The role of cerebral hyperperfusion in postoperative neurologic dysfunction after left ventricular assist device implantation for end-stage heart failure

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Objective: Cerebral hyperperfusion is a life-threatening syndrome that can occur in patients with chronically hypoperfused cerebral vasculature whose normal cerebral circulation was re-established after carotid endarterectomy or angioplasty. We sought to determine whether the abrupt restoration of perfusion to the brain after left ventricular assist device (LVAD) implantation produced similar syndromes.

Methods: We studied the role of increased systemic flow after LVAD implantation on neurologic dysfunction in 69 consecutive HeartMate XVE LVAD (Thoratec, Pleasanton, Calif) recipients from October 2001 through June 2006. Neurologic dysfunction was defined as postoperative permanent or transient central change in neurologic status, including confusion, focal neurologic deficits, visual changes, seizures, or coma for more than 24 hours within 30 days after LVAD implantation.

Results: We found that 19 (27.5%) patients had neurologic dysfunction, including encephalopathy (n = 11), coma (n = 3), and other complications (n = 5). The multivariate analysis showed that an increase in cardiac index from the preoperative baseline value (relative risk, 1.33 per 25% cardiac index increase; $P = .01$) and a previous coronary bypass operation (relative risk, 4.53; $P = .02$) were the only independent predictors of neurologic dysfunction. Reduction of left ventricular assist device flow in 16 of the 19 symptomatic patients led to improvement of symptoms in 14 (87%) patients.

Conclusions: Our findings showed that normal flow might overwhelm cerebral autoregulation in patients with severe heart failure, suggesting that cerebral hyperperfusion is possible in recipients of mechanical circulatory support with neurologic dysfunction.

Left ventricular assist devices (LVADs) have been successfully used in patients with end-stage heart failure, either as a bridge to transplantation or as an alternative to transplantation or destination therapy. Although LVAD implantation has become an accepted therapy for patients with advanced heart failure, the morbidities associated with use of the device have been an ongoing concern. In particular, postoperative neurologic complications are relatively common, and sometimes they can lead to devastating complications that preclude a transplantation and result in very poor quality of life.

According to the 2005 Report of the Mechanical Circulatory Support Device Database, serious neurologic complications have been reported in 14% of 655 recipients with various types of mechanical circulatory support pumps implanted at 60 international centers.[1] In LVAD recipients the reported incidence of postoperative neurologic complications varies by center and pump type, as described in detail by Pae and colleagues.[2] In the largest published single-center studies, the stroke incidence ranges from 3% in 226 HeartMate XVE LVAD (Thoratec, Pleasanton, Calif) recipients[3] and 17% in 288 Novacor LVAD (WorldHeart, Oakland, Calif) recipients[4] to as high as 57% in 23 recipients of the totally implantable LionHeart LVAD (Arrow International, Inc, Reading, Pa).[2]

Most postoperative neurologic complications, including the most serious events, such as strokes, occur within the first few days or weeks after LVAD implantation.[1-4] Hence the incidence of perioperative neurologic complications after LVAD surgery exceeds by several times the relatively small 1.9% incidence noted after other cardiac operations,[5] suggesting an association between the development of neurologic complications and either the device itself or the operation needed to implant it. The exact mechanism by which LVAD implantation contributes to the development of symptoms is not completely understood. Most of the literature assumes that clinically significant neurologic events result either from device-related thromboembolism,[6]

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Abbreviations and Acronyms

CI = cardiac index
CT = computed tomographic
IABP = intra-aortic balloon pump
LVAD = left ventricular assist device
ND = neurologic dysfunction
PRES = posterior reversible encephalopathy syndrome
RR = relative risk

operation-related air embolism,[7] or hemorrhage.[8] Autopsies of patients with fatal neurologic complications, however, did not always reveal evidence of cerebral embolism.[6,7]

In this retrospective review we investigated whether an abrupt increase in systemic blood flow could contribute to LVAD-related neurologic dysfunction (ND) in patients with end-stage heart failure. We hypothesized that restoration of normal cardiac output in this patient group might result in cerebral dysfunction, which is similar to the cerebral hyperperfusion syndrome observed in some patients after carotid artery endarterectomy or angioplasty.[9] This syndrome is believed to result from the inability of chronically hypoperfused cerebral arterioles to accommodate rapidly increasing perfusion pressures.

MATERIALS AND METHODS

Patients

From October 30, 2001, through June 13, 2006, a total of 69 patients underwent HeartMate XVE LVAD implantation at the University of Minnesota Medical Center. We excluded from our analysis recipients of other types of HeartMate LVADs, Novacor LVADs, and axial flow devices, as well as those who required biventricular temporary support before device implantation. The institutional board review approved the study, and all patients provided informed consent to use their clinical data for this study.

Study Design

Because of the possibility of delayed impairment of cerebral autoregulation up to 28 days after increase of cerebral flow reported after carotid endarterectomy,[10] in this study we investigated the relationship between systemic blood flow and ND within the first month after LVAD implantation.

Preoperative clinical data. The following clinical data were available on the day of the operation: patient characteristics and body surface area; cause of heart failure; history of cardiovascular events (including cardiac arrest, myocardial infarction, previous sternotomies, and coronary artery bypass surgery); history of other comorbidities (including stroke, diabetes, or renal dysfunction); laboratory data; left ventricular ejection fraction; and details on medical or device therapy for heart failure (including the use of intravenous inotropes, mechanical circulatory support with an intra-aortic counterpulsation balloon pump [IABP] and mechanical ventilation).

Neurologic dysfunction. We defined perioperative neurologic dysfunction (ND) as a change in neurologic status, including confusion, focal neurologic deficits, visual changes, seizures, or coma, for more than 24 hours within 30 days after LVAD implantation, which is consistent with previously described criteria of cerebral hyperperfusion syndrome.[9]

Hemodynamic changes. Preoperative cardiac output was measured on the day of hospital admission and on the day of LVAD surgery with the use of a Swan–Ganz catheter and was calculated from the Fick equation. After LVAD surgery, the Swan–Ganz catheter was removed. Cardiac output was recorded from the flow displayed on the device monitor at the time of the neurologic event, on the third postoperative day, and on postoperative day 30 or day of hospital discharge, whichever came first. The cardiac index after LVAD implantation was calculated by dividing the device-recorded flow (liters per minute) by the patient's body surface area.

LVAD Surgery

All recipients of LVAD as a bridge to transplantation underwent a complete workup to assess their transplantation candidacy, including carotid and lower-extremity arterial Doppler studies, pulmonary function tests, colonoscopy, a neuropsychiatric evaluation, and an evaluation by a social worker. Patients whose LVADs were intended as destination therapy underwent the same workup. History of stroke or neurologic injury was not a contraindication to LVAD implantation as long as the patient had recovered sufficiently from the neurologic injury, the underlying cause had been corrected, and the risks for stroke recurrence were low. All studied patients had carotid Doppler ultrasonographic analysis performed before LVAD insertion or, in case of emergency implantation, after LVAD insertion to minimize significant intracranial or extracranial cerebral disease. Also, head computed tomographic (CT) analysis was performed in 4 patients who had previous strokes.

LVAD implantation was performed after achievement of general anesthesia, with continuous hemodynamic monitoring. Either preperitoneal or intraperitoneal LVAD implantation was performed through a medial sternotomy. Cardiopulmonary bypass was instituted after full heparinization by means of aortic and right atrial cannulation. Only mild hypothermia was used during the operation (>32°C). The LVAD inflow cannula was secured to the left ventricular apex, and the outflow graft was anastomosed to the ascending aorta. The driveline of the LVAD was usually tunneled out through a right upper quadrant incision. Intraoperative transesophageal echocardiographic analysis was used to confirm the evacuation of air from the cardiac chambers. The operative field was flooded by carbon dioxide to reduce the collection of air inside the heart. Standard maneuvers to evacuate air included filling the heart with blood and ventilating the lungs, along with hand pumping of the LVAD. As the patient was weaned off cardiopulmonary bypass, the LVAD pump was activated with the patient in a steep Trendelenburg position to reduce the risk of cranial air embolism. Once the patient was hemodynamically stable with adequate LVAD flow, protamine was used for reversal of heparin. Appropriate inotropes and vasopressors were administered, as necessary, to maintain hemodynamic stability and to optimize right ventricular function. Postoperatively, the only routine antithrombotic therapy was aspirin (325 mg/d). Warfarin was used only if there were indications for its use, such as pre-existing atrial fibrillation or the presence of a mitral mechanical valve prosthesis.

Statistical Analysis

Preoperative clinical data and hemodynamic changes before and after LVAD implantation were associated with the end point by using univariate analysis to identify risk factors associated with perioperative ND in LVAD recipients. In patients with ND, we compared the hemodynamic measurements at the time of the neurologic event with those of patients who did not have ND by postoperative day 30 or the day of hospital discharge, whichever came first. All continuous variables were treated as such, with the exception of recipient age and body surface area, which were stratified by their means. The risk factors found to be significant by means of univariate analysis at a P value of less than .10 were then entered into the logistic regression model at a P value of less than .05.[10] The figure showing a relationship between the increase in cardiac index (CI) and the predicted probability of postoperative ND was derived from the logistic regression model. The goodness of fit of this model was measured with the Hosmer–Lemeshow statistic.[11] Differences between groups were examined by using χ^2 or Student's t tests. Values are reported as means ± the standard deviation.