## Discussion

### Presenter: Dr Gregory S. Couper

**Dr Ashish S. Shah** *(Nashville, Tenn)*. I would like to thank the Association for the opportunity to discuss this paper and the authors for providing the slides in advance. Despite over 50 years of clinical heart transplantation, the decision to use a heart for transplant rests in the hands of the implanting surgeon, usually late at night, often in the context of multiple forces, including hospital-based resources, regulatory pressures, and fatigue.

The criteria for what is considered an acceptable donor have remained essentially unchanged over the decades and vary from center to center. I think we all worry about using small female hearts, which remain underutilized, certainly in the United States. Over the last several years, however, we have had an emerging and more nuanced view of what constitutes an acceptable donor. Because we're incorporating large datasets and quantifying risk relative to the recipient (not just the donor in isolation), that has helped teams make better decisions. Even more recently, we've been introduced to the idea of myocardial mass between the donors and the recipients. The recent paper from the Cedars-Sinai group examining predicted heart mass and postoperative outcomes has certainly influenced our thinking at Vanderbilt, and I sincerely believe the authors of this study have added another novel dimension in considering right ventricular mass.

You mentioned this earlier, but while 1-year survival is significantly different, the absolute difference is small at 2%. In your multivariable model, your Cox proportional hazards model, it is statistically significant, and you mentioned it—do you think this is clinically meaningful? And the second part of this question is: Have you considered exploring other endpoints, such as the need for postoperative mechanical support, renal failure, and functional status?

**Dr Gregory S. Couper** *(Boston, Mass)*. We did look at the outcomes other than survival, and in that lowest RV-matched group, there was a little bit more graft failure. And of course, the definitions of PGD evolved over the course of the study, and what people inputted as graft failure over our 21 years of database entry could vary.

There was a little bit more rejection, a little bit more renal failure, a little bit more postop dialysis, a little bit more multiorgan failure. We can't pin down what exactly is creating the small difference in mortality. I've always believed that all these things likely roll back to the performance of the allograft right off the bat. It is a relatively small difference, but one of the things we'd like to explore further is whether in this population we can develop the subpopulation in which we really find that this difference is dramatic—where it's not diluted by the vast numbers of patients. The preoperative hemodynamics—pulmonary artery pressure and all those things—were the same in all groups. So that's not really the answer. But it's something we have to explore further by really taking our group of interest and taking the signal and seeing if we can somehow amplify it.

**Dr Shah.** Other studies comparing donor-recipient matching have found an important relationship in preexisting pulmonary hypertension. So maybe restate your conclusion. Did you consider preoperative pulmonary hypertension in this model? Is there any interaction between the undersized donors and preoperative pulmonary hypertension?

**Dr Couper.** In that group of the lowest RV-mismatched group of less than 0%, it's a broad range. It covers a broad range of the LV-mismatched patients below 0%. We could not identify, on the whole, that there was a significant difference in pulmonary artery pressure. Pulmonary vascular resistance, I don't recollect it necessarily being reported frequently or well.

**Dr Shah.** Fair enough. It's certainly something to think about it. We've looked at some of this again with UNOS data and it did seem that undersized donors in patients with pulmonary hypertension, you know, plus or minus an LVAD, you start adding some of these variables together and it may be that your RV mass calculation might be a nice added variable to put in the mix, particularly if you think about this as a risk factor among others. My third question is: Why do you think the oversizing had a mortality to it?

**Dr Couper.** When you begin to express these curves in that parabolic sense, it really becomes obvious that oversizing seems to be almost as big a problem. I don't know the answer to that. My medical colleague Amanda Vest spends most of her clinical and basic research looking into nutritional factors, especially morbid obesity and its impact. These would be obese donors (or more obese donors, presumably) and more male donors at that end of the spectrum. Dr Vest is convinced that the morphologic and phenotypic changes of the obese heart rapidly reverse after transplantation. Certainly within a year of bariatric surgery, there are marked changes toward normalization. I don't know that we know that after transplantation. I think all of us may have had a hard time fitting a really big heart into a space that won't take it, but I don't really think that that's the answer.

**Dr Shah.** All these calculations are based on normal hearts. So if we're able to use calculations based on abnormal hearts (that is, recipients who have restrictive myopathies, hypertrophy or dilated myopathies), can you speculate how relevant these normal heart calculations are to our recipients?

**Dr Couper.** I would agree with you there. These equations were developed to describe the general population, and they probably describe the donor population pretty well, and then we've obviously skewed our selection of donors. These subgroups of patients with smaller-volume hearts, but more dense mass are fascinating, and it would take quite a bit more work, and I'm not sure that we'll have the statistical power there to really make firm statements. But it's an interesting idea.

**Dr Shah**. Well, thank you for that presentation. I just have one comment. I think we do need to start moving away from survival as the as the only endpoint, particularly thinking about future allocation systems. There really are other important functional endpoints like exercise capacity, long-term survival, quality of life that may really affect how we utilize hearts and how we utilize these calculations. Sure, we can get them through the operation—but have we really just transplanted heart failure at a year? So thanks again for the opportunity.

**Dr Couper.** Thank you.

**Dr Scott C. Silvestry** *(Orlando, Fla)*. First, congratulations. I think this study is a phenomenal analysis of an important aspect of transplantation. Eberlein and coauthors reported the first predicted heart mass data in *JACC Heart Failure* in 2014, and we have been using predictive heart mass to guide clinical decisions. Your analysis takes this thinking to another level. If you drill down on your right ventricular mismatched population and look at preop PVR, you will find that the real survival disadvantage occurs in PVRs greater than 2.5.

We have single-center data looking at that, but it's not enough to see—but I think if you rerun your data by mismatch in the pulmonary vascular resistance, there are certain susceptible populations, and I believe this is a sort of a hint of it. I'm glad you're putting the RV calculator out there. My question to you on this data is: How is this changing the decisions that you're making in these patients today moving forward?

**Dr Couper.** I agree with you and Dr Shah that basically, the recipients with elevated pulmonary vascular resistance are probably the fertile area to study further. They're probably the ones at risk of RV mass undersizing. This dataset has not yet really impacted how we look at donor selection. I think a lot of these are attempts to quantify what our surgical intuition has been for decades and how we pick things. I would say that using the total cardiac mass calculator, I am surprised at times that there's a better match, especially younger, female, pretty heavy donors. We've taken a whole lot more of those in recent years than I probably would have dreamed of maybe 5 or 10 years ago.

So I think that by quantifying these things, it brings us to a realization that it's okay. The other thing I would like to just say about the calculators and these parabolic curves is that there are no breakpoints in any of these curves. So there are no absolute thresholds or cutoffs. I think it's all going to be a relative risk-benefit ratio thought process, you know at 2 a.m.

**Dr Carmelo A. Milano** *(Durham, NC)*. I think the other thing that makes this discussion more complicated is that our conventional cold static storage does induce some degree of injury to the right ventricle. And usually that's not particularly significant, but I think in many instances it is significant, and it occurs in an unpredictable manner. So I think continuing to look toward better preservation strategies is a very important topic for our field, and it may affect the way we select organs and what we can get away with and what we can't get away with. Again, thank you for that interesting presentation. Thank you for the discussion around it.