Letters to the Editor

The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors should:

- Include no more than 500 words of text, three authors, and five references
- Type with double-spacing
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Multicenter bridge to transplantation with the HeartMate assist device: Evaluation from another perspective. A rebuttal

To the Editor:

I appreciate the opportunity to comment on the editorial by Copeland[1] concerning our article.[2] I share Copeland's concerns about company-sponsored trials and the possibility of bias in reports that are not verified by Food and Drug Administration (FDA) scrutiny. Company sponsorship always introduces an inherent bias, and the medical literature is replete with articles addressing such concerns. I must point out, however, that all of the data in our report were constantly exposed to third-party critical review by the FDA. Also, as implied in the article, the data from the multicenter trial resulted in FDA approval of the device. As a result, the data we report have the assurance of the accuracy attained by this third-party critical scrutiny.

Copeland's criticism of the control study is inaccurate. The control group was based on the initial trial for approval of the pneumatic HeartMate device (Thermo Cardiosystems, Inc, Woburn, Mass), the first implantable left ventricular assist device (LVAD) to be addressed and approved by the FDA and the only one of the implantable devices to go before the scrutiny of a panel. This control group has also been referred to by other groups seeking approval for LVADs. So, our control group actually represents an important and accepted group for comparison with patients with heart failure treated with an LVAD. The control patients were assigned to treatment, but most could not receive the device due to its unavailability.

The editorialist's discussion of the bleeding complications is unnecessarily lengthy and confusing, and I am not exactly sure what the point is. All LVADs continue to have associated bleeding problems. Such problems, however, improved markedly in the last part of our study through the use of aprotinin and other agents. Moreover, it was not the purpose of our article to address the details of bleeding complications associated with the device. Yet, it is clear that bleeding must be acknowledged as a risk factor in these and all other high-risk LVAD patients.

Copeland also addresses the biologic lining of the device. The concern with biologic linings goes back to the design of the original implantable devices in the 1960s and was part of the focus of the development of LVADs sponsored by the National Heart, Lung, and Blood Institute. One of the consistent and remarkable findings regarding the HeartMate LVAD's biologic lining technology is the low incidence of associated thromboembolic stroke, even in patients who do not receive the anticoagulant warfarin sodium (this device requires aspirin alone). Elsewhere, the biologic lining has been reported to reduce platelets, which may contribute to postoperative bleeding. I think this would have been a good topic for comment by Copeland.

I take issue with Copeland's concern about the adverse events of driveline infections and device malfunctions. Infection was not seen in the pneumatic version of the device but was more of a problem in the electrical device. It also seemed to be associated with the proximity of the driveline exit site to the device. The exit site has since been changed to more closely mimic that of the Novacor device (Baxter Healthcare Corp, Novacor Div, Oakland, Calif), and, with the longer tunnel, the rate of infection seems to be markedly decreased. As for device malfunctions, we noted in our article that 86% of them were malfunctions of external components such as controllers and batteries. No serious complications occurred in patients as a result of these events.

I appreciate Copeland's efforts to put our work into perspective, but also believe that several other points would have been worthy of his comment. First is the fact that LVADs have been used in more than 4000 patients worldwide and have helped save otherwise terminally ill patients in about 70% of cases, a point that an editorialist

could emphasize. Second is the increasing life-saving role of these devices as access to transplants decreases. Third is the fact that all LVADs are still subject to the same entry criteria that were used in the 1970s for patients with acute failure-to-wean-from-bypass. These hemodynamic entry criteria should be reassessed in view of the changing medical therapy and the fact that these implantable pumps are for patients with chronic heart failure on transplant waiting lists who experience worsening of heart failure made manifest primarily by end-organ failure and not by acute hemodynamic compromise.

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doi:10.1067/mtc.2003.69

Cerebral protection with retrograde cerebral perfusion

To the Editor:

In their article Bonser and colleagues[1] claim that the cerebral flow resulting from retrograde cerebral perfusion (RCP) is insufficient to make a major contribution to cerebral oxygenation and that the brain remains ischemic. In the discussion of their impressive work, the authors stated correctly that current data suggest that RCP might provide only little brain perfusion in human subjects compared with antegrade baseline cerebral flow. Should we abandon this adjunct to hypothermic circulatory arrest, or should we explore methods to maximize the benefits from its application? The effort to improve the effectiveness of RCP during hypothermic circulatory arrest should combine reduction of the metabolic activity with simultaneous increase of blood flow to fulfill the residual metabolic requirements of the brain. In a small series my colleagues and I[2] demonstrated that the introduction of vasodilators and anesthetics into the retrograde perfusate tripled RCP flow without increase in pressure and with concomitant suppression of electric activity. In the present study it is not stated whether brain electric activity was monitored, and the individual RCP flow is not specified. Simple pharmacologic manipulations might augment RCP to 20% or 30% of cerebral flow instead of only 10%. The administration of potent anesthetics or other neuroprotective agents might mitigate the metabolic needs of the brain. Such maneuvers will render the brain less ischemic, allowing safer circulatory arrest.

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doi:10.1067/mtc.2003.246

Reply to the Editor:

We thank Elami for his comments concerning our work on retrograde cerebral perfusion (RCP).[1] We acknowledged in our discussion that RCP could contribute to metabolic support during hypothermic circulatory arrest and that this contribution could be increased by the use of vasodilators. It is also possible that the use of anesthetics or neuroprotective agents during RCP might afford neuroprotection. The series quoted by Elami, however, describes only anecdotal evidence from 3 patients undergoing differing pharmacologic interventions.[2] This report described no monitoring of cerebral metabolism or perfusion, therefore making inferences regarding cerebral metabolic activity and blood flow unreliable. We have previously reported that RCP can provide some brain perfusion, but we have questioned what fraction of retrograde flow provides true brain perfusion.[3,4] It is quite possible that increased flow achieved by means of vasodilator administration bypasses the brain through venovenous and venoarterial collaterals.[4] Any assumption that increasing flow increases true brain perfusion and neuroprotection requires rigorous enquiry. We would agree that the jury remains out on RCP and that a beneficial clinical effect remains to be proven. Such therapeutic interventions therefore require assessment as part of randomized controlled trials if their efficacy is to be completely investigated.

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doi:10.1067/mtc.2003.245

Angiogenesis by means of endothelial cell transplantation

To the Editor:

In their article, "Angiogenesis by Endothelial Cell Transplantation," Kim and associates[1] present results of a novel and intriguing approach to angiogenic therapy. Their preliminary report that endothelial cell transplantation into a myocardial scar accelerates angiogenesis suggests a promising alternative to angiogenic gene or protein therapy. About the same time that their article was published, we[2] presented similar results before the American Heart Association at our annual scientific session (Anaheim, Calif) in November 2001.