

Retrospective Study

Video capsule endoscopy in left ventricular assist device recipients with obscure gastrointestinal bleeding

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Abstract

AIM: To assess whether video capsule endoscopy (VCE) affects the outcomes of left ventricular assist devices (LVADs) recipients with gastrointestinal bleeding.

METHODS: This is a retrospective study of LVAD recipients with obscure gastrointestinal bleeding (OGIB) who underwent VCE at a tertiary medical center between 2005 and 2013. All patients were admitted and monitored with telemetry and all VCE and subsequent endoscopic procedures were performed as inpatients. A VCE study was considered positive only when P2 lesions were found and was regarded as negative if P1 or P0 were identified. All patients were followed until heart transplant, death, or the end of the study.

RESULTS: Between 2005 and 2013, 30 patients with LVAD underwent VCE. Completion rate of VCE was 93.3% and there was no capsule retention. No interference of VCE recording or the function of LVAD was found. VCE was positive in 40% of patients ($n = 12$). The most common finding was active small intestinal bleeding (50%) and small intestinal angiodysplasia (33.3%). There was no difference in the rate of recurrent bleeding between patients with positive and negative VCE study (50.0% vs 55.6%,

$P = 1.00$) during an average of 11.6 ± 9.6 mo follow up. Among patients with positive VCE, the recurrent bleeding rate did not differ whether subsequent endoscopy was performed (50% *vs* 50%, $P = 1.00$).

CONCLUSION: VCE can be safely performed in LVAD recipients with a diagnostic yield of 40%. VCE does not affect recurrent bleeding in LVAD patients regardless of findings.

Key words: Heart-assist devices; Capsule endoscopy; Gastrointestinal hemorrhage; Heart failure; Endoscopy; Digestive system

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Core tip: Obscure gastrointestinal bleeding (OGIB) is a common complication for patients receiving left ventricular assist device (LVAD). Although video capsule endoscopy (VCE) is frequently used to investigate OGIB, there is limited data on the safety and usefulness of VCE in LVAD recipients. We found that VCE can be safely performed in LVAD recipients with OGIB and with a 40% diagnostic yield. However, the results of VCE and the subsequent management driven by VCE did not affect the rate of recurrent GIB. Endoscopic intervention thus should be used judiciously, and alternative ways of management should be considered in LVAD patients with OGIB.

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INTRODUCTION

Approximately 50000 patients die from advanced heart failure in the United States each year, with a high mortality rate and life expectancy < 2 years when only medical therapies are utilized^[1]. Although heart transplantation is a definitive therapeutic option for advanced heart failure, only 2200 heart transplants are performed annually due to donor shortage, leaving a large proportion of heart failure patients in need of an alternative therapy^[2]. In recent years, Left Ventricular Assist Devices (LVADs) are used increasingly in this setting as destination therapy, bridge to transplantation, bridge to recovery, or bridge to decision in patients with advanced heart failure^[3]. This approach has increased survival and improved quality of life in advanced heart failure patients^[4].

Since the initial introduction of LVAD therapy, it is well documented that LVADs increase the risk of gastrointestinal bleeding (GIB), with as many as

20%-40% of LVAD recipients manifesting GIB^[5-7]. The mechanism of GIB in LVAD recipients remains incompletely understood, but it is thought to be contributed to by development of angiodysplasia, acquired von Willebrand disease, persistent right ventricular dysfunction, and mucosal ischemia secondary to low pulse pressure^[8,9]. GIB is further exacerbated by the use of anticoagulation in LVAD patients. Although previous reports found that upper GI tract is the most common site of GIB in LVAD recipients^[10], obscure gastrointestinal bleeding (OGIB) remains a frustrating condition frequently encountered in this population.

Video capsule endoscopy (VCE) has made a significant impact on the evaluation of patients with OGIB, with a diagnostic yield of approximately 60%-70%^[11]. However, it is a relative contraindication to use VCE in the setting of implanted electrical medical devices^[12], and there is limited data on both the usage of VCE in LVAD associated OGIB, as well as the safety of VCE in LVAD patients^[13-19].

We retrospectively evaluated our experience with VCE in LVAD patients with OGIB. The aims of our study were to determine the safety and diagnostic yield of VCE, and to assess the outcomes based on management driven by VCE in LVAD recipients.

MATERIALS AND METHODS

Patients

All patients undergoing VCE following implantation of LVAD at Washington University Medical Center between January 2005 and September 2013 were eligible for inclusion in this retrospective study. For inclusion, all subjects were required to have obscure GI bleeding, which was defined as hematemesis, melena, hematochezia, or anemia with positive fecal occult blood, without a definitive source identified on upper endoscopy (EGD) and colonoscopy, thereby requiring VCE for further localization of the bleeding source. Exclusion criteria consisted of patients aged less than 18 years, patients who did not have both EGD and colonoscopy performed prior to VCE, incomplete data collection and studies with unintelligible data. This study protocol was approved by the Institutional Review Board at Washington University in St. Louis.

Data collection

Inpatient and outpatient charts were reviewed in the institution's electronic medical records to extract demographic data, indications for LVAD, types of LVAD implanted, follow-up and GIB data. Patients were followed until heart transplant, death or the last point of contact in the electronic medical records. Patients lost to follow up were not included in the final analyses. Episodes of recurrent GIB were identified and recorded. Recurrent GIB was defined as any recurrence of overt GIB or anemia with positive fecal occult blood. Medical records were reviewed to

Table 1 Characteristics and outcomes of left ventricular assist device recipients undergoing video capsule endoscopy *n* (%)

	Total, <i>n</i> = 30	Positive study, <i>n</i> = 12	Negative study, <i>n</i> = 18	<i>P</i> value
Age (yr)	60.1 ± 10.2	62.6 ± 8.8	58.4 ± 10.9	0.27
Female	6 (20.0)	4 (33.3)	2 (11.1)	0.18
Charlson comorbidity index	4.7	5	4.6	0.70
History of GIB prior to LVAD	3 (10.0)	2 (16.7)	1 (5.6)	0.55
LVAD implant to GIB (mo)	4.8 ± 6.0	5.5 ± 7.0	4.4 ± 5.3	0.65
Overt GIB	23 (76.7)	8 (66.7)	15 (83.3)	0.39
Antiplatelet agents	26 (86.7)	10 (83.3)	16 (88.9)	1.00
Anticoagulants	28 (93.3)	11 (91.7)	17 (94.4)	1.00
Endoscopies prior to VCE (number)	3.2 ± 1.7	3.5 ± 1.9	3.0 ± 1.7	0.46
Length of stay (d)	13.1 ± 12.5	20.3 ± 17.6	8.3 ± 2.3	0.04
Follow-up (mo)	11.6 ± 9.6	9.2 ± 9.3	13.2 ± 9.7	0.28
Recurrent GIB rate	16 (53.3)	6 (50)	10 (55.6)	1.00
Endoscopies after VCE (number)	1.7 ± 2.2	1.8 ± 1.8	1.7 ± 2.5	0.97
Mortality rate	10 (33.3)	4 (33.3)	6 (33.3)	0.90

GIB: Gastrointestinal bleeding; LVAD: Left ventricular assist device; VCE: Video capsule endoscopy.

determine cause of death, and to determine if death was related to GIB when relevant. The Charlson comorbidity index was calculated based on the review of medical records^[20].

Procedures

All VCE studies were performed using PillCam (Given Imaging, Duluth, GA, United States) as inpatients. The risk of capsule retention was assessed by history and radiological imaging studies such as small bowel follow-through or CT enterography per the discretion of GI consult service. Patients were given a half gallon of Golytely (Braintree Laboratories, Braintree, MA, United States) the evening before the procedure and were kept nothing by mouth after midnight. On the day of the procedure, the capsule endoscope was ingested or endoscopically placed in the duodenum if patients had dysphagia or delayed gastric emptying. Patients were monitored by continuous telemetry and evaluated serially by staff. LVADs were monitored continuously by the system controller and interrogated immediately after the VCE *via* the system monitor to evaluate for any changes in function. VCE reports were evaluated for possible LVAD interference and medical records were evaluated for possible LVAD dysfunction related to VCE interference.

Outcomes

The findings on VCE were categorized into 3 types of mucosal abnormalities as previously reported^[21]. P0 lesions were those considered to have no bleeding potential such as normal study, submucosal vein, diverticula without bleeding, or nodule without mucosal break. P1 lesions were those having uncertain bleeding potential such as erosions or red spots. P2 lesions were those thought to have high bleeding potential such as ulcers, angiodysplasias, tumors, as well as active bleeding without lesions identified. The diagnostic yield of the study was assessed by the frequency of P2 lesions. Positive VCE studies were defined as VCE

findings with P2 lesions. VCE findings reported P0 or P1 lesions were considered as negative VCE studies. If VCE did not reach the cecum at the end of recording, it was considered an incomplete study. Safety endpoints included interference of VCE with LVAD function, interference of LVAD with VCE reports, and other previously described adverse events associated with VCE.

Statistical analysis

For statistical analysis, data is reported as mean ± SD unless otherwise indicated. Fisher's exact test and Student's *t*-test were used for categorical variables and continuous variables, respectively. A *P*-value less than 0.05 was required for statistical significance. Logistic regression was used to examine predictors for VCE outcomes.

RESULTS

Thirty LVAD patients underwent VCE over the 8-year study period. No patient was lost to follow up or excluded in this study. All patients were treated and all procedures were performed as inpatients. The mean age was 60.1 ± 10.2 years, and 20% of patients were female (Table 1). Thoratec HeartMate II LVADs were implanted in all of the patients except one patient who had a HeartWare HVAD. The Charlson comorbidity index, the history of GIB prior to LVAD implantation, the interval between LVAD implantation and GIB, and the history of overt GIB did not differ between patients with positive vs negative VCE studies. Twenty-three out of the thirty patients (76.7%) presented with overt OGIB: 21 with melena (70%), 2 with hematochezia (6.7%); whereas 7 patients (23.3%) presented with occult OGIB. Most of our patients received antiplatelets (86.7%) or anticoagulants (93.3%) on presentation. On average 3.2 ± 1.7 endoscopic procedures were performed within 4.1 ± 5.0 d prior to VCE, including 37 EGDs, 17 push enteroscopies, 40 colonoscopies,

Table 2 Locations and findings of positive video capsule endoscopy studies *n* (%)

	Patients (<i>n</i> = 12)
Locations of positive VCE findings	
Stomach and duodenum	2 (16.7)
Small intestine	9 (75.0)
Colon	1 (8.3)
Findings of positive VCE studies	
Small intestinal bleeding with no source or lesion identified (2 in the duodenum, 4 in the jejunum)	6 (50.0)
Angiodysplasia (1 in the duodenum, 3 in the small bowel)	4 (33.3)
Colonic bleeding with no source or lesion identified	1 (8.3)
Gastric ulcer	1 (8.3)

VCE: Video capsule endoscopy.

and 2 sigmoidoscopies. VCE was performed 6.2 ± 2.6 d after the presentation of GIB. VCE was placed endoscopically in 2 patients (6.7%) because one patient had a history of pyloric stenosis, and the other patient failed the swallow study. The mean small bowel transit time of VCE was 3.2 ± 1.1 h. VCE did not reach the cecum in 2 patients (6.7%) over the 8 h recording period, but there was no capsule retention. There was no electromagnetic interference of either VCE or LVAD identified in any patients.

Patients with positive VCE study stayed in the hospital longer than patients with negative VCE study (20.3 d vs 8.3 d, $P = 0.04$). Over the average 11.6 mo follow-up period, there was no statistically significant difference in the recurrent bleeding rate (50% vs 55.6%, $P = 1.00$), the number of endoscopies performed after VCE (1.8 ± 1.8 vs 1.7 ± 2.5, $P = 0.97$), or mortality rate (33.3% vs 33.3%, $P = 0.90$) between patients with positive and negative VCE. The total recurrent bleeding rate in this population was 53.3% ($n = 16$) and the presentation included melena ($n = 12$), hematochezia ($n = 3$) and anemia with positive fecal occult blood ($n = 1$). All 16 patients with recurrent bleeding were hospitalized and underwent transfusion and endoscopic procedures for managing recurrent GIB. The overall mortality rate in this study was 33.3% ($n = 10$): 7 patients died from underlying heart failure, 2 patients died from septic shock, one patient died from subdural hematoma, and none of the patients died from GIB. Four LVAD recipients underwent heart transplantation on average 4.3 mo after VCE and did not develop recurrent GIB afterwards. Before heart transplantation, VCE studies were positive in 2 patients (1 duodenal angiodysplasia and 1 jejunal angiodysplasia) and negative in 2 others.

The diagnostic yield of VCE to detect P2 lesions in this study was 40%. Table 2 demonstrates the locations and the findings of positive VCE studies. Small intestine was the most common site of positive VCE findings (75%). The predominant positive VCE findings in our study were small intestinal bleeding with no source or lesion identified (50%) and small intestinal

angiodysplasias (33.3%). Eighteen VCE studies (60%) were negative, including 13 P0 lesions (12 normal, 1 small nodule) and 5 P1 lesions (red spots). The only patient who had a HeartWare HVAD implanted had a normal VCE study. Despite prior negative upper endoscopies performed 2 and 24 d prior to VCE, two lesions were found within reach of EGD by VCE: one gastric ulcer and one duodenal angiodysplasia (neither VCE was placed endoscopically). One VCE found active bleeding in the colon without the cause of bleeding identified. Angiodysplasia were found in 4 patients: 1 in the duodenum and 3 in the small intestine. In 2 patients where VCE failed to reach the cecum at the end of recording, VCE still detected the cause of GIB: one with gastric ulcer and one with small intestine angiodysplasia. Using logistic regression, we found that higher INR on presentation was associated with a higher probability of positive findings in VCE (OR = 3.62, 95%CI: 1.03-12.7, $P = 0.04$), adjusted for age, gender, and hemoglobin level.

Positive VCE studies led to further endoscopic evaluations in 6 patients out of 12 (50%): 6 push endoscopies and 3 single balloon enteroscopies. The other 6 patients with positive VCE did not have further endoscopies because they had no further bleeding and their hemoglobin had stabilized. During follow-up the overall recurrent bleeding rate in patients with positive VCE was 50% (6 out of 12). In addition, there was no difference in the recurrent bleeding rate whether subsequent endoscopic procedures were performed following positive VCE (3 out of 6 or 50% in each group, $P = 1.00$). Furthermore, after VCE, medications were adjusted in 7 out of 12 patients with positive VCE, and 8 out of 18 patients with negative VCE. These changes included discontinuation or decrease in the dose of aspirin and initiation of proton pump inhibitors. The change of medical management did not affect the rate of recurrent bleeding regardless of whether patients had a positive VCE (40% vs 57.1%, $P = 1.00$), or negative VCE (60% vs 50%, $P = 1.00$). The presentations of recurrent GIB were melena ($n = 4$), hematochezia ($n = 1$) and anemia with positive fecal occult blood ($n = 1$). The clinical course and management of LVAD recipients with positive VCE studies are detailed in Table 3.

DISCUSSION

In this retrospective study spanning 8 years, we demonstrated the safety of VCE and a 40% diagnostic yield of P2 lesions in LVAD recipients with OGIB. We found that the results of VCE were not associated with the rate of recurrent GIB, the number of endoscopic procedures performed, or mortality rate. In addition, the findings of VCE and the subsequent management did not affect the rate of recurrent GIB in LVAD patients.

This study identified 30 LVAD recipients undergoing

Table 3 Clinical course and management of left ventricular assist device recipients with positive video capsule endoscopy studies

No.	Age (yr) and Sex	Presentation	Endoscopic findings and interval prior to VCE (d)	VCE findings	Endoscopic findings and interval after VCE (d)	Recurrent bleeding and interval after VCE (mo)	Management for recurrent bleeding
1	62 M	Anemia	Rectal polyp (2)	Gastric ulcer	N/A	Melena (21)	EGD: GU with visible vessel s/p hemoclip
2	57 M	Anemia	Gastritis, colonic polyp (24)	Duodenal angiodysplasia	PE: Gastritis (2)	No	N/A
3	73 M	Melena	Gastric and jejunal angiodysplasia (4)	Small bowel angiodysplasia	N/A	Melena (1.7)	PE: Bleeding jejunal angiodysplasia s/p APC
4	53 F	Melena	Blood in the terminal ileum (0)	Small bowel angiodysplasia	PE: Bleeding jejunal angiodysplasia s/p APC + hemoclip (2)	No	N/A
5	61 M	Anemia	Colonic diverticulosis, hemorrhoids (3)	Small bowel angiodysplasia	N/A	No	N/A
6	53 M	Anemia	Duodenitis (4)	Stomach and small bowel bleeding	PE: Clean base GU (2)	Melena (0.5)	PE: Gastritis and fresh blood in duodenum without lesions identified
7	70 F	Melena	Gastric angiodysplasia s/p APC (3)	Small bowel bleeding	N/A	Melena (11.4)	PE: DLBCL of stomach
8	61 F	Hematochezia	Sigmoid angiodysplasia s/p APC (2)	Small bowel bleeding	PE: Normal; SBE: Bleeding jejunal angiodysplasia s/p APC+ hemoclip (2)	Hematochezia (11.2)	PE: Gastritis; C-scope: Bleeding sigmoid angiodysplasia s/p APC + hemoclip
9	52 M	Melena	Colonic diverticulosis, hemorrhoids (1)	Small bowel bleeding	N/A	No	N/A
10	59 M	Melena	Duodenal angiodysplasia s/p APC and hemoclip (5)	Small bowel bleeding	PE: Bleeding jejunal angiodysplasia s/p heater probe + APC; SBE: Nonbleeding jejunal angiodysplasia s/p APC (6)	Anemia requiring transfusion (0.7)	C-scope: Bleeding Cecal angiodysplasia s/p hemoclip
11	75 M	Melena	Colonic angiodysplasia s/p hemoclip (6)	Small bowel bleeding	PE: Gastric Dieulafoy's lesion s/p hemoclip; SBE: Bleeding jejunal angiodysplasia s/p APC + hemoclip (2)	No	N/A
12	76 F	Melena	Normal (4)	Colonic bleeding	N/A	No	N/A

APC: Argon plasma coagulation; C-scope: Colonoscopy; DLBCL: Diffuse large B-cell lymphoma; EGD: Esophagogastrroduodenoscopy; F: Female; GU: Gastric ulcer; M: Male; N/A: Not applicable; PE: Push enteroscopy; SBE: Single balloon enteroscopy; VCE: Video capsule endoscopy.

VCE for OGIB. To our knowledge, this is the largest available series of VCE in LVAD patients in the literature^[6,13-19,22] (Table 4). Our results show that VCE is safe to perform in LVAD recipients, without interference between VCE and LVAD and without capsule retention. One prior study found 2 cases of LVAD possibly interfering with capsule images, and suggested that the leads of VCE be placed away from LVAD^[23]. Based on the results of this and other previous studies, the interference between VCE and LVAD is uncommon^[14,16,23]. Consistent with our experience, a recent review article reported that VCE is unlikely to impair the function of cardiac pacemakers, implantable cardioverter defibrillators, and LVAD, although the authors cautioned that wireless telemetry may interfere with VCE recordings^[24].

The diagnostic yield of VCE in LVAD patients in two previous reports was 31% ($n = 13$) and 80% ($n = 5$) (Table 4)^[6,22]. With a larger sample size of 30, the diagnostic yield in our study is 40%. Since only P2 lesions were considered positive, our diagnostic yield

reflects true clinically relevant findings. It is known that the diagnostic yield of VCE is higher when it is performed closer to the presenting GIB event^[25,26], or in patients with overt GIB than with occult GIB^[27,28]. It is also known that the diagnostic yield of VCE is comparable to double balloon enteroscopy (DBE) according to a meta-analysis^[29]. A recent study of DBE in LVAD recipients who presented with overt OGIB found that the diagnostic yield of DBE was 69% when DBE was performed within 24 h of initial presentation^[30]. We suspect that VCE would have a similar diagnostic yield if it is performed within 24 h of overt OGIB. In our study, VCE was performed on average 6.2 d after admission- after coagulopathy was corrected and after other endoscopic procedures failed to identify the cause of OGIB. Using logistic regression, we found that higher INR on presentation was associated with a higher probability of positive VCE. If OGIB is highly suspected in an LVAD patient with a supra-therapeutic INR on presentation, expediting VCE, possibly before coagulopathy is corrected and

Table 4 Previous studies of video capsule endoscopy in left ventricular assist device recipients

Study and the year published	No. of VCE	Diagnostic yield (%)	Findings	Remarks
Girelli <i>et al</i> ^[18] , 2006	1	N/A	No bleeding identified	No follow up reported
Garatti <i>et al</i> ^[15] , 2006	1	N/A	No bleeding identified	No recurrent GIB; received heart transplantation
Seow <i>et al</i> ^[17] , 2006	1	N/A	Duodenal and jejunal angiodysplasia	Push enteroscopy + Octreotide + Sucralfate; no follow up reported
Fenkel <i>et al</i> ^[16] , 2007	1	N/A	Small bowel angiodysplasia	No intervention; no follow up reported
Daas <i>et al</i> ^[14] , 2008	1	N/A	Mid-small bowel active bleeding	Intraoperative enteroscopy; no follow up reported
Bechtel <i>et al</i> ^[19] , 2010	1	N/A	Bleeding in cecum	Colonoscopy; no follow up reported
Elmunzer <i>et al</i> ^[6] , 2011	13	4 (30.8)	3 jejunal angiodysplasias, 1 duodenal Dieulafoy's lesion	1 recurrent bleeding from the same lesion
Meyer <i>et al</i> ^[22] , 2012	5	4 (80.0)	2 jejunal angiodysplasia, 1 cecal ulcer, 1 jejunal mass	1 colonoscopy; 2 SBE; 1 angiography; no follow up reported
Tarzia <i>et al</i> ^[13] , 2013	1	N/A	Small bowel angiodysplasia and small bowel Dieulafoy's lesion	DBE; no follow up reported

DBE: Double balloon enteroscopy; GIB: Gastrointestinal bleeding; N/A: Not applicable; SBE: Single balloon enteroscopy; VCE: Video capsule endoscopy.

other endoscopies performed, may improve the diagnostic yield of VCE in this population.

In a general population with OGIB, > 80% of the bleeding sites are in the small bowel^[11]. The most common location of positive VCE finding in our LVAD patients with OGIB is also small bowel (75%). The most common finding of positive VCE in our study was small bowel bleeding without the cause of bleeding identified, whereas small bowel angiodysplasia was the second most common finding. The source of bleeding can be difficult to identify by VCE in the setting of active bleeding since blood can obscure visualization and VCE cannot clear the visual field with water irrigation. Nevertheless, we surmise that angiodysplasia is the most likely cause of GIB in those with small bowel bleeding without lesions identified given that it has been shown to be the most common cause of GIB in LVAD patients^[6,7,22]. Indeed, 3 patients with small bowel bleeding without lesion identified on VCE were later found to have bleeding small bowel angiodysplasias on subsequent enteroscopies. Of note, in our study 25% of positive VCE findings were within reach of EGD or colonoscopy, underscoring the elusive nature of these lesions and the importance of repeat examinations if necessary.

Our study is the first to report recurrent GIB rate in LVAD recipients after VCE. Although LVAD is thought to predispose patients to GIB through various mechanisms, the recurrent GIB rate (53%) in our LVAD population is similar to OGIB in non-LVAD patients^[31]. Furthermore, there was no difference in the rate of recurrent GIB, the number of endoscopies performed after VCE, and the mortality rate, whether VCE studies were positive or negative. Even among patients with a positive VCE, further endoscopic intervention did not affect recurrent bleeding- the recurrent bleeding rate was 50% regardless of endoscopic intervention (Table 3). On the other hand, the negative VCE study in our cohort was not associated with lower recurrent bleeding rate. It is possible that OGIB may merely be a

reflection of the underlying condition or hemodynamics of LVAD patients, and endoscopic procedures do not necessarily impact their natural courses. Endoscopic evaluation or therapy in this population therefore should be used judiciously, especially given that medical therapy with thalidomide or Octreotide has recently been reported to be effective in LVAD recipients with OGIB^[32,33]. Further study is required to identify the characteristics of patients who may benefit from endoscopic intervention vs supportive care.

Of the 12 patients with positive VCE studies, only 6 patients had subsequent endoscopic procedures because the other 6 patients had no further GI bleeding and their hemoglobin had stabilized, again indicating a dissociation of VCE findings with patients' clinical courses. Given that only 50% of patients with positive VCE had persistent GIB requiring further endoscopic intervention, one possible approach to treat LVAD recipients with OGIB based on our finding is to defer VCE and endoscopies until persistent GIB is observed. The current health care environment creates tremendous pressure on hospitals to shorten patients' stay and expedite diagnostic procedures and treatment. For certain patients in this population, however, it may be more cost-effective to observe and provide supportive medical care without endoscopies. Future studies are needed to test this hypothesis and to determine which subset of LVAD recipients with OGIB would benefit from VCE and subsequent endoscopies.

None of LVAD recipients in this study died from GIB, consistent with a prior report^[34]. All 4 patients who received heart transplantation in our study did not have recurrent bleeding episodes during the study period, which is similar to the result in a recent systematic review that reported 12 patients without recurrent GIB after heart transplantation^[7]. All together, the data indicates that the changes of physiology and hemodynamics associated with LVAD are the causes of GIB, and this process and GIB can

be reversed when LVAD is removed. Consistent with this concept, a previous study found that all LVAD recipients had reduced high molecular weight von Willebrand factor multimers which were normalized after patients received heart transplants^[35].

Our study has limitations. Given that this is a retrospective study from a single tertiary medical center, it has weaknesses similar to other retrospective studies and should be carefully interpreted or generalized. In addition, although this study provides the largest series of VCE in LVAD recipients with OGIB, the sample size of 30 is still limited. We might underestimate the true rate of recurrent bleeding because the follow-up duration may not be long enough. Lastly, in our study VCE were interpreted by several gastroenterologists and the management of patients was not standardized. These variations may affect the results of our study.

In conclusion, our study shows that VCE can be safely performed in LVAD recipients with OGIB and with a 40% diagnostic yield. However, the results of VCE and the subsequent management driven by VCE did not affect the rate of recurrent GIB. Endoscopic intervention thus should be used judiciously in this patient population. An observation-and-supportive care approach could be an alternative way to treat LVAD patients with OGIB. Future studies should answer the questions of what subset of LVAD recipients with OGIB would benefit from endoscopic therapy, and what the most cost-effective way is to take care of this challenging group of patients.

COMMENTS

Background

Gastrointestinal bleeding (GIB) is one of the most common complications in Left Ventricular Assist Devices (LVADs) recipients. The mechanism of GIB in this setting is still unclear, but it is thought to be the results of development of angiodysplasia, acquired von Willebrand disease, persistent right ventricular dysfunction, and mucosal ischemia secondary to low pulse pressure. Moreover, managements of GIB in patients with LVAD are challenging. It is quite difficult to determine the source of GIB and it is not uncommon to not be able to identify the site of bleeding despite extensive workup. Video capsule endoscopy (VCE) has been used extensively for evaluating patients with obscure GIB (OGIB). In this study, we determined the safety and diagnostic yield of VCE, and assessed the outcomes of GIB based on management driven by VCE in LVAD recipients.

Research frontiers

There is limited data on the usage of VCE in LVAD patients. The results of this study provide evidence on the utility and safety of VCE in LVAD patients.

Innovations and breakthroughs

This study showed that VCE can be safely performed in LVAD recipients and the diagnostic yield of VCE was 40%. However, the results of VCE and the subsequent management driven by VCE did not affect the rate of recurrent GIB.

Applications

Although VCE is relatively safe to perform in LVAD recipients, VCE does not necessarily change the course of OGIB in LVAD recipients. Thus, endoscopic intervention should be used carefully in these patients. An observation-and-supportive care approach could be an alternative way to treat LVAD patients with OGIB.

Terminology

LVAD, an implantable mechanical device that helps a heart pumps blood throughout the body. OGIB, gastrointestinal bleeding that is unable to identify the cause after upper endoscopy and colonoscopy are performed. VCE, a small wireless camera that is ingested to examine parts of GI tract.

Peer-review

This is an interesting study for patients with obscure GI bleeding and LVAD receiving VCE.

REFERENCES

- 1 **Peura JL**, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M, John R, Kiernan MS, Mitchell JE, O'Connell JB, Pagani FD, Petty M, Ravichandran P, Rogers JG, Semigran MJ, Toole JM. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. *Circulation* 2012; **126**: 2648-2667 [PMID: 23109468 DOI: 10.1161/CIR.0b013e3182769a54]
- 2 **Miller LW**, Guglin M. Patient selection for ventricular assist devices: a moving target. *J Am Coll Cardiol* 2013; **61**: 1209-1221 [PMID: 23290542 DOI: 10.1016/j.jacc.2012.08.1029]
- 3 **Loor G**, Gonzalez-Stawinski G. Pulsatile vs. continuous flow in ventricular assist device therapy. *Best Pract Res Clin Anaesthesiol* 2012; **26**: 105-115 [PMID: 22910084 DOI: 10.1016/j.bpa.2012.03.004]
- 4 **Rose EA**, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001; **345**: 1435-1443 [PMID: 11794191 DOI: 10.1056/NEJMoa012175]
- 5 **Islam S**, Cevik C, Madonna R, Frandah W, Islam E, Islam S, Nugent K. Left ventricular assist devices and gastrointestinal bleeding: a narrative review of case reports and case series. *Clin Cardiol* 2013; **36**: 190-200 [PMID: 23378047 DOI: 10.1002/clc.22096]
- 6 **Elmunzer BJ**, Padhya KT, Lewis JJ, Rangnekar AS, Saini SD, Eswaran SL, Scheiman JM, Pagani FD, Haft JW, Waljee AK. Endoscopic findings and clinical outcomes in ventricular assist device recipients with gastrointestinal bleeding. *Dig Dis Sci* 2011; **56**: 3241-3246 [PMID: 21792619 DOI: 10.1007/s10620-011-1828-2]
- 7 **Draper KV**, Huang RJ, Gerson LB. GI bleeding in patients with continuous-flow left ventricular assist devices: a systematic review and meta-analysis. *Gastrointest Endosc* 2014; **80**: 435-446.e1 [PMID: 24975405 DOI: 10.1016/j.gie.2014.03.040]
- 8 **Suarez J**, Patel CB, Felker GM, Becker R, Hernandez AF, Rogers JG. Mechanisms of bleeding and approach to patients with axial-flow left ventricular assist devices. *Circ Heart Fail* 2011; **4**: 779-784 [PMID: 22086831 DOI: 10.1161/circheartfailure.111.962613]
- 9 **Sparrow CT**, Nassif ME, Raymer DS, Novak E, LaRue SJ, Schilling JD. Pre-Operative Right Ventricular Dysfunction Is Associated With Gastrointestinal Bleeding in Patients Supported With Continuous-Flow Left Ventricular Assist Devices. *JACC Heart Fail* 2015; **3**: 956-964 [PMID: 26577618 DOI: 10.1016/j.jchf.2015.09.009]
- 10 **Kushnir VM**, Sharma S, Ewald GA, Seccombe J, Novak E, Wang IW, Joseph SM, Gyawali CP. Evaluation of GI bleeding after implantation of left ventricular assist device. *Gastrointest Endosc* 2012; **75**: 973-979 [PMID: 22341716 DOI: 10.1016/j.gie.2011.12.014]
- 11 **Raju GS**, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. *Gastroenterology* 2007; **133**: 1697-1717 [PMID: 17983812 DOI: 10.1053/j.gastro.2007.06.007]
- 12 **Wang A**, Banerjee S, Barth BA, Bhat YM, Chauhan S, Gottlieb KT, Konda V, Maple JT, Murad F, Pfau PR, Pleskow DK, Siddiqui

- UD, Tokar JL, Rodriguez SA. Wireless capsule endoscopy. *Gastrointest Endosc* 2013; **78**: 805-815 [PMID: 24119509 DOI: 10.1016/j.gie.2013.06.026]
- 13 **Tarzia V**, Dal Lin C, Bottio T, Benvenuti S, Chilovi F, Gerosa G. Occult gastrointestinal bleeding in patients with a left ventricular assist device axial flow pump: diagnostic tools and therapeutic algorithm. *J Thorac Cardiovasc Surg* 2012; **143**: e28-e31 [PMID: 22306228 DOI: 10.1016/j.jtcvs.2012.01.033]
 - 14 **Daas AY**, Small MB, Pinkas H, Brady PG. Safety of conventional and wireless capsule endoscopy in patients supported with nonpulsatile axial flow Heart-Mate II left ventricular assist device. *Gastrointest Endosc* 2008; **68**: 379-382 [PMID: 18582876 DOI: 10.1016/j.gie.2008.03.1077]
 - 15 **Garatti A**, Bruschi G, Girelli C, Vitali E. Small intestine capsule endoscopy in magnetic suspended axial left ventricular assist device patient. *Interact Cardiovasc Thorac Surg* 2006; **5**: 1-4 [PMID: 17670498 DOI: 10.1510/icvts.2005.116871]
 - 16 **Fenkel JM**, Grasso MA, Goldberg EM, Feller ED. Capsule endoscopy is safe in patients with pulsatile Novacor PC left ventricular assist device. *Gastrointest Endosc* 2007; **65**: 559-60; author reply 560 [PMID: 17321277 DOI: 10.1016/j.gie.2006.11.029]
 - 17 **Seow CH**, Zimmerman MJ. Capsule endoscopy in the detection of small-intestinal bleeding in patients supported by a nonpulsatile axial-flow Jarvik 2000 left ventricular assist device. *Gastrointest Endosc* 2006; **63**: 1087 [PMID: 16733141 DOI: 10.1016/j.gie.2006.01.018]
 - 18 **Girelli CM**, Tartara P, Vitali E. Lack of reciprocal interference between capsule endoscope and left ventricular assist device. *Endoscopy* 2006; **38**: 94-5; discussion 95 [PMID: 16429365 DOI: 10.1055/s-2005-870458]
 - 19 **Bechtel JF**, Wellhöner P, Charitos EI, Bucsky B, Morshuis M, Sievers HH. Localizing an occult gastrointestinal bleeding by wireless PillCam SB capsule videoendoscopy in a patient with the HeartMate II left ventricular assist device. *J Thorac Cardiovasc Surg* 2010; **139**: e73-e74 [PMID: 19660366 DOI: 10.1016/j.jtcvs.2008.08.073]
 - 20 **Charlson ME**, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383 [PMID: 3558716]
 - 21 **Saurin JC**, Delvaux M, Gaudin JL, Fassler I, Villarejo J, Vahedi K, Bitoun A, Canard JM, Souquet JC, Ponchon T, Florent C, Gay G. Diagnostic value of endoscopic capsule in patients with obscure digestive bleeding: blinded comparison with video push-enteroscopy. *Endoscopy* 2003; **35**: 576-584 [PMID: 12822092 DOI: 10.1055/s-2003-40244]
 - 22 **Meyer MM**, Young SD, Sun B, Azzouz M, Firstenberg MS. Endoscopic evaluation and management of gastrointestinal bleeding in patients with ventricular assist devices. *Gastroenterol Res Pract* 2012; **2012**: 630483 [PMID: 22474445 DOI: 10.1155/2012/630483]
 - 23 **Harris LA**, Hansel SL, Rajan E, Srivathsan K, Rea R, Crowell MD, Fleischer DE, Pasha SF, Gurudu SR, Heigh RI, Shiff AD, Post JK, Leighton JA. Capsule Endoscopy in Patients with Implantable Electromedical Devices is Safe. *Gastroenterol Res Pract* 2013; **2013**: 959234 [PMID: 23710168 DOI: 10.1155/2013/959234]
 - 24 **Bandorski D**, Höltingen R, Stunder D, Keuchel M. Capsule endoscopy in patients with cardiac pacemakers, implantable cardioverter defibrillators and left heart assist devices. *Ann Gastroenterol* 2014; **27**: 3-8 [PMID: 24714370]
 - 25 **Singh A**, Marshall C, Chaudhuri B, Okoli C, Foley A, Person SD, Bhattacharya K, Cave DR. Timing of video capsule endoscopy relative to overt obscure GI bleeding: implications from a retrospective study. *Gastrointest Endosc* 2013; **77**: 761-766 [PMID: 23375526 DOI: 10.1016/j.gie.2012.11.041]
 - 26 **Leclaire S**, Iwanicki-Caron I, Di-Fiore A, Elie C, Alhameedi R, Ramirez S, Hervé S, Ben-Soussan E, Ducrotté P, Antonietti M. Yield and impact of emergency capsule enteroscopy in severe obscure-overt gastrointestinal bleeding. *Endoscopy* 2012; **44**: 337-342 [PMID: 22389234 DOI: 10.1055/s-0031-1291614]
 - 27 **Estévez E**, González-Conde B, Vázquez-Iglesias JL, de Los Angeles Vázquez-Millán M, Pértiga S, Alonso PA, Clofent J, Santos E, Ulla JL, Sánchez E. Diagnostic yield and clinical outcomes after capsule endoscopy in 100 consecutive patients with obscure gastrointestinal bleeding. *Eur J Gastroenterol Hepatol* 2006; **18**: 881-888 [PMID: 16825907]
 - 28 **Robinson CA**, Jackson C, Condon D, Gerson LB. Impact of inpatient status and gender on small-bowel capsule endoscopy findings. *Gastrointest Endosc* 2011; **74**: 1061-1066 [PMID: 21924720 DOI: 10.1016/j.gie.2011.07.019]
 - 29 **Pasha SF**, Leighton JA, Das A, Harrison ME, Decker GA, Fleischer DE, Sharma VK. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. *Clin Gastroenterol Hepatol* 2008; **6**: 671-676 [PMID: 18356113 DOI: 10.1016/j.cgh.2008.01.005]
 - 30 **Edwards AL**, Mönkemüller K, Pamboukian SV, George JF, Wilcox CM, Peter S. Utility of double-balloon enteroscopy in patients with left ventricular assist devices and obscure overt gastrointestinal bleeding. *Endoscopy* 2014; **46**: 986-991 [PMID: 25290096 DOI: 10.1055/s-0034-1377512]
 - 31 **Kushnir VM**, Tang M, Goodwin J, Hollander TG, Hovis CE, Murad FM, Mullady DK, Azar RR, Jonnalagadda SS, Early DS, Edmundowicz SA, Chen CH. Long-term outcomes after single-balloon enteroscopy in patients with obscure gastrointestinal bleeding. *Dig Dis Sci* 2013; **58**: 2572-2579 [PMID: 23430372 DOI: 10.1007/s10620-013-2588-y]
 - 32 **Draper K**, Kale P, Martin B, Cordero K, Ha R, Banerjee D. Thalidomide for treatment of gastrointestinal angiodysplasia in patients with left ventricular assist devices: case series and treatment protocol. *J Heart Lung Transplant* 2015; **34**: 132-134 [PMID: 25447569 DOI: 10.1016/j.healun.2014.09.013]
 - 33 **Loyaga-Rendon RY**, Hashim T, Tallaj JA, Acharya D, Holman W, Kirklin J, Pamboukian SV. Octreotide in the management of recurrent gastrointestinal bleed in patients supported by continuous flow left ventricular assist devices. *ASAIO J* 2015; **61**: 107-109 [PMID: 25232774 DOI: 10.1097/MAT.0000000000000143]
 - 34 **Morgan JA**, Paone G, Neme HW, Henry SE, Patel R, Vavra J, Williams CT, Lanfear DE, Tita C, Brewer RJ. Gastrointestinal bleeding with the HeartMate II left ventricular assist device. *J Heart Lung Transplant* 2012; **31**: 715-718 [PMID: 22425231 DOI: 10.1016/j.healun.2012.02.015]
 - 35 **Uriel N**, Pak SW, Jorde UP, Jude B, Susen S, Vincentelli A, Ennezat PV, Cappelman S, Naka Y, Mancini D. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol* 2010; **56**: 1207-1213 [PMID: 20598466 DOI: 10.1016/j.jacc.2010.05.016]

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