Brain death leads to abnormal contractile properties of the human donor right ventricle

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In a characteristically bold, yet bald, attempt to preserve priority in investigative inquiry, *The Journal of Thoracic and Cardiovascular Surgery* has, in this issue, disinterred an observation first introduced four centuries ago by Macbeth: "The time has been, that when the brains were out, the man would die, and there an end; but now they rise again"¹ The transplantation community is now capable of scooping out your standard donor like a canoe. Thirty different tissue varieties can be successfully restored into welcoming recipients for years of effective functioning. Dying itself is, however, complex. We have evolved to avoid death. Dying provokes a constellation of signals that influence organ function in a receptor-dependent fashion. Receptor expression is gene controlled, and genome-wide scanning has confirmed high heritability correlating with the Framingham Heart Study.² As that great American philosopher Mae West once observed, "Too much of a good thing is wonderful." The editor of the *Journal*, himself no foreigner to stress, has collaborated in studies documenting altered myocardial gene expression and cardiotoxicity related to the death-induced surge in catecholamines.^{3,4} In this issue of *The Journal of Thoracic and Cardiovascular Surgery*, Stoica and colleagues⁵ have extended these observations to the human-donor right ventricle. With apologies to Mae West, too much of a time-tested, life-preserving survival strategy can prove cardiotoxic to a surgical transplantation intervention never imagined by Darwin. Yeh and colleagues³ reported that sympathetic blockade can attenuate brain-death-induced cardiotoxicity. Indications for perioperative beta-blockade are expanding rapidly.⁶ As organ donor husbandry gains in sophistication, an additional indication for prophylactic beta-adrenergic blockade may surface. The study by Stoica and colleagues⁵ represents an important additional step in our understanding of the formidable, multicomponent neurocardiac interface during death.

The authors⁵ appropriately note that the donor-selection criteria for cardiac transplantation remain imperfect, and that despite conscientious and careful evaluation by cardiologists and surgeons, we continue to encounter transplanted hearts with early dysfunction and to occasionally reject hearts that could provide long-term cardiovascular support. The authors evaluated 33 consecutive heart donors and compared their right ventricular pressure-volume loops, dopamine-stimulated contractile reserve, and slope of the end-systolic pressure-volume relationship with those of 10 patients undergoing coronary artery bypass surgery. Taking advantage of this kind of clinical opportunity is the best possible kind of clinical investigation. The authors contend that experimental and clinical data indicate that "brain death" predominantly influences the right ventricle. Therefore, they subjected potential donor hearts to load-independent strategies of right ventricular evaluation. Although the donor hearts exhibited a higher cardiac index than the controls who underwent coronary artery bypass graft surgery, they also displayed impaired load-independent indices. One might anticipate that an increased right ventricular stroke volume (as identified in the donor hearts) would translate into an ejection fraction that was also increased. Clearly, the end-diastolic volume in the donor hearts must be even greater than the increased stroke volume. Similarly, the slope of the end-systolic pressure volume relationship was significantly reduced in the brain-dead donor hearts. As predicted from the discordance between the increased right ventricular stroke volume and the compromised ejection fraction, the right ventricular end-diastolic volume index was higher. These hearts did exhibit some contractile reserve in that they responded to dopamine with an increased cardiac output; however, this further increased

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the right ventricular end-diastolic volume. Perhaps predictably, donor hearts that already exhibited an increased right ventricular end-diastolic volume also demonstrated early postoperative dysfunction. Thus, the authors identified increased right ventricular end-diastolic volume as a predictor of postcardiac transplantation trouble. The authors suggest that brain death provokes right ventricular dysfunction and that this may go undetected with conventional techniques. The authors suggest “refinement of selection criteria to include load-independent indices of performance.” It seems that this might significantly complicate the evaluation of these already unstable patients. It would be valuable for the authors to identify “standard criteria” for donor acceptability and then relate these criteria to preharvest right ventricular volumes with an accompanying relationship between right ventricular end-diastolic volume and successful cardiac function posttransplantation. The authors make the persuasive case that they have identified an important predictor of donor acceptability. It would also be valuable to assess the number of potential donors who are acceptable by “standard criteria” and subsequently exhibit posttransplantation “trouble” that might have been predicted by the “right ventricular end-diastolic volume index.” Similarly, it would be valuable for the authors to estimate the number of donors rejected by standard criteria in whom more precise assessment

of right ventricular volume/function evaluations might identify them as “acceptable.”

We must admire Stoica and colleagues⁵ for persistently chipping away at the intimidating complexities of the neurocardiac axis. We are making progress, but our brains are complex. As observed by Emerson Pugh: “If the human brain were so simple that we could understand it; we would be so simple that we couldn’t.”

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Notices of Correction

Galetta D, Cesario A, Margaritora S, Porziella V, Piraino A, D’Angelillo RM, Gambacorta MA, Ramella S, Trodella L, Valente S, Corbo GM, Macis G, Mulè A, Cardaci V, Sterzi S, Granone P, Russo P. Multimodality treatment of unresectable stage III non-small cell lung cancer: Interim analysis of a phase II trial with preoperative gemcitabine and concurrent radiotherapy. *J Thorac Cardiovasc Surg*. 2006;131:314-21.

The institutional affiliation for Dr. Patrizia Russo is incorrect. Her correct affiliation is Translational Research B (Lung), Department of Integrated Medical Oncology (DOMI), National Cancer Institute, Genova, Italy.

Bodnar E, Blackstone EH. An “actual” problem: Another issue of apples and oranges. *J Thorac Cardiovasc Surg*. 2006;131:1-3.

In the January 2006 issue of the *Journal*, the article contained a lengthy discussion relating to the appropriate use of Kaplan-Meier event estimates versus use of “actual” event data. The statement that the *Journal* will no longer accept articles using “actual” event rates to describe prosthesis longevity was not meant to be included because this approach remains a source of controversy. The *Journal* will allow the author’s discretion as to which event descriptor is most appropriate but reserves the right to subject such articles to statistical review rather than applying an arbitrary standard.

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