)	41 (32.8 %)	**< 0.001**
▪ History of MI	70 (20.3 %)	40 (18.2 %)	30 (24.0 %)	0.20
▪ COPD	51 (14.8 %)	29 (13.2 %)	22 (17.6 %)	0.27
▪ OSA	53 (15.4 %)	32 (14.5 %)	21 (16.8 %)	0.58
▪ LVH	48 (13.9 %)	32 (14.5 %)	16 (12.8 %)	0.65
▪ Pulmonary HTN	26 (7.5 %)	11 (5.0 %)	15 (12.0 %)	**0.02**
▪ CVA	22 (6.4 %)	14 (6.4 %)	8 (6.4 %)	0.99
▪ History of thrombus/thromboembolic event	23 (6.7 %)	17 (7.8 %)	6 (4.8 %)	0.30
Indication for LVAD Implant (n = 340)				
▪ Ischemic cardiomyopathy	125 (36.8 %)	69 (31.5 %)	56 (46.3 %)	**0.02**
▪ Non-ischemic cardiomyopathy	127 (37.4 %)	83 (37.9 %)	44 (36.4 %)	
▪ Acute MI	50 (14.7 %)	39 (17.8 %)	11 (9.1 %)	
▪ Other	38 (11.2 %)	28 (12.8 %)	10 (8.3 %)	
LVAD Type (n = 344)				
▪ Heartmate-II	306 (89.0 %)	192 (87.2 %)	114 (91.9 %)	0.24
▪ Heartmate-III	13 (3.8 %)	9 (4.1 %)	4 (3.2 %)	
▪ Heartware	6 (1.7 %)	3 (1.4 %)	3 (2.4 %)	
▪ Other	19 (5.5 %)	16 (7.3 %)	3 (2.4 %)	
LVAD for bridge to ttransplant (n = 307)	179 (58.3 %)	116 (59.5 %)	63 (56.3 %)	0.58

BMI, body mass index; CHF, congestive heart failure; HTN, hypertension; CAD, coronary artery disease; DM-II, diabetes mellitus, Type 2; CKD, chronic kidney disease; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; LVH, left ventricular hypertrophy; CVA, cerebrovascular accident.
Statistical analysis demonstrated significant association between older age (*P* < 0.001), African American race (*P* = 0.05), Type 2 diabetes (*P* = 0.05), chronic kidney disease (*P* < 0.001), pulmonary hypertension (*P* = 0.02), and ischemic cardiomyopathy as the indication for LVAD implant (*P* = 0.02) and development of gastrointestinal bleeding in the post-LVAD implantation course.

▶ Fig. 1 Cumulative probability of gastrointestinal bleeding by hypertension group,

Patients at risk
No Hyperten 308 179 (0.26) 132 (0.33) 87 (0.35) 59 (0.40) 39 (0.43)
Hyperten 22 11 (0.39) 7 (0.50) 2 (0.72) 2 (0.72) 2 (0.72)

▶ Fig. 3 Cumulative probability of gastrointestinal bleeding by age groups.

Patients at risk
Age ≤60 186 125 (0.14) 92 (0.20) 62 (0.24) 42 (0.28) 28 (0.34)
Age >60 144 65 (0.42) 44 (0.52) 27 (0.56) 19 (0.60) 13 (0.60)

▶ Fig. 2 Cumulative probability of gastrointestinal bleeding by diabetes group,

Patients at risk
No Diabetes 237 146 (0.23) 108 (0.28) 71 (0.32) 49 (0.37) 36 (0.40)
Diabetes 93 44 (0.37) 31 (0.49) 18 (0.53) 12 (0.56) 5 (0.61)

intestinal bleeding events may increase risk of morbidity due to lengthy hospitalizations and the high propensity to develop recurrent gastrointestinal bleedings, often resulting in need for more endoscopic interventions. Endoscopy was demonstrated to be a safe and effective diagnostic and therapeutic modality to manage bleeding lesions in the LVAD population in our study. Nearly half the endoscopic procedures (49.5%) identified a source of bleeding, with an interventional success rate (to achieve hemostasis) of 96.2%. No reported deaths were associated with endoscopic procedures or interventions in our study. A recent retrospective study reviewed a cohort of 87 patients with LVADs implanted at a tertiary care center with a total of 164 gastrointestinal bleeding events [28]. The reported diagnostic yield of endoscopy was significantly lower (30%) as compared to the current study. Given these findings, the authors recommended against routine endoscopic evaluation for occult gastrointestinal bleeding events, unless hemodynamic instability is present or significant transfusions are required; however, with a higher diagnostic yield during the episode of

▶ Table 2 Cox proportional hazards multivariate models for the endpoint of first gastrointestinal bleed.

Parameter	P value	Hazard ratio	95% CI	
			LCL	UCL
Age at implant	<.0001	1.06	1.04	1.08
Male	0.054	0.63	0.40	1.01
African-American race	<.0001	2.75	1.68	4.49
DMII baseline	0.004	1.77	1.20	2.61
Pulmonary HTN baseline	0.012	2.12	1.18	3.82
Acute MI	0.072	0.56	0.30	1.05
Hemoglobin B	0.030	0.87	0.76	0.99

CI, confidence interval; LCL, confidence limit; UCL, upper confidence limit; DM-II, diabetes mellitus, Type 2; HTN, hypertension; MI, myocardial infarction

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▶ **Table 3** Cox proportional hazards multivariate models for the endpoint of all-cause mortality.

Parameter	P value	Hazard	95 % CI	
		ratio	LCL	UCL
Age at implant	0.009	1.03	1.01	1.04
DMII baseline	0.042	1.47	1.01	2.14
NYHA Class	0.007	1.89	1.19	2.98
Td gastrointestinal bleed	<.0001	2.36	1.58	3.53
Td gastrointestinal bleed	0.003	2.10	1.30	3.41
Hemoglobin b	0.022	0.87	0.77	0.98

CI, confidence interval; LCL, lower confidence limit; UCL, Upper confidence limit ; DM-II, diabetes mellitus, type 2; NYHA, New York Heart Association; Td, time dependent

▶ **Table 4** Gastrointestinal bleeding event characteristics.

Event characteristics	Median
Time to first gastrointestinal bleeding event post-LVAD, years Range, years	0.5 0–6.24
LOS, days Range, days	8 0–173
Time to readmission, days[1] Range, days	118 1–1845
Number of readmissions Range	2 1–14
HCT, % at time of gastrointestinal bleeding Event range	22.0 14.0–45.0
HgB, g/dL at time of gastrointestinal bleeding Event range	6.9 4.0–15.0
INR at time of gastrointestinal bleeding event Range	2 1.0–8.6
Platelets at time of gastrointestinal bleeding Event range	213 27–571
PRBC units given Range	4 1–39
FFP units given Range	2 1–8
Platelets given Range	1.5 1–5

LOS, length of stay; HCT, hematocrit, HgB, hemoglobin; INR, international normalized ratio; PRBC, packed red blood cells; FFP, fresh frozen plasma. During the study period, 125 patients had gastrointestinal bleeding events. There were 297 independent bleeding events with a median of two events per patient. Median time from LVAD implant to first gastrointestinal bleeding event was 0.5 years. Median length of stay for gastrointestinal bleeding-associated hospitalizations was 8 days. 59.2 % of patients were readmitted for a subsequent gastrointestinal bleeding event, at a median of 118 days (following prior hemostasis, if the patient had multiple readmissions).
[1] n = 74/125 patients had at least one subsequent readmission (gastrointestinal bleeding-related).

gastrointestinal bleeding, there is clear value of endoscopy in the routine management LVAD patients with a gastrointestinal bleeding event.

Pathophysiology of bleeding in LVAD patients is multifactorial with acquired von Willebrand factor deficiency, hemodynamic flow alterations, and coagulopathy with need for ongoing anticoagulation to prevent pump dysfunction/thrombosis. The majority of the bleeding in these patients is due to GIAD; however, several studies have also reported peptic ulcer disease as a very common source of bleeding in the LVAD patients due to nonsteroidal anti-inflammatory drug (NSAID)-induced damage to the gastrointestinal tract mucosa coupled with platelet inhibitor use and anticoagulation [30].

Endoscopy remains the mainstay in the evaluation of gastrointestinal bleeding events in these patients, with our study indicating upper endoscopy to have the highest diagnostic yield. Push enteroscopy can be considered as an early intervention in recurrent gastrointestinal bleeding events, specifically in patients who present with melena, iron deficiency anemia or occult gastrointestinal bleeding (as the location of the bleeding lesion is most often in the small bowel. This approach is supported in the literature, as it has been reported that performing an enteroscopy early in the course of a gastrointestinal bleeding event may reduce transfusion requirements and increase endoscopic diagnostic yield [31]. For hemodynamically stable patients and those with a negative upper and lower endoscopic evaluation with persistent gastrointestinal bleeding, a VCE with or without computed tomography enterography or a tagged red blood cell scan should be performed. A device-assisted enteroscopy (DAE) would follow, as information gained from VCE and/or radiologic exams would provide the endoscopist with an appropriate target for the procedure. Multiple algorithms have been proposed in the literature [28, 32, 33] for evaluation of gastrointestinal bleeding in LVAD patients; however, there is no standardized guideline for evaluation of these patients and data regarding screening high-risk patients for bleeding prior to LVAD placement are scarce. A recent study reviewed 64 gastrointestinal bleeding events in LVAD patients to evaluate risk of mortality after the index gastrointestinal bleeding event [34]. Their findings suggest increased mortality after

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▶ **Table 5** Endoscopic procedural characteristics.

Procedural characteristics (n = 297 gastrointestinal bleeding)	n (%)
% of procedures performed on inpatients	**257 (86.5 %)**
Antithrombotic use (n = 296)	
▪ Warfarin alone	36 (12.2 %)
▪ Aspirin alone	24 (8.9 %)
▪ Warfarin + aspirin	216 (73.0 %)
▪ Dipyridamole	13 (4.4 %)
▪ Warfarin + aspirin + clopidogrel	5 (1.7 %)
▪ Other	14 (4.7 %)
▪ None	10 (3.4 %)
No. antithrombotic per patient (n = 296)	
▪ 0	9 (3.0 %)
▪ 1	55 (18.6 %)
▪ 2	215 (72.6 %)
▪ 3	17 (5.7 %)
Mean no. antithrombotic agents per patient (n = 296)	1.81
Was antithrombotic held pre-procedure?	
▪ Held	220 (74.1 %)
▪ Continued	30 (10.8 %)
▪ Held & bridged	42 (14.1 %)
▪ Unknown/not reported	5 (1.7 %)
Presenting symptoms of gastrointestinal bleeding[1]	
▪ Symptomatic anemia	150 (50.1 %)
▪ Without other overt signs of gastrointestinal bleeding	77 (25.9 %)
▪ Melena	142 (47.8 %)
▪ Incidentally found anemia	57 (19.2 %)
▪ Hematochezia	42 (14.1 %)
▪ Hematemesis	11 (3.7 %)
▪ Coffee ground emesis	4 (1.3 %)
▪ Hypotension	1 (0.3 %)
Total no. endoscopic procedures performed (gastrointestinal bleeding events)	533
Endoscopic procedures performed	
▪ EGD	228 (42.8 %)
▪ Colonoscopy	125 (23.5 %)
▪ Push enteroscopy	79 (14.8 %)
▪ VCE	68 (12.8 %)
▪ Double-balloon enteroscopy	33 (6.2 %)
▪ Antegrade	26 (78.8 %)
▪ Retrograde	7 (21.2 %)

▶ **Table 5** (Continuation)

Procedural characteristics (n = 297 gastrointestinal bleeding)	n (%)
% of procedures performed on inpatients	**257 (86.5 %)**
Top findings (all gastrointestinal bleeding procedures)	
▪ GIAD	121 (42.2 %)
▪ Ulcer/erosions	38 (13.2 %)
▪ Diffuse bleeding/no pinpoint source	26 (9.1 %)
▪ GAVE	17 (5.9 %)
▪ Bleeding polyps	17 (5.9 %)
▪ Overall diagnostic yield	49.5 %
Top locations of bleeding sources	
▪ Stomach	113 (39.4 %)
▪ Small bowel	83 (28.9 %)
▪ Colon	50 (17.4 %)
Total no. interventions (all gastrointestinal bleeding endoscopic procedures)	226
Top gastrointestinal bleeding interventions	
▪ APC	77 (34.1 %)
▪ Endoclip	67 (29.6 %)
▪ Bicap cautery	57 (25.2 %)
Overall success rate (178/185)	96.2 %
Overall adverse event rate, 30-day	35 (6.6 %)
Non-procedure-related adverse event rate, 30-day	20 (3.8 %)
30-day adverse events (20/533 procedures)	
▪ Death	14 (2.6 %)
▪ CVA	4 (0.8 %)
▪ LVAD pump thrombosis	2 (0.4 %)
Procedural adverse events	15 (2.8 %)
Procedural adverse events (15/533 procedures)	
▪ Bleeding	13 (86.6 %)
▪ Perforation	1 (6.6 %)
▪ Infection	1 (6.6 %)

EGD, Esophagogastroduodenoscopy; VCE, video capsule endoscopy; GIAD, gastrointestinal angiodysplasia; GAVE, gastric antral vascular ectasia; APC, Argon plasma coagulation; CVA, cerebrovascular accident.
Diagnostic yield for procedures was 49.5 %. (Note: procedures performed after source of bleeding found were not included in this calculation). Endoscopic interventions were 96.2 % successful at hemostasis. (Note: there were several procedures with more than one endoscopic intervention; for this calculation each procedure was only once for the denominator). Procedure-related (bleeding, infection, and perforation) adverse events were very minimal (2.8 %). Thirty-day post-procedure adverse events included LVAD pump thrombosis (0.38 %), CVA (0.75 %), and death (2.6 %). No reported deaths were associated with endoscopic procedures or interventions.
[1] Several patients had multiple presenting symptoms, therefore, the total will add up to more than 100 %.

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gastrointestinal bleeding in an LVAD patient, and as a result the authors advocate for assessment of gastrointestinal bleeding risk-factors when patients are being considered for LVAD placement. A nomogram (Utah Bleeding Risk Score) to predict risk of gastrointestinal bleeding in LVAD patients has been proposed in previous literature. This tool incorporates several predictive variables (e. g. coronary artery disease, history of bleeding events, age, etc.) that could potentially be used in the preimplantation period for risk-stratification [35]. Our data suggest that there may be a subset of LVAD patients that have a predisposition to develop a gastrointestinal bleeding. In this cohort, patients that experienced a bleeding event were more inclined to have recurrences; however, there was also a significant proportion (63.8 %) that never had a gastrointestinal bleeding develop in their post-implantation course. Independent risk factors of female sex, African-American race, DMII and pulmonary hypertension were each predictive of a gastrointestinal bleeding event. In existing literature, the only consistently reported risk factor of gastrointestinal bleeding in LVAD patients has been older age at time of implantation [6, 16–19]. If the risk factors demonstrated in our cohort can be validated, appropriate counseling preimplantation and/or endoscopic screening for patients at high risk for post LVAD gastrointestinal bleeding may be considered; however, careful attention should be paid to the risk/benefit profile of such, as pre-LVAD implant patients are at high risk for cardiac events

There are several limitations of this study, inherent to its retrospective design. Our observations and clinical decision-making in management of gastrointestinal bleeding events reflect our single practice, thus results may be difficult to generalize to other institutions. Data were only collected on frequency of endoscopic procedures, not necessarily in the order in which they were performed.

Conclusion

As prevalence of heart failure in the general population continues to rise, the number of patients requiring LVAD implantation is also expected to increase. Evaluation and management of gastrointestinal bleeding in the LVAD population should be well understood by physicians practicing in high-volume LVAD institutions. Our study, with one of the largest cohorts (to our knowledge) of gastrointestinal bleeding in LVAD patients, demonstrated that endoscopy is a useful, effective, and most importantly safe modality, despite this being a high-risk population with necessity for long-term anticoagulant use. A systematic approach is necessary to manage the LVAD population, as risk of developing a gastrointestinal bleeding (most often recurrent GIAD) is inherent due to the requirement for long-term anticoagulation. Thus a multidisciplinary approach is key in management of these patients with close collaboration between the gastroenterology and cardiology teams regarding timing of endoscopy and anticoagulation management. Further studies need to be conducted regarding patient-specific factors that may predict a gastrointestinal bleeding event, the role of screening endoscopy, and the optimal standardized management approach for this population.

Competing interests

The authors declare that they have no conflict of interest.

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