

## Retrospective Cohort Study

# Does endoscopic intervention prevent subsequent gastrointestinal bleeding in patients with left ventricular assist devices? A retrospective study

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## Abstract

### BACKGROUND

Patients with left ventricular assist devices (LVADs) are at increased risk for recurrent gastrointestinal bleeding (GIB) and repeat endoscopic procedures. We assessed the frequency of endoscopy for GIB in patients with LVADs and the impact of endoscopic intervention on preventing a subsequent GIB.

### AIM

To evaluate for an association between endoscopic intervention and subsequent GIB. Secondary aims were to assess the frequency of GIB in our cohort, describe GIB presentations and sources identified, and determine risk factors for recurrent GIB.

### METHODS

We conducted a retrospective cohort study of all patients at a large academic institution who underwent LVAD implantation from January 2011 – December 2018 and assessed all hospital encounters for GIB through December 2019. We performed a descriptive analysis of the GIB burden and the outcome of endoscopic procedures performed. We performed multivariate logistic regression to evaluate the association between endoscopic intervention and subsequent GIB.

### RESULTS

In the cohort of 295 patients, 97 (32.9%) had at least one GIB hospital encounter.

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There were 238 hospital encounters, with 55.4% (132/238) within the first year of LVAD implantation. GIB resolved on its own by discharge in 69.8% (164/235) encounters. Recurrent GIB occurred in 55.5% (54/97) of patients, accounting for 59.2% (141/238) of all encounters. Of the 85.7% (204/238) of encounters that included at least one endoscopic evaluation, an endoscopic intervention was performed in 34.8% (71/204). The adjusted odds ratio for subsequent GIB if an endoscopic intervention was performed during a GIB encounter was not significant (odds ratio 1.18,  $P = 0.58$ ).

## CONCLUSION

Patients implanted with LVADs whom experience recurrent GIB frequently undergo repeat admissions and endoscopic procedures. In this retrospective cohort study, adherence to endoscopic guidelines for performing endoscopic interventions did not significantly decrease the odds of subsequent GIB, thus suggesting the uniqueness of the LVAD population. A prospective study is needed to identify patients with LVAD at risk of recurrent GIB and determine more effective management strategies.

**Key Words:** Gastrointestinal bleeding; Left ventricular-assist device; Endoscopic intervention, Inpatient care; Hospital readmissions; Recurrent bleeding

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**Core Tip:** Patients implanted with left ventricular assist devices (LVADs) whom experience recurrent gastrointestinal bleeding (GIB) frequently undergo repeat admissions and endoscopic procedures. In this retrospective cohort study, a majority of GIB resolved by discharge without intervention and adherence to endoscopic guidelines for performing endoscopic interventions did not significantly decrease the odds of subsequent GIB, thus questioning the role of endoscopy in this population. A prospective study is needed to identify patients with LVAD patients at risk of recurrent GIB and determine more effective management strategies.

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## INTRODUCTION

In the last decade, there has been an overall increase in the implantation of continuous-flow left ventricular assist devices (LVADs), a treatment modality for end-stage heart failure as a bridge to transplant, bridge to recovery, or destination therapy (DT). An overall unchanged rate of heart transplantation has resulted in growing cohort of patients with LVADs[1]. Gastrointestinal bleeding (GIB) is one of the most common adverse event in patients with LVADs[2], cited as affecting 21%-36% of patients[2,3], suggested to be due to chronic anticoagulation (AC) and continuous-flow states[4]. The incidence increases with length of time exposed to LVAD.

Prior cohort studies at tertiary care centers, including one at our institution, describe the GIB sources and outcomes of endoscopic evaluations, suggesting that endoscopic interventions are successful in short-term resolution of GI bleeding[3,5]. Meanwhile, multiple studies have shown that up to 30%-60% of patients experience recurrent bleeding (defined as 2 or more episodes) regardless of intervention[3,4], and a large portion of patients require repeat interventions for recurrent bleeding[6]. There are limited data on whether endoscopic intervention reduces recurrent bleeding, bringing into question its utility in managing this chronic issue.

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The primary aim of this study was to evaluate whether endoscopic intervention could prevent a subsequent GIB in patients with LVADs. Secondary aims were to assess the frequency of GIB in our cohort, describe GIB presentations and sources identified, and determine risk factors for recurrent GIB.

## MATERIALS AND METHODS

### Study population

We performed a retrospective cohort study of all patients  $\geq 18$  years old who underwent LVAD implantation between January 1, 2011 and December 31, 2018 at our large academic institution. For these 319 patients, we reviewed the electronic medical record (EMR) for demographics, and the date, purpose, and type of LVAD implantation. We excluded patients with temporary devices implanted (CentriMag, Thor BiVAD, Total Artificial Heart), resulting in a total of 295 patients. Data were collected from time of LVAD implantation until death, heart transplant, LVAD explantation, or last contact through the EMR, defined as the number of days followed. This chart review was conducted by two clinical physicians and a medical doctorate-trained research assistant.

For each patient, we reviewed the EMR for hospital encounters from January 1, 2011 through December 31, 2019 to identify instances of GIB on admission or during hospitalization, as indicated in discharge summaries, GI consult notes, and/or endoscopic procedure notes. We included encounters as a GIB if there was overt bleeding reported or documented, or the cardiology team documented suspicion for a GIB based on a drop in hemoglobin or other clinical factors with the lack of other explanation. All encounters with procedures for non-bleeding related indications, like colon cancer screening, or iatrogenic bleeding specifically from prior endoscopic procedures were excluded from analysis. Per standard practice by the cardiology team, patients with concern for GIB are managed in the inpatient setting, so there are no outpatient endoscopic procedures.

For each GIB encounter, we recorded laboratory data, blood transfusion requirements, endoscopic data including video capsule endoscopy findings, and relevant patient medications on admission and discharge (AC, antiplatelet, and octreotide). For encounters when GIB was present on admission, we recorded the length of stay. We classified the GIB presentation as overt *vs* occult, where overt indicated bloody output from the GI tract (*i.e.* hematemesis, hematochezia, melena, coffee-ground emesis), and occult indicated no bloody output visualized but the presence of a hemoglobin drop with no other known etiology.

During a GIB encounter, the primary admitting cardiology team would consult the GI service to determine whether to perform an endoscopic procedure. Medical management regarding acid suppression therapy and octreotide was at the discretion of the cardiology team; standard of care was to continue or initiate acid suppression therapy if concerned for upper GI source and only octreotide if concerned for variceal source. Radiologic studies like computed tomography were performed at the discretion of the cardiology team. All endoscopic procedures were performed with GI endoscopists in the inpatient endoscopy operating room under monitored anesthesia care and the presence of an LVAD coordinator. For patients with elevated international normalized ratio (INR)s, endoscopic procedures aside from video capsule endoscopy (VCE) were performed after an INR normalized to 1.5 or below. The decision to proceed with planned endoscopy based on clinical status of the patient and performance of an endoscopic intervention was at the discretion of the GI endoscopist.

This project was reviewed and determined to qualify as Quality Improvement by the University of Pennsylvania's Institutional Review Board.

### Data collection

We reviewed each GIB encounter for endoscopic procedures, including upper endoscopy (EGD) push enteroscopy, single balloon enteroscopy, double balloon enteroscopy, colonoscopy, and VCE. Data were extracted from procedure reports for the presence of a bleeding source and the occurrence of an endoscopic intervention. Endoscopic interventions were defined as epinephrine injection, clip placement, argon plasma coagulation (APC), and bipolar coagulation. For VCE studies, we recorded whether a source was identified and whether an endoscopic procedure occurred afterwards with or without endoscopic intervention.

Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the University of Pennsylvania[7,8]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: (1) An intuitive interface for validated data capture; (2) Audit trails for tracking data manipulation and export procedures; (3) Automated export procedures for seamless data downloads to common statistical packages; and (4) Procedures for data integration and interoperability with external sources.

### **Power calculation**

Based on pilot data suggesting that endoscopic interventions occurred in about a third of encounters, we used a 2:1 allocation ratio. We assumed that endoscopic intervention would decrease the probability of a subsequent GIB from 30% to 50% based on pilot data and what we deemed clinically significant. In order to reject the null hypothesis that endoscopic intervention did not affect subsequent bleeding with a probability (power) of 80% and a type I error probability of 0.05, we needed to study a total of 200 GIB encounters.

### **Independent (exposure) and dependent (outcome) variables**

For the primary aim, the primary outcome variable was a subsequent encounter for GIB. Independent variables included: GIB presentation (overt *vs* occult as defined above), change in AC or antiplatelet therapy, defined as increasing or decreasing doses during the hospitalization or switching agents; days from hospital presentation to endoscopy; source identification during endoscopy or VCE; and endoscopic intervention.

For the secondary aims, the outcome variable was a first GIB. Independent variables included demographics, type of LVAD, purpose of LVAD, and days of exposure to LVAD, defined as the time since LVAD implantation.

### **Statistical analysis**

To evaluate the demographic and clinical differences between those who never had a GIB *vs* those who had at least one, we used a paired *t* test and Wilcoxon rank-sum test for continuous variables that are normally distributed or skewed respectively, and Fisher's exact test for binary and categorical variables. For medians reported, we assessed interquartile range (IQR). We used logistic regression to determine the risk-adjusted impact of endoscopic intervention on subsequent GIB encounters. Risk adjustment variables included age, sex, race, AC status on admission, changes in AC during the admission, source of bleed if applicable, and clinical presentation of GIB. All analyses were performed using STATA version 13.0 (College Station, TX) and reviewed by a biomedical statistician.

## **RESULTS**

### **Frequency of GIB in patients with LVADs**

There was a total of 295 patients who had undergone LVAD implantation during the study period. The devices used were HeartMate2 (57.3%), Heartmate3 (11.2%), and HeartWare (31.5%). 82.3% were male and median age at time of implant was 58.5 years. Patients were followed for a median of 601 d (IQR 165-1138); there were 120 patients who were followed for less than 1 year due to death, device explantation, or heart transplant.

Of the 295 patients, 97 (32.9%) patients presented for at least one GIB encounter. There was a total of 238 bleed encounters, of which 132 (55.4%) were within the first year of LVAD implantation. Time to index GIB was a median of 132 days (IQR 29-338). 87.4% (208/238) of the GIB encounters were in patients on active AC with either warfarin or a direct oral anticoagulant. Aspirin dose was 81mg daily and 325 mg daily in 25.6% (61/238) and 38.7% (92/238) encounters respectively. The most common presentation of GIB was melena (52.9%), followed by other overt GIB (total 21.4%; hematochezia 11.5%, hematemesis 3.0%, coffee-ground emesis 0.4%, not further characterized 6.5%) and occult bleeding (24.0%). Hemoglobin on presentation was a mean of 7.8 g/dL (IQR 6.3-8.8).

Patient characteristics are described in **Table 1** comparing those who had at least one GIB *vs* those without one. Those with GIB were more likely to be older at the time of LVAD implant (age 60.8 *vs* 56.9; *P* = 0.01) and have a higher number of LVAD exposure days (348 *vs* 895, *P* < 0.01). They were also more likely to have the LVAD

**Table 1 Comparative characteristics of patients with left ventricular assistant devices with gastrointestinal bleeding vs no gastrointestinal bleeding, n (%)**

Factor	No GIB	At least 1 GIB	P value
<i>n</i>	198	97	
Age implant, median (IQR)	56.9 (46.9, 67.0)	60.8 (52.7, 69.8)	0.014
Sex (male)	160 (81.2)	82 (84.5)	0.52
Race			0.067
White	113 (57.1)	58 (59.8)	
Black	54 (27.3)	31 (32.0)	
Asian	0 (0.0)	1 (1.0)	
Other	12 (6.1)	5 (5.2)	
Unknown	19 (9.6)	2 (2.1)	
Type of LVAD			0.22
Heartware	66 (33.3)	27 (27.8)	
HeartMate 2	114 (57.6)	55 (56.7)	
HeartMate3	18 (9.1)	15 (15.5)	
LVAD purpose			0.030
Destination (DT)	113 (57.1)	70 (72.2)	
bridge to transplant (BTT)	80 (40.4)	25 (25.8%)	
Bridge to Recovery (BTR)	5 (2.5)	2 (2.1)	
LVAD exposure (d) (IQR)	348 (103, 947)	895 (520, 1433)	< 0.001

The following statistical tests were utilized: Wilcoxon rank-sum test [age, left ventricular-assist device(LVAD)], and Fisher's exact test (sex, race, type of LVAD, LVAD purpose). GIB: gastrointestinal bleeding; IQR: Interquartile range; LVAD: Left ventricular-assist device.

placed as DT (72.2 % vs 57.4 %;  $P = 0.03$ ), though in a logistic regression adjusted for the number of days followed, this was no longer significant ( $P = 0.14$ ). Three patients died during active GIB; in two encounters, the patient had a LVAD thrombosis while AC was held, while in the third, the family declined further evaluation of the GIB.

### Characteristics of endoscopic procedures and interventions

Of the 238 GIB encounters, 204 (85.7%) included at least one endoscopic evaluation including VCE. After excluding 13 encounters with only VCE evaluation, 191 (80.3%) had an invasive procedure. The median number of endoscopic procedures done per encounter was 2 (range 0 to 8). A source was identified in 130/238 (54.6%) encounters; when identified, the source was in the stomach (41.5%), deep small bowel (jejunum and ileum) (30.8%), colon (13.1%), duodenum (13.1%), and esophagus (1.5%). Of 115 encounters where the first procedure was an EGD, 9 (7.8%) included a push enteroscopy later in the same encounter.

An endoscopic intervention was performed in 34.8% (71/204) of encounters with endoscopic evaluation. The most common lesion intervened upon was angioectasias (Table 2). The second most common lesion intervened upon was non-specific oozing, referring to scenarios where there was no identifiable ulcer, angioectasia, or vessel. Other/uncharacterized category includes cases where the documentation did not express the source in the categorical terms. The most common type of intervention was APC and injection was always in conjunction with another intervention.

Among patients who presented to the hospital for a GIB, 45% of encounters with an endoscopic procedure performed within four days resulted in an endoscopic intervention during the hospitalization, compared to 25% if performed on days 5-7 from presentation, and 0 if performed later. Thus, days to the first endoscopic study impacts whether an endoscopic intervention was performed during the encounter [unadjusted odds ratio (OR) 0.80, confidence interval (CI) 0.67-0.96,  $P = 0.018$ ].

Other predictors of endoscopic intervention included overt GIB compared to occult (OR 2.41, CI 1.14-5.10,  $P = 0.022$ ) and transfusion with packed red blood cells (OR 10.0, CI 1.31-76.47,  $P = 0.027$ ).

In encounters for occult bleeding, a culprit lesion was found in 42.1% of cases (24/57). An endoscopic intervention was performed in 10 of 24 (41.6%) and the attributed source was identified as an angioectasia in eight encounters and as oozing

**Table 2 Lesion types and interventions used in endoscopic procedures with interventions, n (%).**

Category		n (%)
Type of intervention	APC	37 (51.4)
	Hemoclip	31 (43.1)
	Injection	23 (31.9)
	Bipolar	16 (22.2)
Culprit lesion	Ulcer	8 (11.1)
	Angioectasia	34 (47.2)
	Dieulafoy	3 (4.2)
	Non-specific oozing	14 (19.4)
	Other/uncharacterized	13 (18.1)

Sum of percentages is greater than 100% as some procedures involved multiple interventions. One encounter had two lesions. APC: Argon plasma coagulation.

without a discrete lesion in the other two encounters. Of 12 encounters where a source was identified in the deep small bowel, six were addressed with endoscopic intervention. Of gastric occult sources, described as erosions, gastropathy, or gastritis, only one (1) underwent intervention.

Excluding the three encounters resulting in death before resolution of GIB, a source was not identified in 46.0% of encounters (108/235), and an intervention was not performed in 69.8% (164/235) encounters, in all of which the GIB resolved on its own by discharge.

### **Subsequent bleeding: Impact of source identification and endoscopic interventions**

Patients who experienced a GIB had a mean of 2.2 encounters for GIB; 55.7% (54/97) of patients with GIB had 2 or more encounters for GIB and 59.2% (141/238) of all encounters were for recurrent GIB (2nd or greater episode). Of all patients with an LVAD, 11.9% (35/295) had 3 or more GIB encounters, resulting in 157 hospitalizations over the span of 7 years (mean 22.4 per year, max 52 in the year 2018).

**Table 3** compares the encounter characteristics of GIB encounters with a subsequent GIB *vs* those without, where multiple encounters regarding the same patient are represented individually. There was no statistical difference in age, race, or sex. There was also no statistical difference whether there was a change in AC, if the GIB was overt *vs* occult, or if a source was identified. Endoscopic intervention during an encounter did not significantly impact the odds of a subsequent GIB (adjusted OR 1.18,  $P = 0.58$ ). The median number of days to a subsequent GIB was 78 d (IQR 21-212) and not statistically different between encounters with endoscopic intervention and those without (**Table 4**). The proportion of encounters with subsequent GIB within 30 d was 29.5% in those with endoscopic intervention and 34.0% for those without, which was also not statistically different ( $P = 0.37$ ). For those with GIB on admission, length of stay was median 12 days (IQR 8-21 d) and not statistically different between encounters with endoscopic intervention and those without ( $P = 0.58$ ).

For subsequent bleeds when a prior source was not identified, a source on the current admission was identified in 20 of 45 (44%). Among the 51 encounters in which a source was identified in both the current GIB and the prior GIB, the source was in the same described area in 36 (70.6%) encounters. Of 22 cases of recurrent bleeding when the prior GIB source was deep small bowel, the current source was also in the deep small bowel in 18; the other 4 encounters sourced the bleed in the duodenum. Of the 28 patients who were found to have a small bowel bleed on at least one encounter, 11 (39.28%) patients had at least one subsequent bleed with a source identified in the small bowel. Otherwise, there was no significant association between the location of bleed identified and the presence of a subsequent bleed.

## **DISCUSSION**

GIB is one of the most common complications in LVAD patients after implantation

**Table 3 Comparative characteristics of gastrointestinal bleeding encounters with a subsequent gastrointestinal bleeding vs no subsequent gastrointestinal bleeding, *n* (%)**

Factor	No subsequent GIB	Had a subsequent GIB	<i>P</i> value
<i>n</i>	97	141	
Change in anticoagulation	56 (64.4)	87 (65.4)	0.89
Overt bleed	75 (78.9)	102 (73.4)	0.36
Hemoglobin, median (IQR)	7.8 (6.8, 9.1)	7.5 (6.2, 8.4)	0.043
Source identified	51 (52.6)	79 (56.0)	0.69
Culprit lesion			1.00
Ulcer	3 (11)	5 (11)	
Angioectasia	13 (48)	21 (48)	
Dieulafoy	1 (4)	2 (5)	
Non-specific oozing	5 (19)	9 (20)	
Other	5 (19)	7 (16)	
Culprit lesion location			0.38
Esophagus	2 (2.2)	0 (0.0)	
Stomach	24 (25.8)	30 (22.6)	
Duodenum	6 (6.5)	11 (8.3)	
Deep small bowel	12 (12.9)	28 (21.1)	
Colon	7 (7.5)	10 (7.5)	
Not identified	42 (45.2)	54 (40.6)	
Endoscopic intervention performed	27 (27.8)	44 (31.2)	0.58
Days to first endoscopic study (mean ± SD)	3.4 ± 7.1	2.9 ± 3.6	0.52

Deep small bowel refers to jejunum and ileum. The following statistical tests were utilized: paired *t* test (days to first endoscopic study), Wilcoxon rank-sum test (age, hemoglobin), and Fisher's exact test (change in anticoagulation, overt bleed, culprit lesion, culprit lesion location, endoscopic intervention performed). GIB: Gastrointestinal bleeding; IQR: Interquartile range; SD: Standard deviation.

**Table 4 Outcomes for gastrointestinal bleeding encounters with endoscopic intervention vs none gastrointestinal bleeding**

Factor	Endoscopic intervention	No endoscopic intervention	<i>P</i> value
Median number of days to subsequent GIB (IQR)	113 (15-302)	72 (24-178)	0.51
	<i>n</i> = 44	<i>n</i> = 97	
Proportion with subsequent GIB within 30 days	29.5%	34.0%	0.37
	<i>n</i> = 44	<i>n</i> = 97	
Median length of stay in days for those with GIB on admission (IQR)	12 (10-23)	12 (8-21)	0.58
	<i>n</i> = 31	<i>n</i> = 86	

The following statistical tests were utilized: Wilcoxon rank-sum test [days to subsequent gastrointestinal bleeding (GIB), length of stay], and Fisher's exact test (proportion with subsequent GIB within 30 d). GIB: Gastrointestinal bleeding; IQR: Interquartile range.

and has become a frequent cause of hospitalization for this population. Patients may have multiple bleeding episodes and nearly 10% of LVAD patients will have 3 or more encounters for GIB. This is the first study to our knowledge that is powered to evaluate whether endoscopic intervention reduces the risk for subsequent GIB. Our results confirm that a high proportion of GIB in our LVAD population clinically stops without endoscopic therapy and that endoscopic intervention does not prevent subsequent bleeding.

Our cohort size is within the wide range of sizes of studied cohorts at other tertiary care centers in terms of the numbers of patients with LVAD implantations and of the encounters for GIB bleeding[3,9,10]. Median time to bleed varies in the prior literature from 55 d to 197 d[3,9,10], where our composite median time of 129 d may reflect a higher proportion of late and recurrent GIB and fewer early GIBs. We found similar factors that correlated with GIB and findings: age correlated with having a GIB[9,11], while overt presentation and need for transfusion support correlated with performing endoscopic interventions[11]. The highest diagnostic yield was confirmed for upper procedures including EGD and push enteroscopy[9,11]. We also found a high burden of GIB caused by angioectasias[5,9]. While Dakik *et al*[6] and Axelrad *et al*[9] found that hemostatic therapy during an index examination was a statistically significant risk factor for a subsequent GIB, this was not the case in our cohort that had more GIB encounters and was followed for a longer period of time. Several factors may have had an impact on this disparity, including cohort size, efficacy of operator specific treatment techniques, selection of significant lesions, nuances in timing, or subtleties in patient demographics.

There are several areas that still warrant further investigation. First, it is unclear if the suboptimal initial diagnostic yield is attributable to delay in endoscopy, impediments imposed by anticipation of INR normalization or completion of bowel preparation, or intermittent visibility and bleeding of lesions such as angioectasias. These variabilities may explain why subsequent GIB encounters are able to isolate a source in some encounters. This low rate of identifying a source is consistent with other studies [9]. While source identification or endoscopic intervention on a visualized lesion did not result in reducing subsequent GIB or readmission rates, other benefits to endoscopy such as shorter length of stay may exist, although we did not find this in our cohort. Addressing these issues may be important in improving the success of endoscopic intervention.

Our findings indicate that minimizing endoscopic utilization may be beneficial for patients and healthcare utilization. There are a few proposed solutions to reduce the burden of low-yield procedures and reduce delay to source identification. Axelrad *et al* [12] proposed an endoscopic algorithm that consisted of push enteroscopy, instead of EGD, or colonoscopy for overt signs of bleeding, along with conservative management without endoscopic evaluation for occult bleeding, and found in a retrospective analysis that this method would improve resource utilization and limit lower-yield procedures. While VCE is often a second line study for persistent bleeding after negative upper and lower endoscopic evaluation[3], Marya *et al*[13] determined that early VCE compared to standard approaches to endoscopy in patients presenting with non-hematemesis GIB increased source localization, with no difference in direct costs of hospitalization. We propose that the VCE be performed urgently in the acute setting while awaiting normalization of the INR prior to possible endoscopy, especially when an endoscopic evaluation has been performed on a prior encounter. This proposal may obviate unnecessary endoscopies should the VCE exclude a targetable lesion, or help identify the most appropriate and high-yield procedure (EGD, push enteroscopy, or balloon enteroscopy) for treatment of an accessible lesion or indicative presence of blood. The yield and cost effectiveness of this strategy deserves further study.

Alternatively, intervention with endoscopic techniques may simply be an inappropriate long-term approach to treatment of certain common hemorrhagic lesions such as angioectasias, which likely represent a systemic process rather than a cluster of focal endoscopic lesions. Designing a randomized trial which withheld endoscopic intervention from some patients with GIB may be impractical given the unclear criteria by which to exclude higher risk patients. However, the creation of a prognostic risk score for patients with LVAD-related GIB could help triage low and high risk patients to different care pathways.

More importantly, recognizing that endoscopy may be only a temporizing measure, there is an urgent need for utilization of medical management protocols to prevent recurrent bleeding. Angioectasia recidivism after endoscopic therapy is common, and endoscopy is rarely a long term solution. Early data suggest that blockade of the angiotensin II receptor activation with angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers may reduce GIB episodes by reducing angioectasia formation[14]. Yin *et al*[10] built a model to predict who may have recurrent bleeding based on age and comorbidities while Welden *et al*[15] found better INR control and early endoscopy within 48 h of admission as clinical predictors of reduced recurrent GIB[15]. AC regimens need better study and standardization to best balance the risks of bleeding and thrombosis[16].



Collaboration amongst gastroenterologists and cardiologists is paramount for achieving optimal patient care, including the management of anti-platelet and AC therapies, LVAD pump speed adjustments, and endoscopic guidance. Alternative pharmaceutical strategies for reducing GIB in this population include the use of octreotide, thalidomide in restricted populations, and desmopressin (which increases the risk for thrombosis); ultimately, cardiac transplantation significantly reduces future GIB, when pulsatile flow and other parameters have been restored[17].

There are several limitations to our study. Our cohort was adequately powered to evaluate for a significant relationship between endoscopic intervention and subsequent GIB, but a larger patient cohort may be able to find statistical significance for a subpopulation, such as those with overt *vs* occult bleeding or with specific sources of bleeding. The retrospective and observational nature of our study limited the ability to show an impact of other parameters like change in AC or change in acid suppression therapy upon admission. Data abstraction was limited for some earlier encounters, including comorbidities and general health condition, due to an interim transition in EMR. There are other factors that contribute to the decisions for GIB management by the individual cardiologists and gastroenterologists that may not have been captured on chart review. We were able to evaluate for GIB encounters within our hospital system and may have missed other GIB admissions, though we think this to be an infrequent scenario as these patients are closely followed by our cardiology colleagues.

## CONCLUSION

Patients with LVAD implantation are at high risk for recurrent GIBs. A majority of episodes of GIB resolve without endoscopic intervention. While endoscopic intervention for GIB is the established practice for the general population, our data do not support this position for patients with LVAD. The percentage of patients who had recurrent bleeding after endoscopic intervention was not statistically different than in those who had no intervention ( $P = 0.92$ ). The rational and focused use of endoscopy, as part of an algorithm for GIB tailored specifically to patients with LVAD, is paramount for providing optimal patient care, limiting risks, and using resources most effectively. We advocate for more prospective evidence which will help support the creation of an evidence-based protocol to manage recurrent GIB and prevent future occurrences.

## ARTICLE HIGHLIGHTS

### **Research background**

Patients with left ventricular assist devices (LVADs) are at increased risk for recurrent gastrointestinal bleeding (GIB) and repeat endoscopic procedures.

### **Research motivation**

There are limited data on whether endoscopic intervention reduces recurrent bleeding, bringing into question its utility in managing this chronic issue.

### **Research objectives**

Our primary aim was to evaluate for an association between endoscopic intervention and subsequent GIB. Secondary aims were to assess the frequency of GIB in our cohort, describe GIB presentations and sources identified, and determine risk factors for recurrent GIB.

### **Research methods**

We conducted a retrospective cohort study of all patients at a large academic institution who underwent LVAD implantation from January 2011 - December 2018 and assessed all hospital encounters for GIB through December 2019. We performed a descriptive analysis of the GIB burden and the outcome of endoscopic procedures performed. We performed multivariate logistic regression to evaluate the association between endoscopic intervention and subsequent GIB.

### Research results

In the cohort of 295 patients, 97 (32.9%) had at least one GIB hospital encounter and recurrent GIB occurred in 55.5% (54/97) of patients. There were 238 hospital encounters, and GIB resolved on its own by discharge in 69.8% encounters. Of the 85.7% (204/238) of encounters that included at least one endoscopic evaluation, an endoscopic intervention was performed in 34.8% (71/204). The adjusted odds ratio for subsequent GIB if an endoscopic intervention was performed during a GIB encounter was not significant (odds ratio 1.18,  $P = 0.58$ ).

### Research conclusions

In this retrospective cohort study, adherence to endoscopic guidelines for performing endoscopic interventions did not significantly decrease the odds of subsequent GIB, thus suggesting the uniqueness of the LVAD population.

### Research perspectives

A prospective study is needed to identify patients with LVAD at risk of recurrent GIB and determine more effective management strategies.

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