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Discussion

DR. W. RANDOLPH CHITWOOD, JR. (Greenville, North Carolina): Dr. Jurkiewicz, Dr. Copeland, Members, and Guests. I would like to congratulate Dr. Van Trigt on a well-designed and well-presented experimental study that attempts to elucidate some of the mechanisms relating to right heart failure after orthotopic cardiac transplantation.

It is well known that recipient pulmonary vascular resistance may offer a formidable afterload and, thus, strain to a heart that is just emerging from hibernation after a harvest that may have occurred many hours earlier.

The intent of this study was to assess factors, other than acute increases in afterload, as determinants of early right ventricular dysfunction after orthotopic cardiac transplantation. Dr. Van Trigt used sonomicrometric cardiac dimension analysis to assess preload recruitable stroke work, which is a load independent determinant of systolic function.

In this study, brain death was shown to have a significant and negative effect on right ventricular contractility. Right ventricular dysfunction was more pronounced than comparative left ventricular systolic impairment. In the cohort without brain death, but transplanted, right ventricular preload recruitable stroke work was reduced as well. Although not defined clearly, this deleterious effect resulted presumably from geometric distortion associated with the biatrial anastomosis.

The reviewer is concerned that there is not an explanation for a potential common mechanism of dysfunction between these two separate models.

My first question: As right ventricular adrenergic receptor density and responsiveness were not affected by brain death, was there any alteration in beta sites in the transplanted group?

Secondly, what would be the effect of combining the two experimental groups so that RV function was studied after transplanting a heart taken after being subjected to several hours of brain death?

Thirdly, could there be a genetic mechanism that switches adrenergic receptors or other effector sites either on or off in response to brain death?

Lastly, have you examined the effect of brain death on right ventricular diastolic function in these models?

Dr. Van Trigt, congratulations on your election to fellowship in the Southern Surgical Association and for the presentation of this provocative and clinically applicable experimental study. I wish to thank the Association for the privilege of discussing this important paper.

DR. WILLIAM L. HOLMAN (Birmingham, Alabama): Dr. Jurkiewicz and Dr. Copeland, Members, and Guests. This paper is important because it gets at one of the most vexing problems in cardiac transplantation—acute failure of the donor right ventricle.

In clinical practice, it is interesting that, although the right heart often struggles for the first few hours or days after implantation, its function then improves and, ultimately, the right ventricle preforms well in the vast majority of patients. Presumably, this recovery is due to an acute decrease in pulmonary vascular resistance, as well as an improvement in right ventricular contractility. Accelerating the improvement in right ventricular function or avoiding right ventricular dysfunction altogether, would obviously be a major advance.

I have two questions, Dr. Van Trigt.

First, did you record the temperature in the right ventricular freewall during the transplant procedure? Was topical hypothermia used as the heart was implanted in the recipient?

Second, did you separately examine the changes in the septal-right ventricular freewall dimension as a source for change in right ventricular performance after brain death or after the transplant operation?

As you know, abnormal septal motion is a common echocardiographic finding after transplantation, as well as after other cardiac operations.

I thank the Association for the privilege of discussing this paper. And, Dr. Van Trigt, I thank you for providing me with a copy of your group's excellent manuscript.

DR. ERLE H. AUSTIN III (Louisville, Kentucky): Dr. Jurkiewicz, Dr. Copeland, Members, and Guests. I also would like to congratulate the authors on what I think is an elegant study dealing with a very important aspect of cardiac transplantation.

Over the past 20 years, we have seen significant improvements in mid- and long-term survival after heart transplantation, but little improvement has occurred with early mortality, which, as Dr. Van Trigt has indicated, is primarily related to the function of the donor heart, especially the right ventricle.

For those of us involved in heart transplantation, there is nothing more frustrating than performing a cardiac transplant and discovering that the donor heart does not have the ability to sustain the recipient circulation.

In a canine model, Dr. Van Trigt and colleagues have demonstrated a major effect of brain death on contractility of the donor heart. I, for one, was amazed to see that the acute onset of brain death was associated with systemic systolic pressures of 400 mm of mercury and pulmonary pressures of 150 mm of mercury—a major workload that must place the donor heart under undue stress.

In this study, brain death alone resulted in a 37% decrease in right ventricular contractility, as measured by preload recruitable stroke work, today's state-of-the-art measurement for ventricular contractility.

In another group of animals, the process of harvesting, preservation and orthotopic implantation resulted in a 43% increase in right ventricular contractility. And by my calculations, by the time the donor heart is implanted, the right ventricle has lost almost 65% of its pre-braindeath contractility. In view of this information, it is amazing that we do as well as we do in clinical heart transplantation.

Nevertheless, the authors have developed a model that beautifully characterizes the effects of brain death as well as standard techniques of harvesting, preservation and implantation on right ventricular contractility.

I would like to ask the authors three questions.

Number one, with this model or other studies in your lab, have you discovered any effects of brain death and/or harvesting on diastolic function? This is a question that Dr. Chitwood also was asking.

Number two, now that you have demonstrated with your model the detrimental effects of brain death, procurement and implantation, do you have plans to use this model to test some interventions that might diminish these effects?

And, finally, I would like to ask Dr. Van Trigt how his experimental work on the effects of brain death on donor heart function has affected the way he evaluates, selects and manages donors for clinical heart transplantation.

I thoroughly enjoyed hearing Dr. Van Trigt's presentation and reading his manuscript. This is exciting work, and I thank the Association for the opportunity to discuss it.

DR. O. H. FRAZIER (Houston, Texas): I appreciate having had the oportunity to hear this well-presented paper on the effects of right ventricular function

However, I disagree with the authors and the previous discussant that right heart function is the chief cause of early donor heart failure, although the normal heart does have problems in pumping against the elevated pulmonary vascular resistance of the recipients.

I recently transplanted what I thought was a reasonable donor heart into a 10-month-old infant who had a PVR of 5 at the time of transplant. The infant was initially weaned from bypass without difficulty, but about an hour later, the right heart failed. This is a scenario familiar to all transplant surgeons. I was able to institute right ventricular assist with a Biomedicus pump in this patient. Before Biomedicus assist began, the infant's blood pressure was about 40 mm Hg. With pump flows of only 1.5 L/minute, blood pressure increased to 55 mm Hg. In the recovery room, the infant was given nitric oxide inhalation therapy. Resistance to flow immediately decreased, and within 1 minute, blood pressure returned to normal. We subsequently tapered the dosage of nitric oxide, and the patient was weaned from Biomedicus assist. At this point, the echocardiograms were normal, and the infant recovered uneventfully. Without such therapy, he surely would have died in the operating room. Thus, although I appreciate the authors' position, I strongly believe that the role of pulmonary vascular resistance is understated.

I congratulate the authors on this excellent study and for bringing this important subject to our attention.

DR. PETER VAN TRIGT III (Closing Discussion): I'd like to thank the discussants for their careful review of the study and for their excellent questions.

One question related to the effect of combining brain death on a heart and subsequent orthotopic transplantation of that heart into a recipient. It was an obvious question that this study raised, and we have performed that in a preliminary group of animals using the newer anastomotic technique of the bicaval and pulmonary venous orthotopic transplantation. After 4 hours of brain death in the instrumented heart, the PRSW values decreased similarly in both the right and left ventricles in the group of animals. After flushing the hearts with cardioplegia and transplanting them in a similar fashion with about 80 to 90 minutes of total global ischemia, there was no further decrease in the PRSW in the right or left ventricle.

The question of diastolic dysfunction in the group of animals was raised, which I think is important in assessing the ventricular function in a complete physiologic fashion in any type of experimental setting. We did measure, in the brain death group, end diastolic pressures, which did significantly increase over time without a concomitant increase in diastolic volumes, which would indicate that there was a loss in compliance of the hearts with progression of brain death.

Questions were raised as to how the receptors can be altered during the process of brain death, and other studies have suggested that beta blockade before brain death or in the early phases of brain death could alter the deleterious effects of brain death on the subsequent function of the heart upon transplantation. We are in the process of looking into that area. We have no data report on that at this time.

I think that in terms of managing our patients clinically with brain death, that attention to blood pressure is especially important, because I feel that the extremes in blood pressure to nonphysiologic ranges—about a fivefold increase in right-sided pressures, about a three- to fourfold increase in left-sided pressures—probably results in the mechanical injury to the contractile elements.

We did not have ultrastructural data on the hearts after brain death as recommended by Dr. Frazier. I think that was an excellent recommendation and something that the study lacks, which we will need to look at in the future.

The routine H & E sections did show the usual catecholamine-induced areas of injury and especially in the subendocardial regions of the hearts undergoing brain death.

The comment about septal freewall dimensions changes during brain death, I think, is an excellent one. In almost all donor hearts assessed by echocardiography, we see some septal dysfunction. This dysfunction was, I think, borne out by the experimental data because the right ventricular PRSW analysis is mainly based on the RV septal freewall dimension, and changes in that dimension are responsible for the decrease in right ventricular PRSW.

I'd like to, again, thank the Association for the opportunity to present these data and the privilege of membership in the Society. Thank you.