Epidemiology and Outcomes Associated With Anemia During Long-Term Support With Continuous-Flow Left Ventricular Assist Devices

DOUGLAS L. JENNINGS, PharmD,[1] JAMIE L. WAGNER, PharmD,[2] LONG TO, PharmD,[2] CARRIE W. NEMEROVSKI, PharmD,[2] JAMES S. KALUS, PharmD,[2] JEFFREY A. MORGAN, MD,[3] AND DAVID E. LANFEAR, MD[4]

Ft. Lauderdale, Florida; and Detroit, Michigan

ABSTRACT

Background: The purpose of this study was to define the prevalence and clinical ramifications of anemia in patients implanted with a continuous-flow left ventricular assist device (CF-LVAD).

Methods and Results: Patients implanted with a CF-LVAD from January 1, 2008, to April 30, 2012, were included in this retrospective cohort study. The primary outcome was the prevalence of anemia throughout the 1st year of device support. Secondary end points included the impact of anemia on rates of readmission to hospital and mortality. Ninety-one patients were included; the prevalence of anemia 360 days after implantation was significantly reduced compared with baseline (61.4% vs 79.1%, respectively; $P = .032$); 65.4% of anemic patients and 34.6% of nonanemic patients were readmitted at least once ($P = .067$). The median number of readmissions in the anemic compared with the nonanemic group was 4 (interquartile range [IQR] 2-6) versus 1.5 (IQR 1-3), respectively ($P < .001$). Furthermore, among those who experienced >3 readmissions during the 1st year, 19 were anemic compared with 1 patient who was not anemic ($P < .001$).

Conclusions: Anemia remains a prevalent condition while on CF-LVAD support and is associated with a significant increase in the number of hospital readmissions. (*J Cardiac Fail 2014;20:387–391*)

Key Words: Anemia, left ventricular assist device, readmission.

Continuous-flow left ventricular assist devices (CF-LVADs) have emerged as a life-prolonging treatment modality in patients with advanced heart failure.[1] These devices have been shown to prolong survival, increase exercise capacity, improve liver and kidney function, and alleviate heart failure symptoms.[1–6] Furthermore, several studies have demonstrated that CF-LVAD implantation can result in significant improvement in quality of life, as measured with the use of the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Minnesota Living With Heart Failure Questionnaire.[2,6–8]

Anemia is commonly associated with heart failure, and has been linked with poor outcomes in this patient population. One small study of patients with first-generation LVADs suggested that anemia remains a prevalent condition during device support.[9] However, those devices are no longer used, but no studies evaluating the presence and potential impact of anemia during contemporary device support have been conducted. Therefore, the purpose of the present study was to examine the epidemiology and clinical outcomes associated with anemia during long-term support with CF-LVAD support.

Methods

This retrospective cohort study included all patients who were at least 18 years old and implanted with either a Heartmate II or Heartware device for end-stage heart failure from January 1, 2008, to April 30, 2012, at our institution. Patients were excluded if they received a right ventricular, biventricular, or replacement left ventricular device, were <18 years old, or received post-implantation care at another institution. At our institution, all patients have regular monitoring of hemoglobin values at least once

From the [1]Nova Southeastern University Department of Pharmacy Practice, Ft. Lauderdale, Florida; [2]Henry Ford Hospital Department of Pharmacy Services, Detroit, Michigan; [3]Henry Ford Hospital Department of Cardiac Surgery, Detroit, Michigan and [4]Henry Ford Hospital Department of Cardiovascular Medicine, Detroit, Michigan.

Manuscript received November 11, 2013; revised manuscript received March 18, 2014; revised manuscript accepted April 3, 2014.

Reprint requests: Dr Douglas L. Jennings, PharmD, AACC, BCPS (AQ-Cardiology), Nova Southeastern University, College of Pharmacy, 3200 South University Drive, Fort Lauderdale, FL 33328. Tel: 954-262-1362. E-mail: djennings@nova.edu

All decisions regarding this manuscript were made by a guest editor.
See page 390 for disclosure information.
1071-9164/$ - see front matter

http://dx.doi.org/10.1016/j.cardfail.2014.04.012

Table 1. Pre-implantation Demographic Characteristics of Patients Stratified According to the Presence of Anemia

Variable	Overall (n = 91)	Anemia (n = 72)	No Anemia (n = 19)	*P* Value
Age (y)	55 (46–62)	55 (44–65)	53 (41–66)	.672
Male, n (%)	65 (71.4)	49 (68.1)	16 (84.2)	.254
Race, n (%)				.443
White	51 (56)	42 (58.3)	9 (47.4)	
Nonwhite	40 (44)	30 (41.7)	10 (52.6)	
Heartmate II, n (%)	78 (85.7)	64 (88.9)	14 (73.7)	.135
Bridge to transplant, n (%)	38 (41.8)	29 (40.3)	9 (47.4)	.609
Intermacs score	2.68 ± 0.868	2.63 ± 0.846	2.89 ± 0.937	.230
Serum creatinine (mg/dL)	1.34 ± 0.44	1.40 ± 0.47	1.30 ± 0.25	.453
Creatinine clearance (mL/min)	63.14 ± 23.55	61.36 ± 23.84	69.86 ± 21.75	.163
BUN (mg/dL)	23.87 ± 13.95	22.56 ± 14.17	28.84 ± 12.17	.081
Hemoglobin (mg/dL)	11.36 ± 1.70	10.73 ± 1.23	13.76 ± 0.92	<.001
Hematocrit (%)	33.92 ± 5.03	32.04 ± 3.56	41.02 ± 3.01	<.001
MCV (fL)	86.99 ± 8.44	85.87 ± 8.75	91.26 ± 5.50	.012
LDH (IU/L)	292.50 ± 118.93	286.61 ± 108.96	314.90 ± 156.03	.509
Haptoglobin (mg/dL)	124.06 ± 92.94	143.24 ± 93.11	62.70 ± 67.06	.091
Vitamin B_{12} (pg/mL)	740 ± 445.67	713.8 ± 493.08	871.0	.785
Ferritin (ng/mL)	170.00 ± 159.69	167.67 ± 171.62	179.33 ± 127.88	.915
Iron saturation (%)	14.76 ± 8.39	15.18 ± 8.90	12.40 ± 4.51	.504

BUN, blood urea nitrogen; MCV, mean corpuscular volume; LDH, lactate dehydrogenase.
All values are presented as mean ± SD unless otherwise indicated.

monthly, and decisions regarding further diagnostic testing for anemia are at the discretion of the treating physician. Iron deficiency, if detected, is generally treated with oral supplementation. Any patients with overt signs of gastrointestinal bleeding (GIB) were evaluated with endoscopy or colonoscopy. Significant evidence of hemolytic anemia prompts further work-up for device thrombosis. Finally, erythropoietin-stimulating agents are not routinely used in our anemic patients.

Patient demographics and data variables were gathered with the use of inpatient electronic medical records and clinical heart failure databases. Key data collection included hemoglobin and hematocrit, iron studies, hemolysis studies (ie, lactate dehydrogenase and haptoglobin), and serum creatinine values for assessment of renal function. Patients were divided into an anemic group and a nonanemic group at baseline and were followed for up to 1 year after device implantation. The primary outcome was the prevalence of anemia (defined as a hemoglobin <13 mg/dL for men and <12 mg/dL for women) at 180 days after implantation. Anemia prevalence was also assessed at 90, 270, and 360 days after implantation. Additionally, all readmissions to hospital were collected; readmissions due to an anemia-related cause (defined as the occurrence of GIB, device hemolysis, or any bleeding episode) were analyzed separately. All-cause mortality during the 1-year follow-up period and any occurrence of GIB were also recorded.

Continuous variables were expressed as median ± interquartile range (IQR) and analyzed with the use of the Mann-Whitney *U* test. Differences between the anemic and nonanemic group of patients at 180 days of CF-LVAD support were analyzed with the use of the McNemar test. Comparisons of categoric variables were made with the use of a χ^2 test. If the expected number in any given data subgroup was <5, the Fisher exact test was used. A *P* value of <.05 was considered to be significant for all comparisons. Statistical testing was completed with the use of SPSS 19.0 (IBM, Armonk, New York).

Results

Ninety-one patients met the criteria for inclusion during the study period (Table 1). Before implantation, 79% of the patients were anemic. Both at baseline and 180 days after implantation, the anemic and nonanemic groups were similar with the exception of hemoglobin, hematocrit, and mean corpuscular volume (MCV; Table 2).

In the overall population, anemia was present in 68.3% of the patients after 180 days of CF-LVAD support, which was similar to the pre-implantation prevalence (Fig. 1). However, the prevalence of anemia 360 days after implantation was significantly reduced compared with baseline

Table 2. Laboratory Characteristics 180 Days After Implantation, Stratified According to the Presence of Anemia

Variable	Normal Values	Anemia (n = 56)	No Anemia (n = 26)	*P* Value
Serum creatinine (mg/dL)	[<1.03]	1.26 ± 0.46	1.20 ± 0.30	.502
Creatinine clearance (mL/min)*	—	65.55 ± 23.58	67.25 ± 16.10	.705
BUN (mg/dL)	[10–25]	19.48 ± 8.45	20.69 ± 10.45	.578
Hemoglobin (mg/dL)	[12–15]	10.91 ± 1.32	13.61 ± 0.99	<.001
Hematocrit (%)	[36–46]	32.54 ± 3.99	40.34 ± 2.76	<.001
MCV (fL)	[80–100]	87.62 ± 6.62	85.47 ± 10.00	.252
LDH (IU/L)	[100–220]	269.48 ± 74.44	304.50 ± 61.91	.203
Haptoglobin (mg/dL)	[30–200]	54.33 ± 129.98	23.90 ± 33.80	.761
Reticulocytes (%)	[0.5–1.5]	2.7 ± 0.42	NA	NA
Iron saturation (%)	[15–50]	14.43 ± 5.65	NA	NA

Abbreviations as in Table 1.
*Calculated with the use of the Cockcroft-Gault equation.