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Guest Editorial

Neurological Dysfunction Associated With Mechanical Circulatory Support: Complications That Still Need Attention

> . . . fewer than half of the patients in the LVAD group had a neurological event . . .
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> Lazar et al., *Circulation* 2004;109:2423–7(1)

While infection and bleeding are clearly the most prevalent complications in mechanical circulatory support, neurological complications can perhaps be the most devastating. These complications are a leading cause of morbidity, mortality, increased hospital stay, and cost. These complications impact not only the patient, but also the entire health-care delivery team, and the patient's friends and family.

While a certain baseline level of neurological complications including cerebrovascular accidents (CVAs), transient ischemic attacks (TIAs), or other neurologic deficits can be reasonably expected in the extremely moribund patient population receiving mechanical circulatory support, it is still unclear what this baseline level should be. Perhaps the most valuable insight in this area came from the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study, which through randomization of the control group to optimal medical management delineated the impact of mechanical circulatory support on neurological events as highlighted in Table 1.

Mechanical circulatory support is clearly a risk factor for potential neurological complications. Potential mechanisms include intra-operative low systemic flow, dislodgement of a ventricular thrombus, inadequate ventricular assist device (VAD) deairing, device-related thrombus formation, inadequate anticoagulation/antiplatelet therapy, chronic low blood flow, mismatching of effective stroke volume to the volume of the ventricle, exacerbation of preexisting anticoagulation disorders, and others. However, a major part of the problem in addressing neurological complications with mechanical circulatory support is the lack of comprehensive data sets regarding neurological dysfunction in mechanical circulatory support recipients.

CONTEMPORARY COMPLICATION RATES

Differing definitions and level of reporting of neurological complications can make comparisons quite difficult. Hopefully, researchers and clinicians can more widely embrace the use of common definitions and level of reporting, during future clinical trials and in reporting research results in the literature. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) adverse event definitions are certainly a major step in this direction, and all those in this field should be encouraged to utilize these common well-thought-out definitions.

Data from the large registries of mechanical circulatory support patients do provide some insight into contemporary neurological complication rates (Table 2). The Mechanical Circulatory Support Device (MCSD) Database of the International

TABLE 1. *Neurological event rates in the REMATCH study (1)*

Neurological events*	LVAD group ($n = 68$)	Medical therapy group ($n = 61$)
Number of events	42	4
Number of patients with events	30	4
Percent of all patients with events	44%	7%
Number of stroke events	12	2
Number of patients with stroke events	11	2
Percent of all patients with stroke events	16%	3%

* Stroke, transient ischemic attack, toxic-metabolic, other.

TABLE 2. *Neurological event rates from the MCSD database and INTERMACS (2,3)*

Neurological dysfunction*	MCSD database ($n = 413$)	Intermacs ($n = 348$)
Number of events	—	79
Number of patients with events	58	58
Percent of all patients with events	14%	17%

* Stroke, transient ischemic attack.

Society for Heart and Lung Transplantation covering 413 patients implanted between 2002 and 2004 reported neurological dysfunction in 14% of all patients (2). The most recent report from INTERMACS covering 348 patients implanted between 2006 and 2007 reported neurological dysfunction events in 17% of all patients (3). Unfortunately, more detailed analysis of these databases in terms of event severity and outcomes have yet to be reported.

While the majority of the data in the large data registries are from pulsatile devices, recent reports with continuous flow (e.g., nonpulsatile) devices suggest similar neurological complication rates. The largest detailed report in this area is for the HeartMate II device (Thoratec, Pleasanton, CA, USA) (4). This observational study in 133 patients between 2005 and 2006 reported 8 patients with ischemic strokes (6%), 3 patients with hemorrhagic strokes (2%), 5 patients with TIAs (4%), and 8 patients with other neurologic events (6%). Of particular note, over half of the ischemic strokes in this group occurred during the first 2 days.

Data are also now emerging for several of the centrifugal-based nonpulsatile devices, which are now entering clinical evaluation, which also suggest a similar level of neurological complications (Table 3). For example, the VentrAssist (Ventracor, Chatswood, Australia) results from the US bridge to transplant feasibility study of 28 patients reported 18% of all patients experienced neurological dysfunction (5). Additionally, data from the first 23 implants of the HeartWare device (HeartWare, Sydney, Australia) followed out to 180 days (6) reported 13% of all patients experiencing neurological dysfunction.

While the available data help to provide a top-level overview of the issue of neurological complications in mechanical circulatory support, there is certainly a lack of detailed research literature on the topic. Lazar et al. provided a detailed review of the REMATCH results in terms of neurological complications (1). Furthermore, Tsukui et al. provided a single center retrospective review of the experience at the University of Pittsburgh Medical Center (7), Pae et al. provided details on the LionHeart experience (8), and Thomas et al. provided a device-specific experience (Novacor; WorldHeart, Ottawa, Canada) at a single center (9). These reports and others provide some important insight into issues surrounding neurological complications during mechanical circulatory support; however, further research efforts are clearly needed to address this devastating complication.

ADDRESSING NEUROLOGICAL COMPLICATIONS

A key focus must be on tailoring specific anticoagulation/antiplatelet therapy to individual patients. This can be accomplished through extensive preoperative screening for coagulation disorders (heparin-induced thrombocytopenia, lupus anticoagulant, etc.) and tailoring specific regimens based on these conditions (7). Monitoring of coagulation status using thromboelastography can also be an important tool for tailoring antiplatelet therapy on an ongoing basis.

Infection is also clearly implicated as a risk factor for neurological events (10), and abnormal white blood cell (WBC) counts even in the absence of infection have recently been suggested as an increased risk factor for CVAs (7). Therefore, closer monitoring of coagulation parameters should be adopted, especially in the presence of elevated WBC counts.

TABLE 3. *Neurological event rates for early reports with two centrifugal-based continuous flow devices (VentrAssist, HeartWare) now undergoing clinical evaluation (5,6)*

Neurological dysfunction*	VentrAssist ($n = 28$)	HeartWare ($n = 23$)
Number of events	6	3
Number of patients with events	5	3
Percent of all patients with events	18%	13%
Number of stroke events	4	2
Number of patients with stroke events	3	2
Percent of all patients with stroke events	11%	9%

* Stroke, transient ischemic attack.

Some other areas of investigation worthy of some consideration which relate to neurological complications are outlined below:

Influence of cannula design/placement

A recent retrospective study of 216 patients implanted with INCOR axial-flow pump (Berlin Heart, Berlin, Germany) also sheds important light into the issue of neurological complications related to cannula design and placement (11). In this study, the length of the apical tip protruding into the ventricle (24 vs. 34 mm) was found to have had a significant impact on the incidence of stroke. The incidence of stroke was reduced from 23% in patients with the short cannula ($n = 138$) to just 4% in patients with the longer cannula ($n = 78$). The authors suggest that the increased intraventricular length prevented thrombus formation caused by trabecula interference, and altered flow patterns, thus preventing growth of fibroplastic tissue around the cannulation site (11). The sizable impact of this relatively minor design revision further highlights the importance of carefully assessing cannula placement during implantation using transesophageal echocardiography.

Intra-aortic filtration

Since mechanical circulatory support patients are at an increased risk for neurological complications, greater use of neurologic protection devices such as intra-aortic filters may be warranted in this high-risk patient group. Intra-aortic filtration is not definitively proven to reduce neurological complications, but it has been shown to capture a substantial amount of particulate matter, thus, use may be warranted in high-risk patients (12). Given the substantial aortic manipulation during mechanical circulatory support device implantation as well as the risk for releasing preexisting ventricular thrombi during device implantation, intra-aortic filtration may provide the means to reduce particulate matter that could be responsible for early neurological events.

Restoration of blood flow and device operating modes

Cerebral hyperfusion syndrome, an early neurological complication most commonly associated with carotid endarterectomy, has also been reported in mechanical circulatory support recipients (13). This syndrome, a result of prolonged hypoperfusion and impaired autoregulation of cerebral blood flow, results in increases of cerebral blood flow of up to 100% over baseline following intervention, and can also lead to cerebral edema and stroke. This syndrome is also analogous in some ways to mechanical circulatory support wherein patients with chronic low flow states are dramatically returned to normal flow states following device implantation. In the single report of this syndrome occurring in mechanical circulatory support patients, Boyle et al. implemented device flow restrictions in two patients which led to complete neurological recovery (13). These findings suggest that there may be some potential strategies of implementing innovative device operating modes which allow for a more gradual restoration of blood flow levels post implant. This concept, while unsupported by specific evidence at this time, highlights an area where very little research has been conducted. Interestingly, while weaning patients off mechanical circulatory support devices has been studied quite extensively, very little work has been conducted on the best approach to weaning patients onto these devices. Gradually restoring blood flow levels over time after implantation may be advantageous in addressing the neurological complications associated with mechanical circulatory support.

CONCLUSIONS

Neurological complications remain one of the most devastating complications for mechanical circulatory support device recipients, and have been a leading cause of morbidity, mortality, increased hospital stay, and cost. Given these potentially devastating consequences, an enhanced scientific focus in this area is certainly warranted. Perhaps the next educational conference on mechanical circulatory support should focus on neurological complications, instead of simply rehashing the clinical results of various new devices. Just as our collective efforts in the past have led to significant achievements in this field, an interdisciplinary group of experts brought together to focus on neurological complications can begin to shed some light on this most troubling complication.

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REFERENCES

1. Lazar RM, Shapiro PA, Jaski BE, et al. Neurological events during long-term mechanical circulatory support for heart failure: the Randomized Evaluation of Mechanical Assistance

for the Treatment of Congestive Heart Failure (REMATCH) experience. *Circulation* 2004;109:2423–7.
2. Deng MC, Edwards LB, Hertz MI, et al. Mechanical Circulatory Support Device Database of the International Society for Heart and Lung Transplantation: second annual report—2004. *J Heart Lung Transplant* 2004;23:1027–34.
3. Data Collection and Analysis Center University of Alabama at Birmingham. INTERMACS—Quarterly Statistical Report. Implant Dates March 2006–November 30, 2007. Available at: http://www.intermacs.org. Accessed March 2008.
4. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. *N Engl J Med* 2007;357:885–96.
5. Boyle A, Griffith B, Ascheim D, et al. The VentrAssist LVAD: results of the U.S. BTT feasibility trial. Slide Presentation. Available at: http://www.ventracor.com. Accessed April 2008.
6. Wieselthaler GM, Strueber M, O'Driscoll GA, Jansz P, Khaghani A. A report on the first 23 human implants: experience with the novel HeartWare LVAS with hydromagnetically levitated rotor in a multi-institutional trial. Slide Presentation. Available at: http://www.heartware.com. Accessed April 2008.
7. Tsukui H, Abla A, Teuteberg JJ, et al. Cerebrovascular accidents in patients with a ventricular assist device. *J Thorac Cardiovasc Surg* 2007;134:114–23.
8. Pae WE, Connell JM, Boehmer JP, et al. Neurologic events with a totally implantable left ventricular assist device: European LionHeart Clinical Utility Baseline Study (CUBS). *J Heart Lung Transplant* 2007;26:1–8.
9. Thomas CE, Jichici D, Petrucci R, Urrutia VC, Schwartzman RJ. Neurologic complications of the Novacor left ventricular assist device. *Ann Thorac Surg* 2001;72:1311–5.
10. Ramasamy N, Vargo RL, Kormos RL, Portner PM. Intracorporeal support: the Novacor left ventricular assist system. In: Goldstein DJ, Oz MC, eds. *Cardiac Assist Devices*. Armonk, NY: Futura Publishing Co., 2000;323–39.
11. Schmid C, Jurmann M, Birnbaum D, et al. Influence of inflow cannula intraventricular length in axial-flow pumps on neurologic adverse event rate: results from a multi-center analysis. *J Heart Lung Transplant* 2008;27:253–60.
12. Banbury MK, Kouchoukos NT, Allen KB, et al. Emboli capture using the Embol-X intraaortic filter in cardiac surgery: a multicentered randomized trial of 1289 patients. *Ann Thorac Surg* 2003;76:508–15.
13. Boyle AJ, Park SJ, Colvin-Adams MM, et al. Cerebral hyperfusion syndrome following LVAD implantation. *J Heart Lung Transplant* 2003;1:S203. Abstract.