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Pre-operative and post-operative risk factors associated with neurologic complications in patients with advanced heart failure supported by a left ventricular assist device

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Abstract

BACKGROUND—Neurologic complications (NCs) are the major adverse events after left ventricular assist device (LVAD) surgery. Pre-operative and post-operative factors associated with NCs in patients with LVADs were investigated.

METHODS—We reviewed 307 consecutive patients undergoing LVAD surgery (167 HeartMate I and 140 HeartMate II devices) at Columbia University Medical Center between November 2000 and December 2010. Clinical characteristics and hemodynamic and laboratory indexes were analyzed. NC was defined according to the Interagency Registry for Mechanically Assisted Circulatory Support definition of neurologic dysfunction, including transient ischemic attack (TIA) and ischemic or hemorrhagic cerebrovascular accident (CVA).

RESULTS—NCs developed in 43 patients (14.0%) at 91.8 ± 116.3 days post-operatively. The frequency of NC development was similar in HeartMate I and II patients. Patients with NC showed a higher frequency of pre-LVAD CVA history (27.9% vs 15.5%, $p = 0.046$), lower pre-operative sodium (129.0 ± 7.0 vs 132.1 ± 8.1 mg/dl, $p = 0.018$) and albumin concentrations (3.5 ± 0.7 vs 3.7 ± 0.6 mg/dl, $p = 0.049$), lower post-operative hematocrit (34.9% ± 5.1% vs 37.8% ± 6.1%, $p = 0.0034$), sodium (131.6 ± 7.7 vs 134.4 ± 6.4 mg/dl, $p = 0.010$) and albumin concentrations (3.7 ± 0.5 vs 3.9 ± 0.5 mg/dl, $p = 0.0016$), and higher frequency of post-operative infection (39.5% vs 19.3%, $p = 0.003$) than those without NC. Multiple regression analysis revealed that CVA history (odds ratio, 2.37, 95% confidence interval, 1.24 –5.29; $p = 0.011$) and

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post-operative infection (odds ratio, 2.99, 95% confidence interval, 1.16 –10.49; $p = 0.011$) were highly associated with NC development. The combination of CVA history, pre-operative and post-operative sodium and albumin, and post-operative hematocrit and infection could discriminate patients developing NCs with a probability of 76.6%.

CONCLUSIONS—Previous stroke, persistent malnutrition and inflammation, severity of heart failure, and post-LVAD infections are key factors associated with development of NCs after LVAD implantation.

Keywords

ventricular assistventricular assist device; neurologic complications; heart failure; risk factor

Cardiac transplantation provides considerable survival benefits for patients with end-stage heart failure (HF); however, its use is severely limited due to donor shortage.[1,2] A growing number of heart transplant candidates require long-term support by a left ventricular assist device (LVAD) while they await cardiac transplantation. LVAD therapy has evolved into a standard therapy for patients with advanced HF,[3–5] not only as a bridge to cardiac transplantation but also as a destination therapy or a bridge to myocardial recovery.[6,7]

Long-term LVAD support, however, can result in serious complications such as cerebrovascular accidents (CVAs), hemorrhage, and infection.[4,8] CVA remains the leading cause of death and the primary reason for withdrawal from transplant eligibility in LVAD-supported patients. In addition, transplant recipients with a history of CVA face tremendous difficulties in their post-operative course, including higher morbidity and mortality and problems to reintegrate into society, often for years after transplant.[4,5,8,9] An incidence of ischemic and hemorrhagic CVAs after LVAD placement of 8% to 25% has been reported.[5,10,11] This study was initiated to assess the pre-operative and post-operative factors associated with the development of neurologic complications (NCs) in patients undergoing LVAD placement, and we investigated factors associated with NCs after LVAD surgery in our single-center experience.

Methods

Patients and study design

We reviewed 307 consecutive patients who underwent HeartMate I or II (Thoratec Corp, Pleasanton, CA) LVAD placement at Columbia University Medical Center between November 2000 and December 2010. Patients who underwent other types of LVAD surgery were excluded. Definition of NC was based on the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) definition of neurologic dysfunction: any new, temporary or permanent, focal or global neurologic deficit, including transient ischemic attack (TIA) that resolves within 24 hours, and ischemic or hemorrhagic intracranial CVA that persists beyond 24 hours or less than 24 hours with infarction on an image study.[8,12] In patients with multiple episodes of NC, the first episode of CVA was used for the analysis for patients developing CVA, and the first TIA episode was used for the analysis of patients with only TIA and not progressing to CVA.

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Aspirin (81 mg daily) was initiated early post-operatively in all patients who received a HeartMate I device; however, warfarin was not initiated for the first month, even if patients had a history of atrial fibrillation. The anti-coagulation protocol for patients with HeartMate II device included heparin, warfarin, and anti-platelet agents, such as aspirin and/or dipyridamole, except for those with contraindication to the medication or/and active bleeding. Heparin was used as a bridge therapy until patients taking warfarin reached a therapeutic international normalized ratio (INR). A target INR was 1.8 to 2.5 for the studied patients. Various anti-coagulation treatments were optimized according to tailored management to each patient's clinical condition.

We performed 2 different analyses. First, univariate and multivariate analyses were performed on 43 patients to define pre-operative and post-operative factors associated with NCs, including TIA and CVA. Second, after excluding the 10 patients who only developed TIA but not CVA, we analyzed factors associated with CVA. All patients were first divided into 2 groups: those who developed NC at any time after LVAD placement (Group NC) and those who did not develop any NC throughout the post-operative period (Group non-NC). After excluding patients with only TIA from those in Group NC, patients who developed CVA were classified as Group CVA.

Clinical characteristics, pre-operative hemodynamic data, and laboratory examinations were compared between patients with and without NCs as well as between patients with CVA and without CVA. In addition, pre-operative LV end-diastolic diameters and ejection fractions derived from echocardiograms were assessed by biplane Simpson's method and compared among the groups.

Post-operative laboratory examinations, infection, and warfarin or/and aspirin administration were also compared among the groups. Pre-operative variables were obtained within 7 days before surgery. Post-operative laboratory data for patients with NC or CVA were collected within 7 days before the events, and data for patients without NC were collected within 7 days from the end of observation or device removal due to transplant, recovery, or death. A post-operative infection was defined as >2 positive cultures when the patient developed any symptom of an infection. Urinary tract infection was defined as >2 positive urine cultures with $>10^5$ colonies/ml with signs of urinary tract infection.

Statistical analysis

Data are presented as means ± standard deviation. Normality was evaluated for each variable on the basis of normal distribution plots and histograms and by the Kolmogorov-Smirnov test. Clinical characteristics, hemodynamic, and laboratory data were compared among groups using Student's unpaired two-tailed *t*-test or chi-square analysis. Univariate logistic regression analysis was used to select factors associated with NC or CVA for inclusion in subsequent multivariate analysis. A stepwise forward selection method was used to select variables that discriminated patients with NC or CVA from those without any episodes of NC. The partial F value of 0.2 was used for selection criteria. The discriminant score and discriminant probability were calculated using a discriminant function test. All statistical analyses were performed using JMP 7.0 software (SAS Institute, Cary, NC).

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Results

The clinical course of 307 patients (167 patients with HeartMate I device and 140 patients with HeartMate II device) was retrospectively analyzed (Figure 1). Patients were a mean age of 54 ± 14 years at the time of surgery, and the mean post-operative observation period was 259 ± 304 days. The mean observation periods were 138 ± 224 days (range 3–1,434 days) for HeartMate I patients and 277 ± 333 days (range, 3–2,069 days) for HeartMate II patients.

A total of 51 NC events occurred in 43 patients (14.0%, 0.23 events/patient per year) after a mean of 92 ± 116 days after LVAD surgery, consisting of 27 events in 24 patients (14.4%) with HeartMate I and 24 events in 19 patients (13.6%) with HeartMate II. These 43 patients were classified as those in Group NC. A total of 39 CVA events occurred in 33 patients (10.7%, 0.18 events/patient per year) at 80 ± 103 days after the surgery, consisting of 22 events in 19 patients (11.4%, 0.34 events/patient per year) with HeartMate I and 17 events in 14 patients (10.0%, 0.16 events/patient per year) with HeartMate II. They were considered as Group CVA. The duration from the LVAD surgery to all NC events is shown in Figure 2, which revealed that 37 of 51 events (72.5%) occurred within 6 months after LVAD surgery.

Multiple NCs occurred in 6 patients (2.0%); however, analysis was performed based on 1 event/patient using the first episode of CVA in patients with CVA or the first episodes of TIA in patients with only TIA to avoid double- or triple-counting of those patients' clinical data and to purely discriminate patients with NC or CVA from those who remained free of NC.

Comparison of variables in patients with NC (CVA and TIA) and those without NC

Clinical characteristics of all patients are summarized in Table 1. Age, sex, body surface area, baseline heart disease, and type of LVAD were not significantly different between Group NC and Group non-NC. The proportion of patients with a history of CVA was higher in Group NC than in Group non-NC. Other factors of patients' previous medical histories, including atrial fibrillation, were not significantly different among the groups. There was no difference among the patients in simultaneous surgical procedures at the time of LVAD implantation such as patent foramen ovale closure, tricuspid reconstructions, or left atrial exclusion.

Table 2 summarizes pre-LVAD hemodynamic, laboratory, and echocardiographic parameters within 7 days before surgery. Hemodynamic variables did not differ significantly between Group NC and Group non-NC. Pre-operative serum sodium and albumin concentrations were lower in Group NC than in Group non-NC. The LV end-diastolic diameters and ejection fractions were not significantly different between the groups.

Table 3 summarizes post-LVAD warfarin and aspirin administration and laboratory examinations in all patients. The proportion of patients with warfarin or/and aspirin administration was not significantly different between the NC and non-NC groups. Post-operative hematocrit was lower, and again, serum sodium and albumin concentrations were lower in Group NC than in Group non-NC.

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Table 4 summarizes the comparison of post-LVAD infection between the groups. The infections analyzed were sepsis, LVAD-related infection, including driveline, pocket, and/or wound infection, and urinary tract, respiratory, or other infections, including gastrointestinal, and/or pressure ulcer infection. The frequency of LVAD-related infections alone was significantly higher in patients in Group NC than those in Group non-NC; however, the aggregate end point of all types of infection was significantly higher in patients in Group NC as well as in Group CVA than those in Group non-NC (Table 4).

Comparison of variables in patients with only CVA and those without any episodes of NC

After excluding patients with only TIAs, the comparison between patients with CVA and patients without any NC did not show any significant differences in clinical characteristics (Table 1), pre-LVAD hemodynamic data (Table 2), and post-operative warfarin and aspirin administration (Table 3). Pre-operative and post-operative sodium and albumin concentrations were lower in patients with CVA than in non-NC patients (Tables 2 and 3). The proportion of patients who developed infections was also higher in Group CVA than in Group non-NC (Table 4).

Multivariate analysis of factors associated with NC and CVA after LVAD surgery

As a result of this comparative analysis between Group NC and Group non-NC, history of CVA, pre-operative sodium and albumin, post-operative sodium, hematocrit, and albumin, and post-operative infection were selected for inclusion in a subsequent multivariate analysis.

Stepwise forward selection analysis revealed that history of CVA and post-operative infection were independently associated with the development of NCs after LVAD surgery (Table 5). A discriminant function test revealed that a discriminant score (Z), defined by using the following equation, yielded a discriminant probability of 76.6%:

$$\begin{aligned} \mathrm{Z}=14.065+[1.1\times(\text{history of CVA;1=yes, 0=no})] \\ -(0.034\times \mathrm{pre}-\mathit{operative\ sodium},\mathrm{mg/dl}) \\ -(0.59\times \mathrm{pre}-\mathit{operative\ albumin},\mathrm{mg/dl}) \\ -(0.036\times \mathrm{post}-\mathit{operative\ sodium},\mathrm{mg/dl}) \\ -(0.059\times \mathit{post}-\mathit{operative}\mathrm{Hct},\%) \\ -(0.43\times \mathrm{post}-\mathit{operative\ albumin},\mathrm{mg/dl}) \\ +[1.0\times(\mathrm{post}-\text{operative infection;1=yes, 0=no})] \end{aligned}$$

A result of Z > 0 indicates patients developing NC; Z < 0 indicates patients not developing NC after LVAD.

Multiple stepwise forward selection analysis for CVA development after excluding patients with only TIA revealed that pre-operative sodium, and post-operative sodium and albumin levels, and infection were discriminant factors for development of CVA. Among those variables, only post-operative infection was independently associated with CVA (Table 4).

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Discussion

In the present study, we have demonstrated that:

1. overall frequency of NC including TIA was 14.0% after LVAD placement and that the frequency of ischemic/hemorrhagic CVA was 11.4%;
2. the frequency of NC was not different between patients with HeartMate I vs HeartMate II devices;
3. history of CVA and post-operative infection were factors independently associated with development of NCs after LVAD placement;
4. the combination of prior CVA, pre-operative sodium and albumin, post-operative sodium, hematocrit and albumin, and post-operative infection could discriminate patients who develop NCs with a discriminant probability of 76.6%; and
5. an analysis done for CVA patients after excluding patients with only TIA yielded similar results.

NC is a devastating adverse event after LVAD placement.[4–9] The incidence of CVA after LVAD placement was reported to be 8% to 25%,[5,10,11] The Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure (REMATCH) trial showed that sepsis was the leading cause of death and CVA was the third leading cause of death (9.0%) after LVAD placement.[4] An analysis of the INTERMACS database, which includes pulsatile-flow and continuous-flow devices, also reported that NC was one of the leading causes of death.[13] NCs affect not only the device outcome, but also a patient's quality of life, even after transplantation.[4,5,8,9] Therefore, discrimination of patients who are at high risk for NCs is key to achieving an acceptable short-term and long-term outcome after LVAD placement. A reliable system to distinguish patients at high risk for NC would allow special attention to be given to these patients to prevent NCs and potentially even initiate preventive interventions to avoid the development of NCs.

It is noteworthy that post-operative infection was the single factor independently associated with both NC and CVA development. Association between infection and atherosclerotic coronary artery disease has been reported previously.[14,15] We speculate that infection causes changes in the microvascular structure, reactivity, and overall function as well as coagulation abnormalities that altogether result in a higher risk of NC development.[16,17] Nakajima et al[9] reported that longstanding HF with right heart dysfunction before LVAD placement and infection after LVAD placement was associated with CVA development after LVAD placement.

Patients with biventricular failure likely require a long duration of inotropic support before and after LVAD, which may lead to line infections and systemic infection. Owing to the retrospective nature of this study, we could not include right ventricular variables derived from pre-operative echocardiography, because not all patients with severe HF requiring LVAD surgery could provide good right ventricular images that permit a quantitative

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assessment. The relationship between pre-LVAD biventricular failure and post-LVAD complications requires additional investigation.

Furthermore, in the present study, hypoalbuminemia, hyponatremia, and post-LVAD anemia were also discriminant factors for NC development. Hypoalbuminemia has been often described in patients with severe HF and is associated with poor outcome.[18,19] Hyponatremia is also a common problem in patients with HF, indicates activation of the renin-angiotensin-aldosterone system, and also predicts poor prognosis.[20,21] In addition, anemia was also reported to be related to adverse outcomes in patients with LVAD support.[22]

Our findings indicate that malnutrition and inflammation, pre-LVAD and post-LVAD factors that are known to be associated with severity of HF, are also associated with the development of major complications after LVAD placement such as NC and infection. Thus, major complications after LVAD placement, such as NC and infection, may also have a cause-and-effect relationship with each other. Also, patients who were severely ill pre-operatively with deterioration of general condition would likely develop complications after LVAD implantation. Our observation may support the findings that the INTERMACS levels identified patients at risk for developing complications after mechanical circulatory support.[23,24] Of note, we evaluated a number of variables and showed that not a single comorbidity, but the combination of variables, could predict NC development. Further investigation is required to investigate the mechanism underlying these interactions.

In the present study, the anti-coagulation status reflected by INR, as well as history of atrial fibrillation, were not significantly different among patients with NC or CVA and those without NC. We did not perform an analysis by dividing patients with ischemic events and hemorrhagic events due to the small number of events in the sub-groups. Also, several patients developed multiple NCs, with both ischemic and hemorrhagic events, with varying degrees of anti-coagulation. In fact, some of those patients developed subsequent events within 24 to 48 hours after the first event regardless of the intense or less intense anti-coagulation condition. We speculate that a patient who is prone to develop an ischemic NC is also prone to develop a hemorrhagic NC, and vice versa, although the anti-coagulation state remains within a therapeutic range. We will further review the anti-coagulation status of patients with NC, focusing on serial changes of INR levels before the events. In addition, more detailed observations, such as pre-operative transesophageal echocardiograms and post-operative evaluation for device-related thrombus formation by the use of speed ramp studies, would be helpful for further prospective analysis.

Previous studies reported that the event rate of NC was considerably reduced in continuous-flow devices compared with pulsatile-flow devices.[5,13] In the present study, the overall frequency of developing NC was not significantly different between patients supported with HeartMate I vs II devices. Because the observation period of HeartMate II patients was significantly longer than that in HeartMate I patients ($p = 0.0057$) in the present study and because most events occurred in the early post-operative period in both devices (Figure 2), we could not simply compare the event rate/patient per year in both devices by the patient's

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cohort. Further investigation would be required to investigate actual events rate associated with the different devices in a different study design.

In conclusion, we demonstrated that previous CVA, persistent malnutrition, persistent inflammation, severity of HF, and post-LVAD infections are key factors associated with NC as well as CVA development after LVAD implantation. Our study did not reveal differences in frequency of NC development between devices in different generation. These findings provide helpful guidance for risk stratification and clinical management strategies of patients with advanced HF receiving LVAD support.

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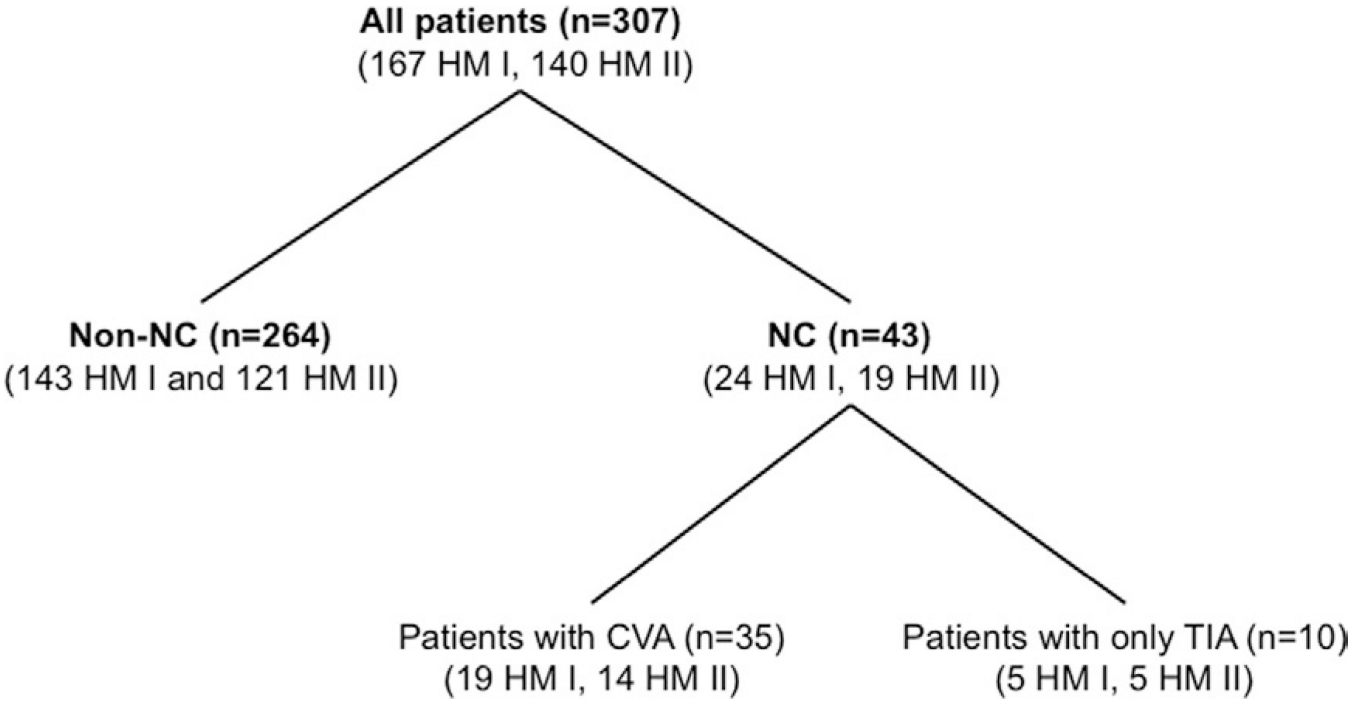

Figure 1.

Patients who underwent placement of a HeartMate I (HM I) or HeartMate II (HM II) device were divided into 2 groups: those with any neurologic complication (NC), including transient ischemic attack (TIA; Group NC), and those who did not develop NC after the surgery (Group non-NC). After excluding patients with only TIA episodes, patients with ischemic or hemorrhagic cerebrovascular accident (CVA) were classified as Group CVA. The analysis was performed between Group NC and Group non-NC, and between Group CVA between Group non-NC.

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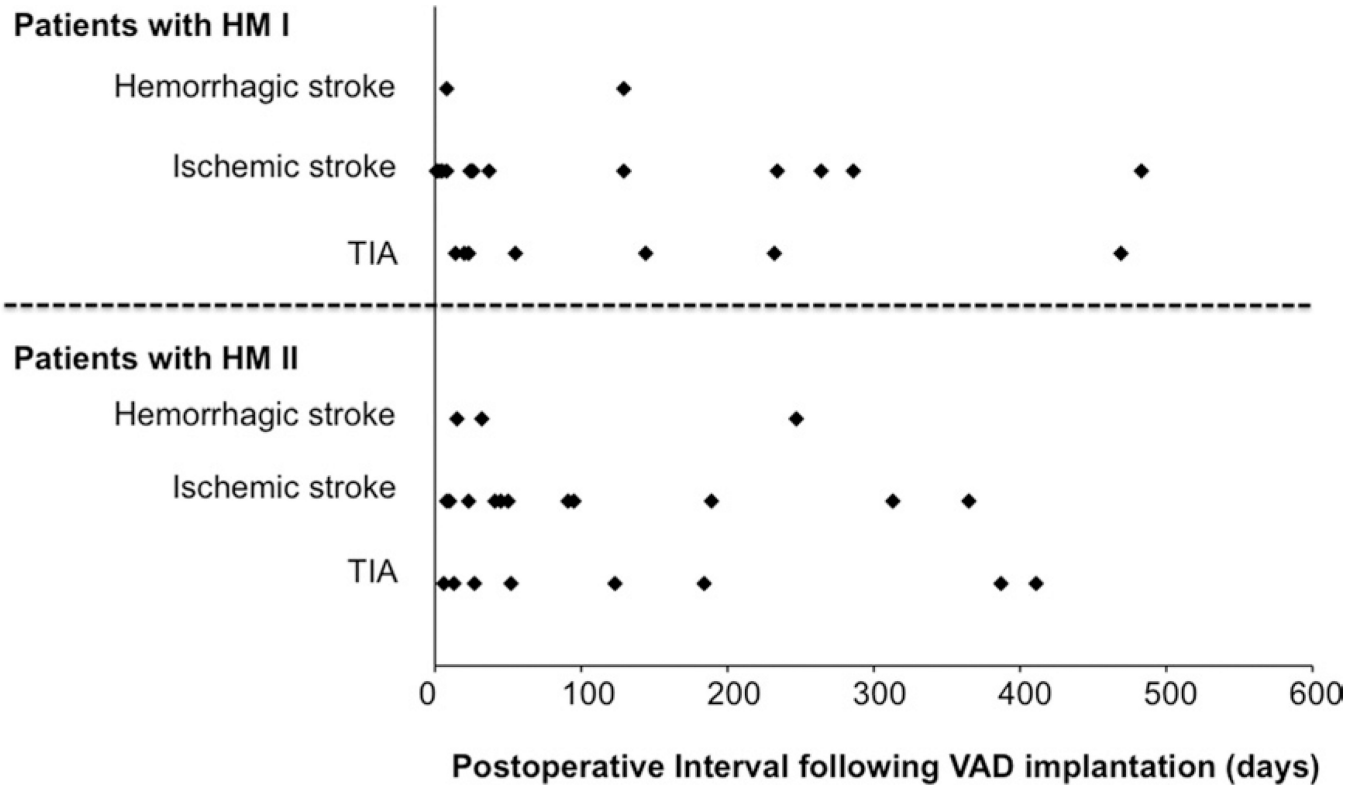

Figure 2.

Complications during the post-operative observation period after placement of a HeartMate I (HM I) or HeartMate II (HM II) ventricular assist device (VAD). The study cohort sustained 51 events. TIA, transient ischemic attack.

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Table 1

Clinical Characteristics

Variable[a]	Group non-NC (*n* = 264)	Group NC (*n* = 43)	*p*-value (Non-NC vs NC)	Group CVA (*n* = 35)	*p*-value (Non-NC vs CVA)
Age, years	53.6 ± 12.6	54.4 ± 13.1	0.701	54.1 ± 15.6	0.830
Male sex	216 (79.1)	33 (76.7)	0.126	29 (82.9)	0.266
Body surface area, m^2	1.96 ± 0.24	1.91 ± 0.21	0.578	1.93 ± 0.22	0.484
Medical history					
Stroke	41 (15.5)	12 (27.9)	0.046	10 (28.6)	0.054
Diabetes mellitus	77 (29.1)	12 (27.9)	0.866	10 (28.6)	0.941
Hypertension	120 (47.0)	18 (40.9)	0.660	18 (51.4)	0.505
Hyperlipidemia	84 (31.8)	13 (30.2)	0.836	13 (37.4)	0.527
PVD	29 (11.0)	8 (18.6)	0.225	7 (20.0)	0.124
Renal failure	76 (28.8)	11(25.0)	0.665	9 (25.7)	0.704
Atrial fibrillation	134 (50.8)	25 (58.1)	0.369	23 (62.8)	0.096
Etiology of heart disease					
Ischemic	207(78.8)	28 (65.1)	0.056	25 (71.4)	0.352
Non-ischemic	57(21.2)	15 (34.9)	0.056	10 (28.6)	0.352
Type of LVAD					
HeartMate I	143 (54.2)	24 (55.8)	0.804	19 (54.3)	0.989
HeartMate II	121 (55.8)	19 (44.2)	0.804	16 (45.7)	0.989

CVA, cerebrovascular accident; LVAD, left ventricular assist device; NC, neurologic complication; PVD, peripheral vascular disease.

[a]Continuous data are presented as mean ± standard deviation; categoric data as number (%).

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Table 2

Results of Pre-operative Hemodynamic and Laboratory Examinations

Variable[a]	Group non-NC (*n* = 264)	Group NC (*n* = 43)	*p*-value (Non-NC vs NC)	Group CVA (*n* = 35)	*p*-value (Non-NC vs CVA)
Hemodynamic variables					
Cardiac index, liters/min/m^2	1.8 ± 0.4	1.7 ± 0.3	0.118	1.7 ± 0.5	0.179
PAWP, mm Hg	28.4 ± 8.1	2.3 ± 8.9	0.268	28.8 ± 10.0	0.790
Mean pressure, mm Hg					
Pulmonary artery	36.2 ± 9.4	38.5 ± 9.7	0.140	37.2 ± 12.0	0.568
Right atrial	12.9 ± 7.9	13.2 ± 7.8	0.817	12.6 ± 8.0	0.833
Atrial	79.1 ± 12.8	76.3 ± 9.6	0.171	77.1 ± 10.0	0.375
Vascular resistance, WU					
Peripheral	3.8 ± 2.2	3.9 ± 2.4	0.785	3.7 ± 2.5	0.804
Systemic	23.1 ± 6.3	23.8 ± 9.2	0.530	23.8 ± 7.9	0.550
Laboratory examinations					
White cell count, ×10^3/μl	8.2 ± 2.3	9.0 ± 3.9	0.060	9.0 ± 3.8	0.078
Lymphocytes, %	11.4 ± 5.2	10.9 ± 3.7	0.545	10.3 ± 4.6	0.234
Hematocrit, %	33.2 ± 5.9	32.4 ± 6.2	0.304	32.1 ± 6.3	0.414
Platelets, ×10^3/μl	191 ± 86	190 ± 80	0.898	189 ± 85	0.876
Bilirubin, mg/dl					
Total	1.7 ± 1.3	1.8 ± 1.5	0.678	1.6 ± 1.6	0.375
Direct	0.6 ± 0.5	0.7 ± 0.7	0.254	0.7 ± 0.9	0.322
Sodium, mEq/L	132.1 ± 8.1	129.0 ± 7.0	0.018	129.1 ± 7.1	0.038
Potassium, mEq/L	4.3 ± 0.5	4.4 ± 0.5	0.225	4.4 ± 0.4	0.257
Blood urea nitrogen, mg/dl	37 ± 18	35 ± 19	0.460	34 ± 18	0.442
Creatinine, mg/dl	1.6 ± 0.4	1.5 ± 0.9	0.224	1.5 ± 0.7	0.212
Albumin, mg/dl	3.7 ± 0.6	3.5 ± 0.7	0.049	3.5 ± 0.7	0.030
ALT, IU/liter	99 ± 100	88 ± 96	0.509	91 ± 91	0.661
AST, IU/liter	72 ± 86	55 ± 77	0.231	60 ± 77	0.428
BNP, pg/ml	1835 ± 1117	2101 ± 1046	0.145	1921 ± 946	0.663
International normalized ratio	1.4 ± 0.5	1.3 ± 0.4	0.213	1.3 ± 0.3	0.249
Echocardiographic parameters					

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Variable[a]	Group non-NC (*n* = 264)	Group NC (*n* = 43)	*p*-value (Non-NC vs NC)	Group CVA (*n* = 35)	*p*-value (Non-NC vs CVA)
LVEDD, mm	69.5 ± 12.1	71.9 ± 12.8	0.240	70.7 ± 12.5	0.588
LVEF, %	18.4 ± 10.0	20.0 ± 12.4	0.353	19.1 ± 10.8	0.713

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; CVA, cerebrovascular accident; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NC, neurologic complication; PAWP, pulmonary arterial wedge pressure.

[a]Data are presented as mean ± standard deviation.

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Table 3

of Post-operative Medication and Laboratory Examinations in All Patients

Variable[a]	Group non-NC (*n* = 264)	Group NC (*n* = 43)	*p*-value (Non-NC vs NC)	Group CVA (*n* = 35)	*p*-value (Non-NC vs CVA)
Medication					
Warfarin	195 (73.8)	36 (83.7)	0.165	29 (82.9)	0.249
Aspirin	238 (90.1)	38 (88.4)	0.828	32 (91.4)	0.721
Laboratory examinations					
White cell count, $\times 10^3/\mu L$	7.9 ± 2.3	8.5 ± 3.4	0.142	8.2 ± 3.5	0.499
Lymphocytes, %	13.0 ± 6.2	12.1 ± 4.9	0.365	12.3 ± 4.6	0.520
Hematocrit, %	37.8 ± 6.1	34.9 ± 5.1	0.003	34.7 ± 6.3	0.005
Platelets, $\times 10^3/\mu l$	189 ± 90	201 ± 82	0.402	199 ± 85	0.54
Bilirubin, mg/dl					
Total	1.6 ± 2.9	1.9 ± 3.1	0.534	1.7 ± 2.6	0.846
Direct	0.8 ± 2.2	1.0 ± 1.8	0.572	0.8 ± 0.9	0.937
Sodium, mEq/L	134.4 ± 6.4	131.6 ± 7.7	0.010	131.9 ± 7.1	0.033
Potassium, mEq/L	4.3 ± 0.6	4.4 ± 0.4	0.292	4.3 ± 0.4	0.848
Blood urea nitrogen, mg/dl	33 ± 14	32 ± 18	0.866	33 ± 17	0.755
Creatinine, mg/dl	1.5 ± 0.6	1.5 ± 0.7	0.623	1.4 ± 0.7	0.717
Albumin, mg/dl	3.9 ± 0.5	3.7 ± 0.5	0.016	3.7 ± 0.7	0.036
ALT, IU/liter	67 ± 99	66 ± 38	0.921	61 ± 51	0.716
AST, IU/liter	79 ± 86	58 ± 80	0.140	60 ± 77	0.222
BNP, pg/ml	802 ± 894	673 ± 685	0.571	712 ± 746	0.663
International normalized ratio	1.5 ± 0.9	1.6 ± 0.7	0.532	1.5 ± 0.3	0.845

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; CVA, cerebrovascular accident; NC, neurologic complication.

[a]Categoric data are presented as number (%), and continuous data as mean ± standard deviation.

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Table 4

Post-operative Infection Data in All Patients

Infection type[a]	Group non-NC (*n* = 264)	Group NC (*n* = 43)	*p*-value (non-NC vs NC)	Group CVA (*n* = 35)	*p*-value (non-NC vs CVA)
All forms	51 (19.3)	17 (39.5)	0.003	13 (37.1)	0.016
Sepsis	41 (15.1)	9 (20.9)	0.377	7 (20.0)	0.498
LVAD related[b]	30 (11.4)	10 (23.3)	0.031	7 (20.0)	0.145
Urinary tract	45 (17.0)	11 (25.6)	0.179	9 (25.7)	0.082
Respiratory	30 (11.4)	6 (14.0)	0.624	5 (14.2)	0.613
Others[c]	14 (5.3)	4 (9.3)	0.874	2 (5.7)	0.577

CVA, cerebrovascular accident; NC, neurologic complications.

[a]Data are presented as number (%).

[b]Left ventricular assist device-related infection of the driveline, pocket, or/and wound infections.

[c]Includes gastrointestinal, genital, otorhinolaryngologic and/or pressure ulcer infections.

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Table 5

Stepwise Forward Selection Analysis of Factors Associated With Neurologic Complication and Cerebrovascular Accident After Left Ventricular Assist Device Placement

Factors	OR (95% CI)	*p*-value
Associated with overall NC development		
History of CVA	2.37 (1.24–5.29)	0.011
Pre-operative factor		
Sodium	0.93 (0.90–1.12)	0.208
Albumin	0.51 (0.21–1.37)	0.079
Post-operative factor		
Hematocrit	0.96 (0.71–1.22)	0.184
Sodium	0.84 (0.68–1.21)	0.075
Albumin	0.71 (0.46–2.42)	0.143
Infection	2.99 (1.16–10.49)	0.011
Associated with CVA development		
Pre-operative factor		
Sodium	0.95 (0.92–1.01)	0.057
Post-operative factor		
Sodium	0.92 (0.90–1.02)	0.060
Albumin	0.43 (0.23–0.98)	0.050
Infection	4.24 (1.69–14.58)	0.0005

CI, confidence interval; CVA, cerebrovascular accident; NC, neurologic complication; OR, odds ratio.