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Association of Nasal Mucosal Vascular Alterations, Gastrointestinal Arteriovenous Malformations, and Bleeding in Patients With Continuous-Flow Left Ventricular Assist Devices

Snehal R. Patel, MD,[a] Shivank Madan, MD,[a] Omar Saeed, MD,[a] Mohammed Algodi, MD,[a] Anne Luke, NP,[b] Marc Gibber, MD,[c] Daniel J. Goldstein, MD,[b] Ulrich P. Jorde, MD[a]

ABSTRACT

OBJECTIVES This study sought to determine whether the nasal mucosa can serve as a surrogate for evaluating arteriovenous malformations (AVMs) related gastrointestinal (GI) bleeding in patients supported by continuous-flow left ventricular assist devices (CF LVADs).

BACKGROUND Bleeding from the mucosal surfaces of GI tract, particularly AVMs, is the most common complication of CF LVAD support. The pathophysiology of AVM formation during CF LVAD support is of critical interest yet poorly understood; in large part because of the length and accessibility of the GI tract. Nasal endoscopy is a minimally invasive, bedside test giving access to a mucosal surface possibly representative of the GI tract.

METHODS Eighty subjects (35 with CF LVAD, 30 with heart failure reduced ejection fraction [HFrEF], and 15 controls without heart failure) underwent nasal endoscopy for systematic evaluation of the intranasal mucosa for the presence of hypervascularity (HV). Patient records were reviewed for episodes and etiology of GI bleeding.

RESULTS Nasal HV was present in 63%, 57%, and 20% of the LVAD, HFrEF, and control groups, respectively ($p = 0.018$). Although the prevalence was similar, the severity of nasal HV was significantly higher in the CF LVAD group compared with the HFrEF group. Of the baseline characteristics in the entire cohort, only a history of heart failure was associated with HV (odds ratio: 4.8; 95% confidence interval: 1.02 to 22.31; $p = 0.040$) in adjusted logistic regression modeling. HV was strongly associated with GI bleeding in the CF LVAD cohort: the incidence was 32% in subjects with HV compared with 0% in subjects with normal mucosa ($p = 0.023$).

CONCLUSIONS In this pilot study, HV of the nasal mucosa was associated with GI bleeding in subjects with CF LVADs. Nasal endoscopy has significant potential to further investigation into mechanisms of bleeding and risk stratification during CF LVAD support. (J Am Coll Cardiol HF 2016;4:962–70) © 2016 by the American College of Cardiology Foundation.

Continuous-flow left ventricular assist devices (CF LVADs) have revolutionized the treatment of advanced heart failure (HF). At present, approximately 5,000 CF LVADs are implanted annually in the United States alone, in majority of cases as destination therapy (1,2). With survival rates approaching 70% at 2 years in patients with CF LVADs as destination therapy, the

From the [a]Division of Cardiology, Department of Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York; [b]Department of Cardiovascular and Thoracic Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York; and the [c]Department of Otorhinolaryngology-Head and Neck Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York. This study was supported by intramural research funds. Dr. Jorde has served as an unpaid consultant for St. Jude Medical. Dr. Goldstein has has served as a consultant for St. Jude Medical and HeartWare, Inc.; is a national principal investigator for the St. Jude Medical-sponsored MOMENTUM 3 trial; and has received travel support from St. Jude Medical to attend meetings related to the MOMENTUM 3 trial. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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primary treatment goal has moved from survival to increased quality of life. Consequently, prevention and management of adverse events have taken center stage for attempts to advance the field (3).

During CF LVAD support, mucosal bleeding is the most common adverse event, manifesting primarily as gastrointestinal bleeding (GIB) in an astonishing one-third of patients (4,5). From an observational perspective, 2 unique features of GIB in CF-LVAD patients have evolved: 1) mucosal bleeding is often the result of arteriovenous malformation (AVM), an otherwise uncommon cause of GIB; and 2) there is an almost universal development of acquired von Willebrand syndrome after CF LVAD implantation (5–8). Although these important observations were made nearly a decade ago, little progress has been made since in understanding the mechanisms of mucosal bleeding. This lack of progress is in large part the result of the dynamic nature of AVMs and logistic difficulties in assessing mucosal surfaces of the small bowel.

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Epistaxis, or bleeding from the nasal mucosa, is common in patients with CF LVADs, and its pathophysiological underpinnings may be identical or similar to those of bleeding from the gastrointestinal (GI) tract. Therefore, the nasal mucosa, with a limited surface area and ease of access by nasal endoscopy, may represent an ideal site to further investigate mucosal bleeding during CF LVAD support.

Accordingly, we systematically explored nasal mucosal vascular alterations by endoscopy in subjects with CF LVADs. Further, to test whether nasal mucosal vascular alterations may represent a systemic process, we linked the presence of *nasal* mucosal alterations to clinical *GIB*. Finally, we compared the prevalence of these nasal alterations in subjects with CF LVADs with the prevalence in subjects with HF and in normal controls.

METHODS

SUBJECTS. Eighty subjects (35 with CF LVADs, 30 with HF reduced ejection fraction [HFrEF], and 15 healthy controls without HF) were recruited from the Heart Failure and Advanced Cardiac Therapies Institute at Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York. All subjects with CF LVADs were >60 days post-LVAD implantation and were ambulatory outpatients at the time of nasal endoscopy. Important inclusion criteria for the HFrEF group included a diagnosis of systolic HF for longer than 6 months, New York Heart Association functional class III or IV, and left ventricular ejection fraction (LVEF) ≤ 35%. The primary exclusion criterion in all groups was the presence of anatomic abnormalities such as choanal atresia or deviated septum that would prevent passage of the nasal endoscope. All subjects were considered to be medically optimized, and medications were continued on the day of study. The Montefiore Medical Center Institutional Review Board approved this study, and all subjects gave written informed consent.

For each subject, the medical record was reviewed by a trained physician for demographic and clinical data including instances of GIB. GIB was defined according to INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) criteria as clinical evidence of GIB including melena, hematochezia, hematemesis, or rectal bleeding occurring ≥7 days post-LVAD implantation and requiring transfusion of 1 or more units of packed red blood cells (9). At our institution, all patients presenting with GIB undergo exhaustive evaluation to ensure that the source of bleeding is clearly identified. This evaluation includes routine and simultaneous upper endoscopy, video capsule endoscopy, and colonoscopy, as well as double-balloon enteroscopy if necessary. For the assessment of LVEF and left ventricular size, echocardiographic data were retrieved pre-implantation in the CF LVAD group. For the HFrEF group, echocardiographic parameters were retrieved from the study closest to the time of nasal endoscopy. To assess pulsatility, an aortic valve opening score was calculated in the CF LVAD group from echocardiography performed closest to the time of nasal endoscopy on the basis of a 10-beat average: 0 = no opening; 1 = intermittent opening; and 2 = regular opening (every beat, if atrial fibrillation >7/10). For the CF LVAD group, Doppler blood pressure was measured, and LVAD parameters were recorded at the time of testing. This testing included the HeartMate II (St. Jude Medical, St. Paul, Minnesota) pulse index, which is calculated by the device as follows: (maximum power − minimum power) / (average power) averaged over 15 s (10).

NASAL ENDOSCOPY. All nasal endoscopic procedures were performed by a board certified otorhinolaryngologist (M.G.). First, the nasal cavity was topically anesthetized and decongested with a combination of tetracaine (Pontocaine) and oxymetazoline. Then, rigid endoscopy was performed with a 0° and 30° Hopkins rod telescope. The nasal endoscope was passed along the floor of the nose to

ABBREVIATIONS AND ACRONYMS

AVM = arteriovenous malformation

CF = continuous flow

GI = gastrointestinal

GIB = gastrointestinal bleeding

HF = heart failure

HFrEF = heart failure reduced ejection fraction

HV = hypervascularity

LVAD = left ventricular assist device

LVEF = left ventricular ejection fraction

TABLE 1 Ordinal Scale for Grading Hypervascularity

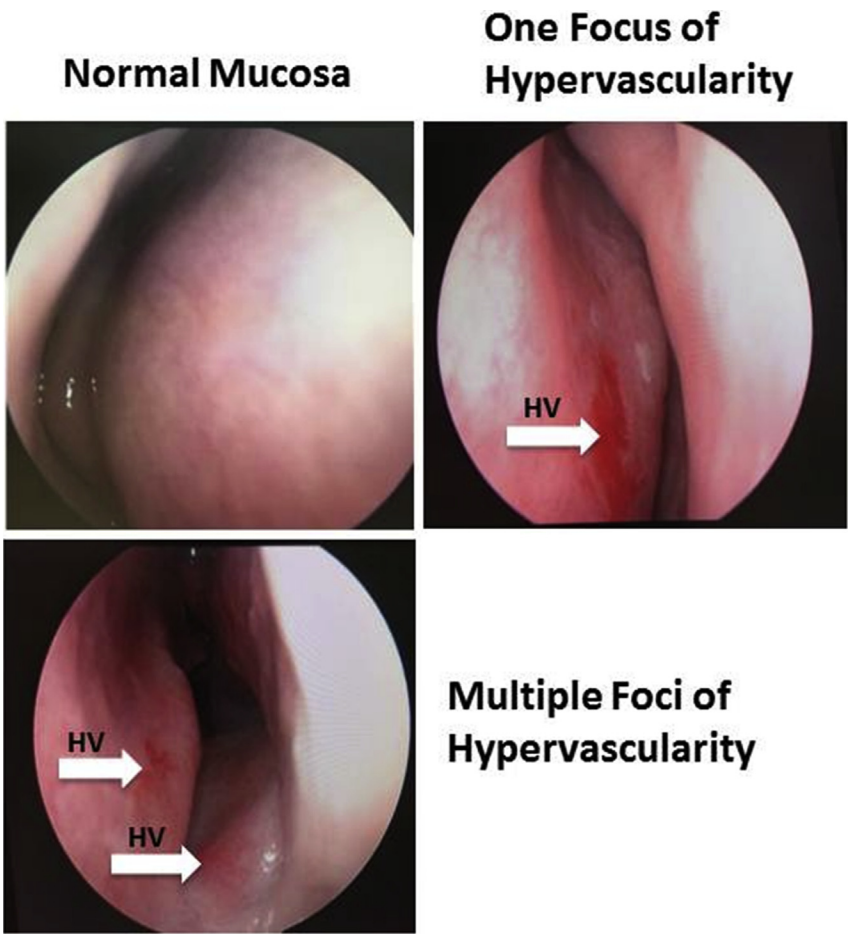
Grade	Description
0	None: no hypervascularity
1	Mild: 1 focus of hypervascularity
2	Moderate: >1 focus of hypervascularity
3	Severe: diffuse hypervascularity

examine the inferior turbinate, the inferior meatus, and the floor of the nose. It was then passed through the upper portion of the nasal cavity to the nasopharynx to assess the septum and middle turbinate, the lateral nasal wall, the osteomeatal complex, and the sphenoethmoidal recess. Any anatomic or vascular abnormalities and the presence of epistaxis were documented and video recorded.

Standard nomenclature for nasal mucosal vascular alterations in patients without hereditary hemorrhagic telangiectasia currently does not exist. Therefore, for the purposes of this study, we devised the following terminology and grading systems: *hypervascularity* (HV) was characterized by a visible dilated blood vessel coursing below the mucosa and easily identified during endoscopy. Patients were graded categorically on the presence or absence of HV, as well as on an ordinal scale, as described in Table 1. Figure 1 provides examples of HV.

STATISTICAL ANALYSIS. The baseline characteristics were described as frequencies (percentage) for categorical variables, mean ± SD for continuous variables with a normal distribution, and median with interquartile range for continuous variables with a non-normal distribution. Comparison among groups was made using the chi-square test for categorical variables, analysis of variance for continuous variables with a normal distribution, and the Wilcoxon

FIGURE 1 Examples of HV



HV = hypervascularity.

rank sum test for continuous variables with a non-normal distribution. We evaluated the association between various baseline characteristics and the presence of nasal HV by using unadjusted and adjusted logistic regression models. All statistical analysis was performed with STATA version 13 (StataCorp, College Station, Texas), and a 2-sided p value <0.05 was considered significant.

RESULTS

PATIENT POPULATION. Baseline demographics of the 3 groups are depicted in Table 2, as are characteristics pertinent to the HFrEF and CF LVAD groups. The HFrEF group was older and more likely to have hypertension and chronic kidney disease stage 4 or 5 as compared with both the group with CF LVADs and normal controls. The LVEFs of the CF LVAD (pre-implant) and HFrEF groups were similar (25% vs. 25%; p = 0.137), as was the percentage of patients with ischemic cause (34% vs. 17%; p = 0.107).

HYPERVASCULARITY. The mean duration from LVAD implantation to nasal endoscopy was 342 ± 270 days. As shown in Figure 2A, HV was present in 63%, 57%, and 20% of the LVAD, HFrEF, and control groups, respectively (p = 0.623 for CF LVAD vs. HFrEF; p = 0.018 across groups). When assessed by the ordinal scale, the degree of HV was more severe in the LVAD group as compared with the HFrEF group and, in turn, was more severe in the HFrEF group versus the control group (p = 0.018 for CF LVAD vs. HF; p = 0.013 across all groups) (Figure 2B).

To assess for predictors of HV, the entire study group was combined, for a total of 80 subjects. Of the analyzed variables, including age, sex, race, diabetes, hypertension, and chronic kidney disease, only a history of HF and sex were associated with the presence of HV in unadjusted logistic regression analysis (Figure 3). After adjustment for differences in baseline characteristics, only a history of HF remained associated with HV (odds ratio: 4.8; 95% confidence interval: 1.02 to 22.31; p = 0.040). Similarly, the LVAD and HFrEF groups were combined, for a total of 65 subjects, and were analyzed for cardiac-specific factors associated with HV. None of the examined variables, including cause of HF, LVEF, use of vasodilator drugs, or anticoagulant agents, were associated with the presence of HV (Figure 3).

Table 3 examines the CF LVAD group alone and divides it into subjects with and without HV. There were no significant differences in the baseline characteristics including duration of support at the time of testing. The 2 assessed measures of pulsatility, the aortic valve opening score and the HeartMate II pulse index, were similar between subjects with and without mucosal abnormalities.

TABLE 2 Baseline Demographics

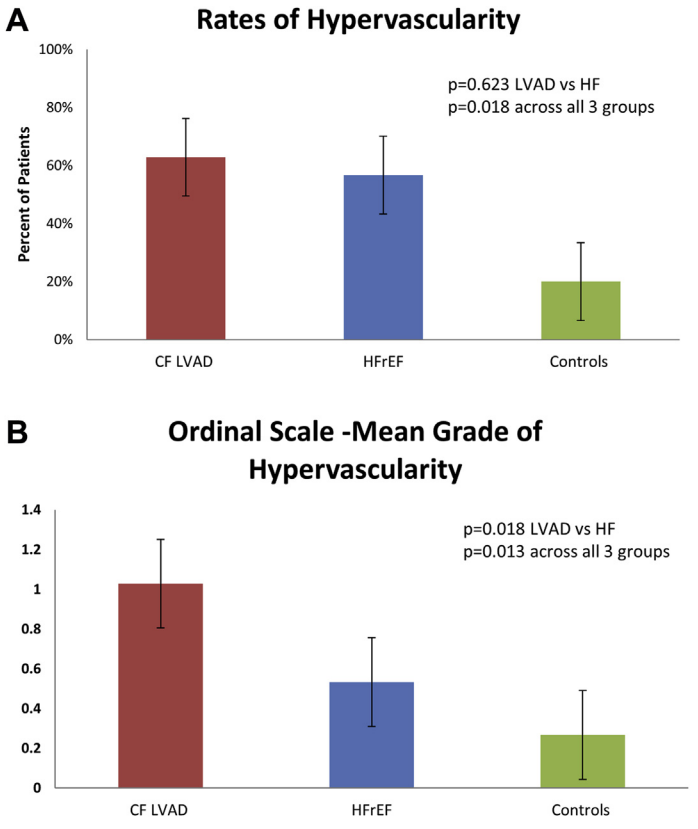
	CF LVAD (n = 35)	HFrEF (n = 30)	Controls (n = 15)	p Value*	p Value†
Age (yrs)	55 (44–68)	67 (56–73)	33 (30–69)	0.011	0.007
Female (%)	6 (17)	5 (17)	9 (60)	0.959	0.002
Race				0.032	0.003
Caucasian (%)	6 (17)	1 (3)	3 (20)		
African American (%)	10 (29)	19 (63)	1 (7)		
Hispanic (%)	15 (43)	8 (27)	9 (60)		
Asian (%)	4 (11)	2 (7)	2 (13)		
Hypertension (%)	17 (49)	23 (77)	4 (27)	0.024	0.004
Diabetes (%)	15 (43)	13 (43)	3 (20)	0.969	0.255
CKD 4/5	1 (3)	6 (20)	0 (0)	0.042	0.021
Ischemic etiology of HF (%)	12 (34)	5 (17)	–	0.107	–
LVEF (%)	25 (20–30)	25 (25–33)	–	0.137	–
Medications					
Warfarin (%)	32 (91)	15 (50)	–	<0.001	–
Aspirin (%)	29 (83)	19 (63)	–	0.074	–
ACE or ARB (%)	22 (63)	20 (67)	–	0.869	–
Hydralazine (%)	10 (29)	14 (47)	–	0.093	–
Nitrates (%)	7 (20)	12 (40)	–	0.090	–
Beta blocker (%)	34 (97)	29 (97)	–	0.283	–
Type of LVAD					
HeartMate II (%)	30 (86)	–	–	–	–
HeartWare (%)	5 (14)	–	–	–	–

Values are mean (range) or n (%). *CF LVAD versus HFrEF. †Across all 3 groups.

ACE = angiotensin-converting enzyme inhibitor; ARB = angiotensin converting blocker; CF = continuous flow; CKD = chronic kidney disease; HF = heart failure; HFrEF = heart failure reduced ejection fraction; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction.

ASSOCIATION OF HYPERVASCULARITY WITH CLINICAL EVENTS. Of the 35 subjects with CF LVADs, 7 (20%) experienced GIB after LVAD implantation but before nasal endoscopy. At the time of the bleeding, 6 of the 7 subjects were taking aspirin, and all patients were taking warfarin, with a median international normalized ratio (INR) at the time of GIB of 1.9 (range 1.3 to 3.1). The median INR during the time at risk did not differ between those with and without GIB (2.0 [Q1 to Q3: 1.7 to 2.1] vs. 2.0 [Q1 to Q3: 1.7 to 2.2]; p = 0.690). The cause of GIB was identified as an AVM in 5 of 7 (71%) subjects, a hemorrhoid in 1 subject, and a cecal ulcer in the remaining subject. The median times from LVAD implantation to any GIB (52 days; range 28 to 538 days) and from LVAD implantation to AVM bleeding only (60 days; range 52 to 538 days) did not differ. Time from GIB to nasal endoscopy was 241 days (range 130 to 480 days). There was a strong association between GIB during LVAD support and HV on nasal endoscopy: all 7 of the episodes of GIB occurred in patients with HV. As demonstrated in

FIGURE 2 Hypervascularity Assessment



Rates of hypervascularity as assessed categorically **(A)** and ordinal scoring of hypervascularity **(B)** in continuous flow (CF) left ventricular assist device (LVAD), heart failure (HF) reduced ejection fraction (HFrEF), and controls (n = 35, n = 30, and n = 15, respectively).

Figure 4A, in the CF LVAD cohort, the incidence of GIB was 32% in subjects with HV compared with 0% in subjects with normal mucosa (p = 0.023).

In the HFrEF group, 5 (17%) patients had GIB before endoscopy. The distribution of GIB causes in this group was as follows: gastric ulcer, 40%; hemorrhoids, 40%; and unidentified cause, 20%. As shown in Figure 4B, there was no association between the presence of HV on nasal endoscopy and GIB in the HFrEF group (HV vs. normal mucosa: 12% vs. 23%; p = 0.410). In terms of antiplatelet and anticoagulant therapy, 3 patients taking warfarin, 1 was taking aspirin, and 1 was taking neither drug at the time of GIB. None of the normal control patients had a history of GIB.

DISCUSSION

We examined the association of nasal mucosal vascular alterations with GIB and its substrate etiology during CF LVAD support. Our principal findings are as follows: 1) 63% of the subjects with LVADs demonstrated HV of the nasal mucosa in comparison with 20% of controls; 2) subjects with HF had an overall prevalence of nasal HV similar to that observed in subjects with CF LVADs, but the average HV severity index was twice as high in the subjects with CF LVADs; and 3) all the subjects with CF LVADs who experienced clinical GIB had nasal HV, whereas no GIB episodes occurred in subjects with normal nasal mucosa. We believe that these findings have important implications for our understanding of mucosal bleeding during CF LVAD support and demonstrate the potential of nasal endoscopy as a tool to investigate this disease process further.

Mucosal bleeding has emerged as the most common and challenging complication of CF LVAD support. It manifests primarily as GIB, with documented rates approaching 33%, although the actual incidence of all mucosal bleeding is much higher when other sites such as nasal mucosa and the genitourinary tract are included. In a large, single-center analysis, Uriel et al. (4) found that 65% of patients who were more than 65 years old require blood transfusion for mucosal bleeding in the first year after CF LVAD implantation. These are alarming rates and have accordingly spawned intense focus on the pathophysiology of this process.

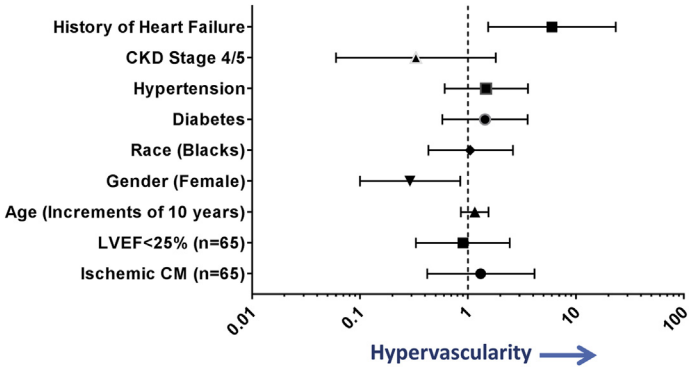
It is now clear that, similar to the description of Heyde syndrome in aortic stenosis, there are both hematologic and anatomic abnormalities at play in the specific pathophysiology of CF LVAD-associated GIB (11,12). Hematologically, numerous investigators, beginning with Geisen et al. in 2008 (6), have shown that rotary pumps create a nearly universal depletion of the high-molecular-weight multimers of von Willebrand factor (i.e., acquired von Willebrand factor deficiency) (6). This depletion is believed to result from the imposition of high shear stress on the blood elements while traversing the pump (13). Anatomically, as documented by Demirozu et al. (5) and others, most episodes of mucosal bleeding are caused by AVMs. The combination of these 2 pathological processes accounts for the excessive bleeding seen in patients during CF LVAD support because high-molecular-weight multimers are critical to hemostasis at areas of high flow such as AVMs (14). The unanswered question in this paradigm is "Why AVMs are so prevalent in subjects with CF LVADs?" There has been little progress in answering this question, largely because investigations have been stunted by the length (~10 m) and accessibility of the GI tract.

In search for a suitable surrogate for the mucosal surfaces of the GI tract, we systematically investigated the nasal mucosa in patients with CF LVADs, patients with HF, and normal controls. We found that 63% of the studied subjects with LVADs evidenced nasal HV. Although we refrained from using the histologically defined term "arteriovenous malformation," the anatomic observation is identical to what is seen during GI endoscopy (**Figure 5**). This prevalence is much higher than the 20% HV rate noted in the group of normal controls ($p = 0.018$); however, it was surprisingly similar to the 57% HV rate in the HFrEF group ($p = 0.623$). This is an important observation and could imply that HF *itself* predisposes to mucosal vascular alterations then then become clinically relevant only after CF LVAD implantation. This suggestion is consistent with a 2-hit hypothesis that is commonly accepted in many other causes of GIB whereby acquired von Willebrand factor deficiency or another hematologic perturbation caused by the device provides the second hit (15).

To confirm these findings, the entire study group was analyzed for characteristics associated with HV, and indeed only a history of HF was significant in multivariate modeling (**Figure 3**). When nasal HV was analyzed by an ordinal scale, the LVAD group was found to have significantly higher degrees of severity of HV than the HFrEF group. This finding is consistent with the assumption that the LVAD group had a more advanced degree of HF. Under this construct, HF predisposes to mucosal vascular alterations that become progressively severe with advancing degrees of HF. Although at present the exact mechanism whereby HF predisposes to mucosal vascular alterations is unknown, it is established that serum levels of angiogenic factors are elevated during HF (16,17). In an attempt to maintain adequate capillary density, these factors, which include vascular endothelial growth factor and angiopoietin-2, are stimulated during HF by pathological myocardial hypertrophy, which induces myocardial oxygen supply/demand mismatch (i.e., ischemia). Although HF investigations have focused on the myocardial effects of up-regulated serum angiogenic factors, there has been little reason until now to consider their potential *noncardiac* effects. Indeed, published reports from the neurosurgical realm have linked angiopoietin-2 to brain AVMs, thus offering a plausible mechanism for AVM formation in HF (18). This is an area in need of further study.

In a specific analysis of the CF LVAD cohort, measures of pulsatility (aortic valve opening and the HeartMate pulse index) were similar between subjects with and without HV. This finding stands in distinction to the aforementioned suggestion as well as previously published reports that found an association between pulsatility and mucosal bleeding (19).

FIGURE 3 Association of Baseline Features With Nasal Hypervascularity



*On multiple logistic regression analysis with the above variables, only a history of heart failure had a significant association (OR: 4.8; 95% CI: 1.022 to 22.31, $p = 0.04$).
CI = confidence interval; CKD = chronic kidney disease; CM = cardiomyopathy; LVEF = left ventricular ejection fraction; OR = odds ratio.

TABLE 3 Comparison of Characteristics of Hypervascularity Versus Normal Mucosa in Subjects With CF LVAD

	Normal Mucosa (n = 13)	Hypervascularity (n = 22)	p Value
Age (yrs)	55 (42-65)	58 (44-71)	0.412
Female (%)	3 (23)	3 (14)	0.474
Ischemic etiology (%)	3 (23)	9 (41)	0.283
Diabetes (%)	5 (38)	10 (45)	0.686
Hypertension (%)	4 (31)	13 (59)	0.105
CKD 4/5 (%)	1 (8)	0 (0)	0.187
LVEF (%)	20 (15-30)	20 (12-25)	0.894
LVEDD (cm)	6.7 (5.5-7.3)	5.5 (4.9-6.1)	0.108
Type of LVAD			0.133
HeartMate II	13 (100)	17 (77)	
HVAD	0	5 (23)	
Mean duration of LVAD support (days)	327	351	0.802
Aortic valve opening*	0.75	0.68	0.824
HeartMate II PI	5.7	5.8	0.863
Doppler blood pressure (mm Hg)	92 (84-102)	85 (78-90)	0.083
HeartMate II speed (rpm)	9,000 (8,800-9,200)	9,000 (8,800-9,200)	0.809
LVAD flow (l/m)	4.9 (4.3-5.3)	4.4 (4.0-5.2)	0.439
All gastrointestinal bleeding (%)	0 (0)	7 (32)	0.023
AVM gastrointestinal bleeding (%)	0 (0)	5 (23)	0.063

Values are mean (range), n (%), or %. *Aortic valve opening, scored over a 10-beat average as follows: 0 = no opening; 1 = intermittent; and 2 = closed.
AVM = arteriovenous malformation; LVEDD = left ventricular end-diastolic diameter; PI = pulse index; other abbreviations as in Table 2.

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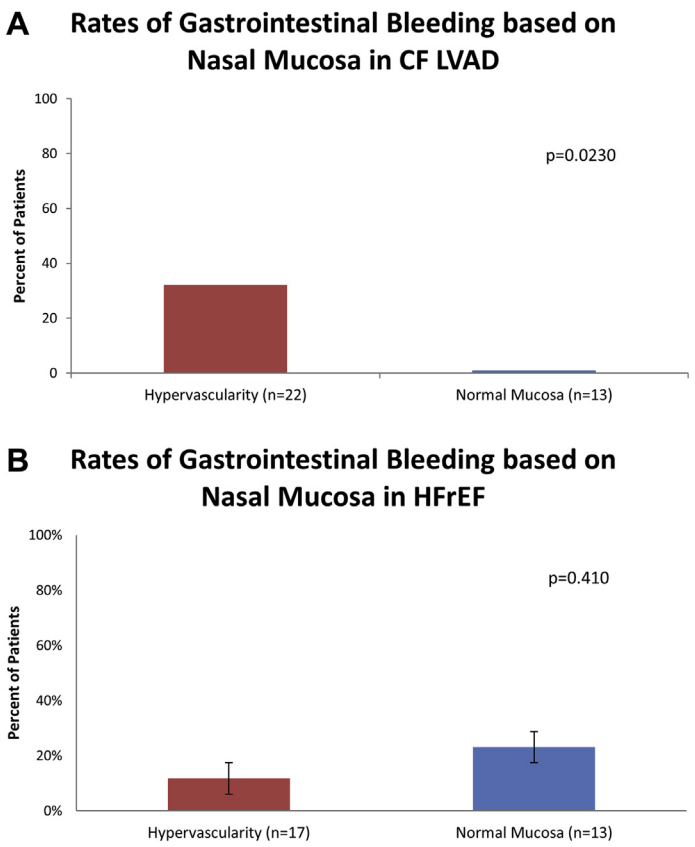
FIGURE 4 Risk of Gastrointestinal Bleeding on the Basis of Hypervascularity



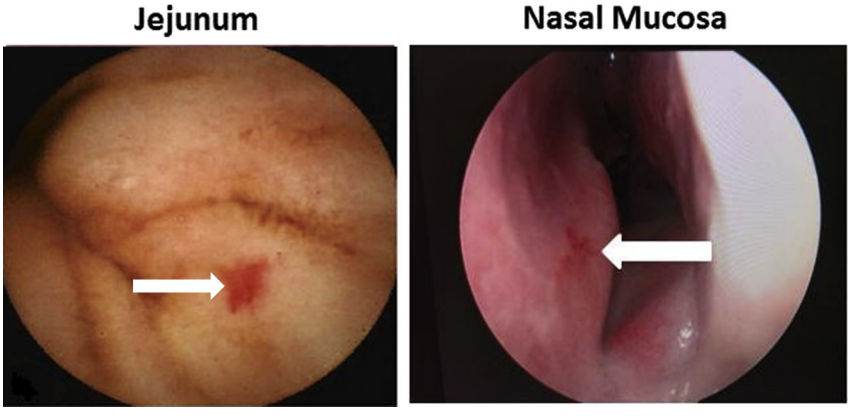
(A) Continuous flow left ventricular assist device (CF LVAD). **(B)** Heart failure reduced ejection fraction (HFrEF).

The lack of association between these measures of pulsatility and HV in our study quite likely could be explained by the relative lack of sensitivity of these tools to assess pulsatility. In this regard, developing better measures of pulsatility will be critical for future investigation in this area (20).

The high prevalence of vascular alterations in the nasal mucosa and the association with GIB in patients with CF LVADs suggest that this is a systemic process and not limited to the nasal mucosa. In this study, we were unable simultaneously to image the entire GI tract to confirm this hypothesis. In lieu of this, we examined whether the GI manifestation of AVMs during CF LVAD support (i.e., GIB) was more prevalent in subjects with nasal HV. As illustrated in Figure 4, this was clearly the case and may imply that mucosal vascular abnormalities are systemic. Additionally, the remarkable finding that none of the subjects with normal nasal mucosa experienced GIB may lead one to speculate that the nasal mucosa is indeed representative of mucosal surfaces at large and that we have identified nasal HV as a risk factor and a sine qua non condition for AVM bleeding during CF LVAD support. In comparison, the HFrEF group demonstrated no association between nasal HV and GIB, once again supporting the notion that a second hit from CF LVAD inclines AVMs to bleed. Clearly, these are preliminary observations and need more careful validation.

STUDY LIMITATIONS. The first limitation of the present study, a pilot project, is the small sample size. As is common to most LVAD studies, the small sample size may limit the generalizability of the findings. The 3 study groups had important baseline differences

FIGURE 5 Comparison of Nasal Hypervascularity and Arteriovenous Malformation of the Gastrointestinal Tract



that could have affected the observations of nasal HV. We also chose not to adjust for multiple comparisons when analyzing HV severity because this was a limited pilot study. Second, we were unable *simultaneously* to link HV of the nose to AVM of the GI tract. We therefore used the surrogate of clinical AVM bleeding of the GI tract. We found that a slightly higher percentage of GIB episodes were caused by AVMs (71%) than is commonly cited in the literature. Although we cannot be certain, we believe that this finding reflects our institutional approach of exhaustive evaluation of each bleeding episode so that the source is always identified. Finally, our data do not provide any insights on the fate of HV observed before LVAD implantation or on the development of HV and/or GI AVMs after LVAD implantation. Despite these important limitations, we believe this is vital work that demonstrates the potential of a more feasible model to study mucosal bleeding during CF LAD support. Ideally, future studies can build on these findings and clarify outstanding issues, including the correlation between GI and nasal AVMs, their true incidence in HF, and prospective follow-up for the progression and evolution of AVMs pre- and post-LVAD implantation.

CONCLUSIONS

Nasal mucosal HV is common in patients with CF LVADs and is strongly associated with GIB. In fact, in this pilot study, bleeding from GI AVMs occurred exclusively in patients who also had nasal HV. This finding, if validated in appropriately powered studies, may identify the nasal mucosa as a surrogate for mucosal vascular alterations in the GI tract and may thus greatly facilitate risk stratification for and understanding of bleeding episodes in patients supported by CF LVADs.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Snehal R. Patel, Division of Cardiology, Heart Failure, Cardiac Transplantation, and Mechanical Circulatory Support, Montefiore Medical Center, Albert Einstein College of Medicine, 3400 Bainbridge Avenue, Medical Arts Pavilion-7th Floor, Bronx, New York 10467. E-mail: snepatel@montefiore.org.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: GIB is the most common bleeding complication of CF LVAD support. The source of bleeding is most often mucosal AVM, an otherwise uncommon cause of GIB.

TRANSLATIONAL OUTLOOK 1: Study of AVM bleeding during CF LVAD support has been limited by the length and accessibility of the GI tract. The nasal mucosa may provide a more readily available surrogate to study this disease.

TRANSLATIONAL OUTLOOK 2: The traditional assumption is that mucosal vascular abnormalities are induced by CF LVAD, although there is no evidence to support this premise. It is possible that advanced HF itself is associated with mucosal vascular alterations, and this finding requires further investigation.

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