

tion and improvement in physiologic status may be achieved to improve survival following the transplant.<sup>3</sup>

A possible scoring system for better selection of patient criteria is sought. In this context the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system, a multiparameter, physiology-based predictor of outcome, might be helpful. It can aid in both selection and timing of LVAD implantation, particularly in patients not meeting normal hemodynamic criteria for LVAD usage.<sup>4</sup>

Development of right ventricular failure often causes poor results in patients with LVADs. It is important to take into consideration the predictive factors including the need for circulatory support, female gender, and nonischemic etiology, along with the hemodynamic alterations including low pulmonary artery pressure and low right ventricle stroke work index, that might indicate poor right ventricular outcome.<sup>5</sup> Careful observation of the above would assist both in patient selection and clinical handling of isolated LVAD implants.

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## Reply to the Editor:

We thank Dr Ashraf for his comments on our recent article concerning the use of left ventricular assist devices (LVADs) in patients with chronic congestive heart failure.<sup>1</sup> His letter invites us to discuss several important points.

First, to clarify the device type used predominantly at our center and used exclusively in our study, we favor the HeartMate XVE (single-lead vented electric) LVAD (Thoratec Corp, Pleasanton, CA) for its relative ease of implantation, durability, and lack of need for systemic anticoagulation. Our long-term experience with this device has paralleled an evolution in design, resulting in improved bridge-to-transplant and posttransplant survival rates.<sup>2</sup>

Next, we could not agree more with Dr Ashraf's observation that the timing of transplantation following LVAD insertion plays a critical role in determining survival. Our own unpublished data show near normalization of blood urea nitrogen, creatinine, and liver function values at approximately 3 months of support time, bolstering the concept of enhanced end-organ perfusion by the LVAD. Moreover, the smooth transition to cardiac rehabilitation and nutritional optimization throughout the recovery period are of critical importance.

Although we do not employ the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system ourselves, we use similar clinical and laboratory-based parameters to select LVAD candidates. All patients referred for LVAD are generally refractory to maximal medical therapy, which often includes the use of intravenous inotropes, vasopressors, and intra-aortic balloon pumps. Exclusion is therefore done on the basis of such factors as ventilatory status, elevated pulmonary pressures, and prolonged prothrombin time.

Despite the physiologic benefits of LVADs, even as they apply to the right ventricle, right heart failure (RHF) occurs in approximately 15% to 20% of patients postoperatively.<sup>3,4</sup> Multiple studies have sought to identify demographic and hemodynamic risk factors predictive of the development of RHF, but in practice, these parameters often exhibit variable outcomes. Although the best treatment for RHF is avoidance, when it does become manifest, a low threshold should be maintained to promptly start inotropic (ie, milrinone) and pulmonary vasodilator (ie, ni-

tric oxide) therapy, with a right ventricular assist device close at hand.

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## Apoptosis in ischemic spinal cord injury

### To the Editor:

We read the article of Suzuki and associates<sup>1</sup> titled "Experimental study on the protective effects of edaravone against ischemic spinal cord injury" with great interest. They studied the effect of a free radical scavenger named "edaravone" in a rabbit model of transient aortic occlusion and claimed its protective effect on the ischemia-reperfusion injury of spinal cord by suppressing the level of reactive oxygen species (ROS). We congratulate Suzuki and associates for their excellent study. We think that the introduction of microdialysis method to determine the production of ROS in the neuronal tissue after transient ischemia for the first time in the literature by the authors is a great contribution to our current knowledge.

Recently, data has accumulated that programmed cell death or apoptosis of motor neurons in spinal cord after transient ischemia is an outstanding mechanism of postoperative paraplegia or paraparesis.<sup>2,3</sup> The neuronal injury following transient aortic occlusion occurs in 2 phases, namely, early and delayed. Ischemic insult in spinal cord

activates apoptosis by plasma membrane death receptor pathway, activation of caspase enzymes, and release of cytochrome c from mitochondria. Although blood flow to the spinal cord is restored during reperfusion, the motor neurons that seem to survive ischemic insult may undergo delayed selective death, particularly 7 days after the procedure.<sup>4</sup> Despite that the etiology of delayed selective neuronal death has been proposed to be the activation of Akt protein, Grp78, and caspase 12 proteins, further studies should be warranted. In the present study, the authors claimed the protective effect of edaravone on spinal cord injury according to the histologic examination and levels of ROS. However, it is known that these neurons might be apoptotic despite the normal cellular architecture seen on the hematoxylin and eosin (H & E) staining. The authors did not focus on apoptotic mechanisms and demonstrated only necrotic (ghost) neurons with H & E staining without considering the neurons undergoing apoptosis. In this regard, we believe that addition of the neuronal apoptosis would increase the statistical power of this study.

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## Reply to the Editor:

We thank Dr AK for his insightful comments on our recently published article. Paraplegia or paraparesis occurring in the late postoperative period is well described in the literature. The mechanism of this delayed spinal deficit is presumed to be related with apoptosis. Sakurai and colleagues<sup>1</sup> evaluated the relationship between delayed paraplegia and apoptosis using immunohistochemical techniques. In their experimental study, the transient spinal ischemic time was 15 minutes. Two days after the reperfusion, the mean Johnson score was  $4.9 \pm 0.894$ , and 3 of the 5 rabbits had normal hind-limb function. In our study,<sup>2</sup> we applied a spinal ischemic time of 30 minutes. Two days after the reperfusion, all rabbits in the control group were completely paraplegic with a Johnson score of 0. The focus of our investigation was to assess whether prophylactic administration of edaravone could suppress necrosis and not apoptosis of the spinal cord. Consequently, a longer spinal ischemic time was employed and only hematoxylin-eosin staining was used for histopathologic evaluation. As suggested by AK, motor neurons that appear intact on hematoxylin and eosin staining as a result of the prophylactic administration of edaravone might suffer delayed apoptosis-related injury. Because we did not use any marker for apoptosis in our study, we are not in a position to comment on this. However, we agree with Dr AK that further studies need to be undertaken to clarify this issue. We are indeed planning to embark on a protocol that involves the use of markers of apoptosis in a model of shorter spinal ischemic time and longer duration of observation.

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study on the protective effects of edaravone against ischemic spinal cord injury. *J Thorac Cardiovasc Surg.* 2005;130:1586-92.

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## Surgical treatment for congestive heart failure with autologous adult stem cell transplantation

### To the Editor:

Patel and colleagues<sup>1</sup> have provided further evidence of the benefit of autologous stem cell transplantation in patients with ischemic cardiomyopathy. However, even if, in the past years, observational studies and some randomized controlled trials have established that autologous stem cell transplantation has led to significant improvement in myocardial infarction and congestive heart failure, this study unfortunately has not specifically addressed several clinically relevant questions: What dose of CD34+ cells for stem cell therapy in this area should we use? Furthermore, what is the best cell type and the best cell dose for each cell type?

In recent studies, doses of CD34+ cells ranging from  $10^6$  to  $10^8$  have been used; however, if the optimum dose of CD34+ cells needed is proven to be much less than  $10^6$ , procedures involved in collecting sufficient amounts for therapeutic use can be less time-consuming and thus potentially cost-saving. Furthermore, the expression of CD34 surface antigen characterizes a heterogeneous population of cells including hematopoietic progenitor cells, endothelial progenitor cells, mature endothelial cells, and tissue-committed stem cells as recently reported.<sup>2</sup> It is still not clear whether the beneficial effect of these cells in regeneration can be explained by the transdifferentiation of hematopoietic stem cells, the paracrine secretion of angiopoietic factors from bone marrow-derived stem cells,<sup>3</sup> or the presence of tissue-committed stem cells for myocardium or endothelium. We believe that there is a pressing need to standardize therapeutic protocols to allow tailor-made therapies for these patients.

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