

Study: Two-sizes-too-small 'Grinch' effect hampers heart transplantation success

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Current protocols for matching donor hearts to recipients foster sex mismatching and heart size disparities, according to a first-of-its kind analysis by physicians at the University of Maryland School of Medicine. Matching by donor heart size may provide better outcomes for recipients, who already face a scarcity of resources as they await a transplant.

The analysis of 22 years of adult [heart transplant](#) data in the United States, published in *JACC: Heart Failure* by the American College of Cardiology, critically reappraises the current practice of matching donors and recipients by [body weight](#) rather than [heart](#) size. While two people may weigh the same, their hearts could have vastly different sizes – often requiring a smaller donor heart to strain to do the necessary work. The researchers dubbed this the "Grinch" effect, referring to the Dr. Seuss character whose heart was "two sizes too small."

The contrast is especially amplified when a match based on body weight doesn't factor in sex differences. "Men who receive women's hearts are 32 percent more likely to die in the first year after transplantation, and this is entirely because of suboptimal sizing," says the study's principal author, Robert M. Reed, M.D., assistant professor of medicine at the University of Maryland School of Medicine and a transplant pulmonologist at the University of Maryland Medical Center. "Even if the weights of donor and recipient are similar, the female heart is considerably smaller, while women are more often given men's hearts that are larger."

According to study co-author Keshava Rajagopal, M.D., Ph.D., a University of Maryland heart and lung transplant surgeon, the research emphasizes the peril of undersizing. "Undersizing a donor heart is very dangerous. It's like putting a motorcycle engine into a truck," says Dr. Rajagopal, assistant professor of surgery at the University of Maryland School of Medicine. "We need to figure out a better way to reliably ascertain heart size to best match donor and recipient. Some of the heart size models we utilize in this study may provide those predictive tools."

Transplant centers typically limit the pool of acceptable heart donors to those whose body weight is within 30 percent of the recipient's body weight. "This research shows that the current system allows some less-than-optimal matches to occur, while simultaneously reducing access to an already very limited resource for people waiting for heart transplants," says Dr. Reed. He and his team propose a new strategy to determine compatibility based on the predicted total heart mass for recipient and donor pairs.

The research conclusions are based on a retrospective analysis of more than 31,000 donor-recipient adult heart transplant pairings from the United Network for Organ Sharing (UNOS) transplant registry between October 1989 and June 2011. The study focused on heart size matching, comparing outcomes based on body weight, predicted heart mass and sex. The study evaluated risk of death after transplantation at one year and five years.

The body weight sizing analysis reflected the prevailing weight-based matching criteria: 86 percent of donor weights were within 30 percent of the corresponding recipient's weight. Donor-recipient weight differences were distributed similarly across categories of sex matching. Survival was similar among groups with weight mismatches when compared against the best weight-matched group. "These findings confirm that weight differences are not associated with any difference in survival,"

says Dr. Reed.

The sex comparison revealed that 77 percent of recipients were male (median age 55) and 71 percent of donors were male (median age 29). Overall death rates at one and five years post-transplant were 12 percent and 23 percent respectively. Nearly 71 percent were sex-matched recipient-donor pairs, while 29 percent were sex-mismatched pairs. Differences in predicted cardiac size accounted for the survival differences associated with donor-recipient sex mismatch.

The comparison of predicted heart mass shows the risk of death rose markedly when the donor heart's predicted mass was 10 to 15 percent below the predicted mass of the recipient's heart. The group that had the most undersized hearts was 25 percent more likely to die in the first year after transplant.

Finally, the study found that heart size plays a role in the need to treat acute organ rejection during the first year after transplant. Rejection was treated nearly 50 percent more often in the most undersized compared to the most oversized heart pairings.

The study did not pinpoint why undersized hearts produce worse outcomes, but Dr. Reed speculates that problems result because the heart has to grow to meet the needs of its new body. "The undersized [donor heart](#) has to bulk up to deal with the work load of a body it was never meant for. I suspect this growth occurs in an unhealthy way."

This research complements prior work on lung sizing in transplantation done by Dr. Reed in collaboration with the study's senior author, Michael Eberlein, M.D., Ph.D., a transplant pulmonologist and assistant professor of medicine at the University of Iowa Roy J. and Lucille A. Carver College of Medicine.

Dr. Eberlein notes that lung transplant candidates in the United States are listed for acceptable donor height ranges, with body height used as a surrogate for lung size. A series of studies conducted by Drs. Eberlein and Reed have shown that the body height standard for lungs has shortcomings similar to the body weight standard for hearts.

"This thoracic transplantation research tells us there are better ways to manage the organ size- matching process," says Dr. Eberlein. "Instead of body weight for hearts and body height for lungs, we show that such parameters of estimated organ size as the predicted heart mass and predicted total lung capacity are clinically more relevant for the size-matching decision."

More than 3,700 people worldwide undergo heart transplantation annually. About 3,570 people are currently on the heart transplant waiting list in the United States, according to the Organ Procurement and Transplantation Network.

"Heart transplantation has made great strides in recent years; now, thanks to this research, clinicians have a new calculus that promises better donor-recipient matching and better-functioning hearts," says E. Albert Reece, M.D., Ph.D., M.B.A., vice president for medical affairs at the University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and Dean of the University of Maryland School of Medicine. "In an era of new models of healthcare delivery and accountable care, studies such as this can reveal what is best for the patient and can help optimize placement of rare thoracic donor organs."

More information: Reed RM, Netzer G, Hunsicker L, Mitchell BD, Rajagopal K, Scharf S, Eberlein M. "Cardiac size and sex matching in heart transplantation: Size matters in matters of sex and the heart." J AM COLL CARDIOL HF, January 8, 2013, [DOI: 10.1016/j.jchf.2013.09.005](https://doi.org/10.1016/j.jchf.2013.09.005)

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