Influence of Donor Sex and Mechanism of Death on Cardiac Transplant Recipient Early pAMR Incidence and Cardiovascular Death

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Purpose

Recent studies indicate that both donor and recipient innate immune responses participate in initiating and accelerating adaptive immune responses. Hypoxia is the primary stimulus for elaboration of reactive oxygen species (ROS). ROS activates the innate immune systems of the donor (in the allograft) and the recipient (during ischemia reperfusion) which unleashes a systemic inflammatory state. We sought to investigate donor mechanism of death (MOD) as a predictor of adverse recipient outcomes using in depth donor chart review. Based on previous work, we also investigated the effect of donor sex on recipient outcomes.

Methods

We analyzed charts of local adult (18-64) donors in a database on 711/1135 donors where adequate data was available. We linked records to recipients and their adverse cardiac outcomes including cardiovascular (CV) death by UNOS criteria. We also looked at the incidence of early antibody-mediated rejection (pAMR) after transplant (>2 episodes in 90 days post transplant). Data was analyzed using logistic regression, log rank test of differences and Tukey Contrasts.

Discussion

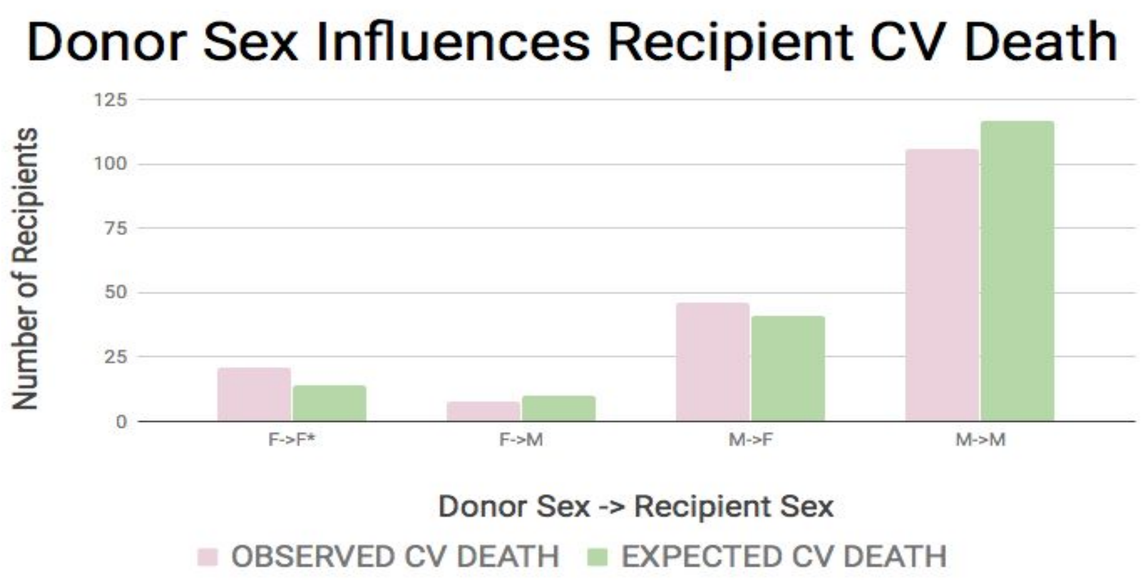
The data show that that female donor hearts, especially when transplanted into female recipients result in a higher incidence of recipient cardiovascular death, and have a higher observed frequency of early pAMR. Early pAMR is associated with a higher incidence of CV death. Female donors and recipients have stronger innate immune responses and might trigger stronger alloimmune responses in recipients.

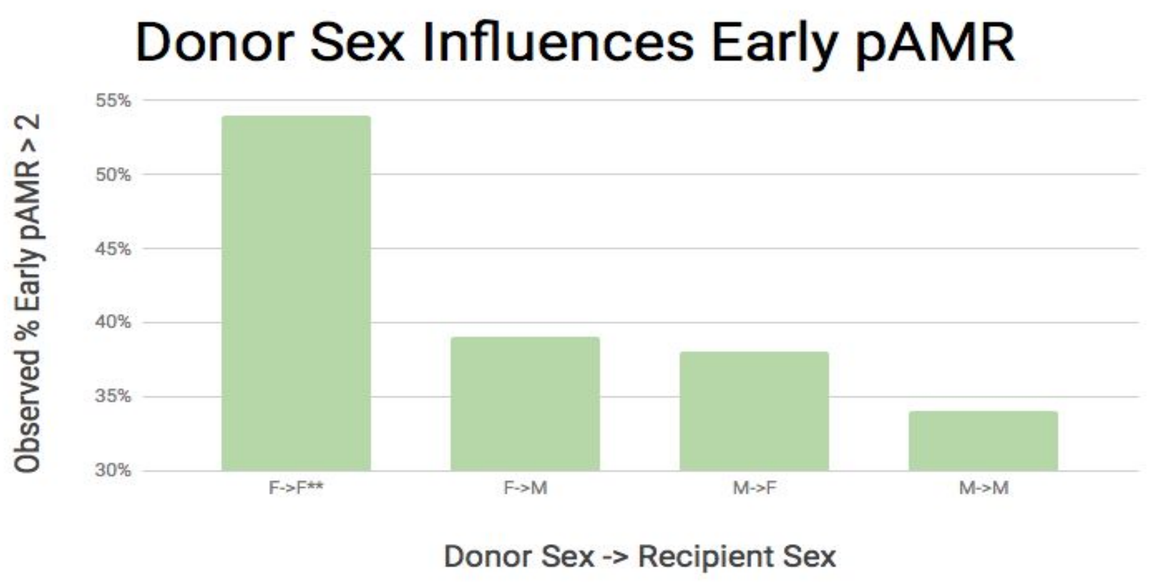
Donor MODs associated with serious trauma (MVA and ICH) led to CV death more frequently. The donor MOD most strongly associated with early pAMR was ICH. Coagulation system defects are present in donors with ICH. These defects, expressed by increased fibrin deposits in the heart, are more likely to lead to early pAMR in the recipient. Triggering of the coagulation system is a fundamental part of the innate immune response.

Conclusion

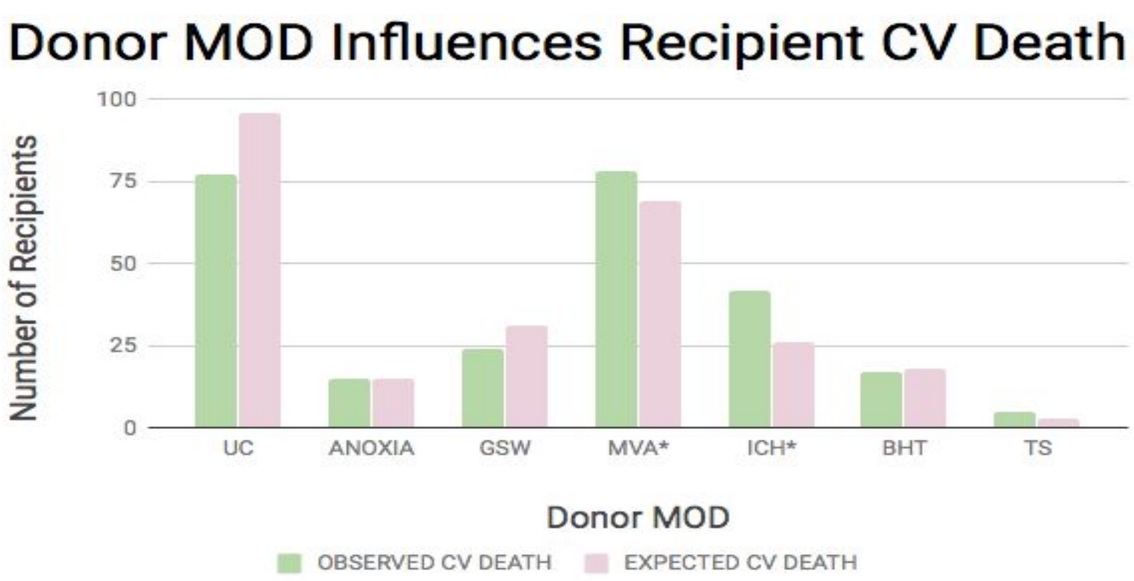
Female donors produce worse outcomes in recipients, likely because of their heightened immune responsiveness. Any MOD with long standing and/or severe trauma (MVA and ICH) activate the innate immune responses of the donor which predisposes recipient for pAMR or CV death. A shift in provider awareness to mind donor risk factors might help improve recipient outcomes.

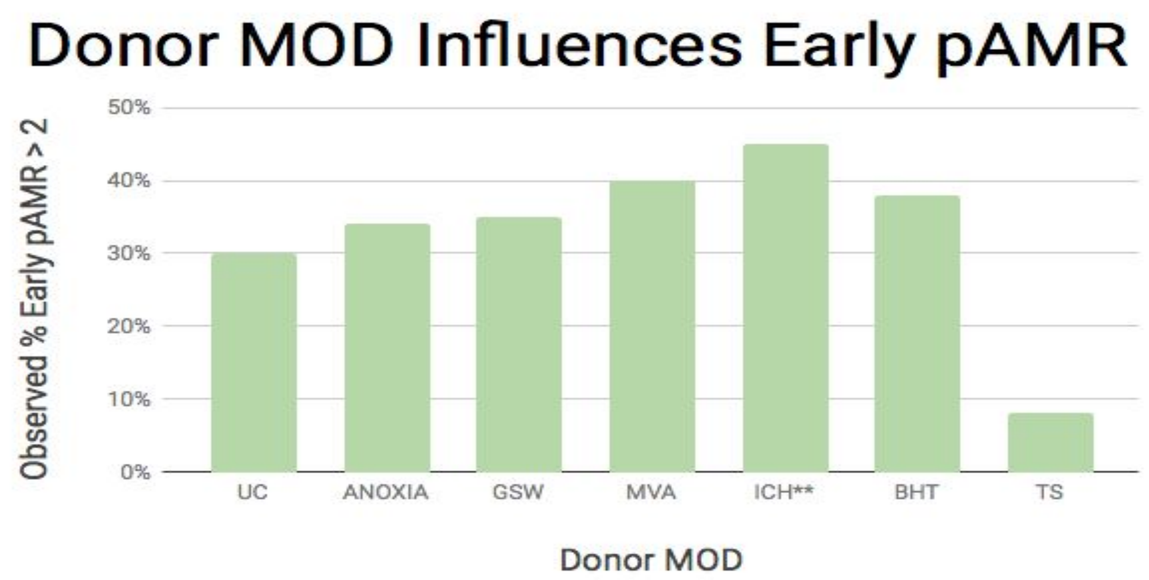
Results





*p=0.048 by log rank test for donor sex; p=0.083 for recipient sex **p =0.0496 FF vs MM by Tukey Contrasts (expected versus observed events)





*p<0.007 versus unclassified MOD for CV death **p<0.002 (pAMR compared to unclassified MOD)

UC=Unclassified, GSW=Gunshot Wound, MVA=Motor Vehicle Accident, ICH=Intracranial Hemorrhage, BHT=Blunt Head Trauma, TS=Tumor Surgery. Unclassified MOD represents the donors whose records did not specify MOD. This was used as the control group for the study.

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