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. 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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References

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 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 ± 0.894, and 3 of the 5 rabbits had normal hind-limb function. In our study, 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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References

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

To the Editor:
Patel and colleagues 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 specified 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 10⁶ to 10⁸ have been used; however, if the optimum dose of CD34+ cells needed is proven to be much less than 10⁶, 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. 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, 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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Letters to the Editor

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