Asymmetric Pattern of Cerebrovascular Lesions in Patients After Left Ventricular Assist Device Implantation

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Background and Purpose—Stroke is a major adverse event after left ventricular assist device (LVAD) surgery. The purpose of this study was to describe differences in hemispheric distribution of stroke in LVAD patients.

Methods—We reviewed 317 consecutive patients who underwent LVAD surgery between November 2000 and July 2011. Stroke during LVAD support was analyzed.

Results—In total, 46 strokes occurred at 76.0±96.8 days postoperatively. Among the 46 strokes, 27 events (58.7%) occurred in right hemisphere, 13 events (28.2%) in the left hemisphere, 3 events (8.7%) occurred bilaterally, and 2 events (4.3%) were vertebrobasilar lesions. The right hemispheric stroke was significantly more common in patients with postoperative infection compared with left hemispheric events.

Conclusions—Stroke after LVAD implantation has a right hemispheric predominance. This finding suggests LVAD-related thrombus in the setting of infection and/or the anatomic configuration of LVAD outflow cannula-ascending aorta anastomosis to be highly associated with stroke after LVAD surgery. (Stroke. 2012;43:872-874.)

Key Words: acute stroke ■ cardiac surgery ■ infectious disease

Cardiac transplantation provides considerable survival benefits for patients with end-stage heart failure; however, its use is severely limited because of donor shortage. A growing number of heart transplant candidates require long-term support with left ventricular assist devices (LVAD) while they await cardiac transplantation. LVAD therapy has evolved into a standard therapy for patients with advanced heart failure, not only as a bridge to cardiac transplantation but also as a destination therapy. Long-term LVAD support, however, can result in serious complications, such as stroke, bleeding, and infections. The incidence of stroke after LVAD placement is reported to be 8% to 25%. Cerebral embolic events after cardiac surgery are frequently distributed more often in the right cerebral hemisphere. Kim et al reported recently that right hemispheric infarcts are associated with cardiogenic embolism, whereas left hemispheric infarcts are more associated with aortic embolism. In the present study, we investigated the distribution of stroke in patients undergoing LVAD implantation and whether clinical characteristics differed in LVAD patients experiencing right versus left hemispheric stroke.

Methods
The present study was approved by the institutional review board of Columbia University Medical Center. We retrospectively reviewed 317 consecutive patients who underwent LVAD placement at Columbia University Medical Center between November 2000 and July 2011. Diagnosis of stroke was made based on the Interagency Registry for Mechanically Assisted Circulatory Support definition of ischemic or hemorrhagic intracranial stroke. According to the clinical and brain computer tomography findings, lesions of stroke were classified into right, left, bilateral hemispheric, or vertebrobasilar lesions. Patients with transient ischemic attack were excluded from the analysis. Anticoagulation protocol included heparin, warfarin, and antiplatelet agents, such as aspirin and/or dipyridamole, except for those patients with contraindication to the medication or/and active bleeding.

Clinical characteristics, postoperative infection frequency, and anticoagulant status associated with right and left hemispheric stroke were compared. We excluded bilateral and vertebrobasilar stroke from the comparison analysis. Postoperative information was collected within 10 days of the event. A postoperative infection was defined as symptoms of infection with concomitant positive microbiological cultures. The diagnosis of sepsis and LVAD-related infection was made when the patient showed ≥2 positive cultures to avoid the possibility of contamination of the culture site. LVAD-related infection was defined as drive line, LVAD pocket, and/or wound and device infection. Urinary tract infection was defined as a single positive urine culture with >10^5 colonies per milliliter with clinical signs of urinary tract infection, such as dysuria and/or pyuria. Data were presented as mean±SD. Data were compared between groups using the Student unpaired t test or χ² test. All of the statistical analyses were performed using JMP 7.0 software (SAS Institute).
Results

A total of 46 strokes occurred in 41 patients (12.9%; 24 events per 100 patients per year) after LVAD surgery during an observation period of 254±324 days (Figure). There were 38 ischemic and 8 hemorrhagic strokes. Among those, 27 events (58.7%) occurred in the right hemisphere, 13 events (28.2%) occurred in the left hemisphere, 3 events (6.5%) occurred bilaterally, and 2 events (4.3%) were in vertebrobasilar lesions.

Age, sex, and body surface area were not significantly different between patients developing right and left hemispheric stroke. Type of LVAD (continuous flow device or pulsatile flow device) was not significantly different between patients with right and left hemispheric events. Mean duration from LVAD surgery to stroke was 90.8±111.0 days in the right hemispheric event and 42.7±69.9 days in the left hemispheric event, which was not statistically different.

Arteriosclerotic risk factors, such as hypertension, diabetes mellitus, previous history of stroke, and ischemic heart disease, as baseline heart disease for LVAD requirement tended to associated less often with right hemispheric stroke than with left hemispheric stroke (25.9% versus 30.8%, 29.6% versus 46.2%, 14.8% versus 30.8%, and 40.7% versus 61.5%, respectively), whereas pre-LVAD atrial fibrillation was more often associated with right hemispheric stroke (48.2% versus 23.1%); however, these findings were not statistically significant. Neither anticoagulant medication of warfarin and/or aspirin administration nor international normalized ratio within 10 days before the stroke was significantly different between the groups. Infection frequency (sepsis and LVAD-related infection) preceding the events was significantly higher with right hemispheric stroke than with left hemispheric stroke (Table). The analysis for ischemic stroke alone revealed that, among a total number of 35 ischemic events, 24 events (61.5%) occurred in the right hemisphere and 11 events (28.2%) were in the left hemisphere (28.2%). Infection was also more frequently seen in right hemispheric stroke compared with left hemispheric stroke (59.3% versus 23.1%; P=0.028).

Discussion

In the present retrospective study, we have demonstrated that stroke after LVAD implantation has a right hemispheric predominance and right hemispheric stroke after LVAD implantation was more often associated with infection compared with left hemispheric stroke. The incidence of stroke after LVAD placement was reported previously to be 8.0% to 25.0%.2-4 The overall incidence of stroke in our cohort was 12.9%.

Regarding the hemispheric distribution of stroke, the results of our observation are consistent with previous reports describing the mechanism of right-hemispheric dominance of cardiogenic embolisms after cardiac surgery.5-8 Considering any thrombus inside the LVAD pump as a part of cardiac embolic material in addition to actual intracardiac thrombi, right-to-left propensity of stroke after LVAD can be easily explained by anatomic alignment of the arteries arising from aortic arch. Moreover, surgical manipulation of LVAD outflow cannula-to-ascending aorta anastomosis may also direct embolic material toward the brachiocephalic trunk. It is noteworthy that postoperative infection was highly associated with right compared with left hemispheric stroke. We reported recently that patients with postoperative infection are

### Table. Post-LVAD Infection Associated With Right and Left Hemispheric Stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>Right Hemisphere (n=27)</th>
<th>Left Hemisphere (n=13)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any forms of infection, no. of patients (%)</td>
<td>16 (59.3)</td>
<td>3 (23.1)</td>
<td>0.028</td>
</tr>
<tr>
<td>Sepsis, no. of patients (%)</td>
<td>13 (48.2)</td>
<td>2 (15.4)</td>
<td>0.037</td>
</tr>
<tr>
<td>LVAD-related, no. of patients (%)</td>
<td>5 (18.5)</td>
<td>0 (0.0)</td>
<td>0.039</td>
</tr>
<tr>
<td>Urinary tract, no. of patients (%)</td>
<td>12 (44.4)</td>
<td>3 (23.1)</td>
<td>0.182</td>
</tr>
<tr>
<td>Respiratory, no. of patients (%)</td>
<td>5 (11.4)</td>
<td>1 (7.7)</td>
<td>0.345</td>
</tr>
</tbody>
</table>

LVAD indicates left ventricular assist device.
more prone to develop stroke than those without infection after LVAD implantation. Infection precipitates coagulation abnormalities that may lead to a high frequency of LVAD-related thrombus formation resulting in right hemispheric stroke.

Limitation of this study is that it is a single-center, retrospective analysis in a small cohort of patients. The present study included both ischemic and hemorrhagic stroke because of the small number of total events. However, we assume that a certain amount of hemorrhagic strokes in LVAD patients may occur as a result of asymptomatic microemboli, and the underlying mechanism of hemorrhagic and ischemic stroke could not be separated.

The asymmetry of stroke distribution in LVAD patients may have important implications for understanding the mechanism of this devastating adverse event after LVAD placement. Further study would be needed to explore the potential mechanisms behind right-left asymmetry of cerebrovascular accident after LVAD, which may lead to a preventive strategy.

Disclosures
Y.N. is a consultant for Thoratec and Terumo Heart. U.J. is a consultant for Thoratec and Jarvic Heart.

References
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