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The association of donor vasoactive drugs with pancreas transplant graft survival

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Introduction

- Vasoactive drugs (VaD) are commonly used to correct abnormal haemodynamics of organ donors in Intensive Care Units (ICU).
- VaDs can differentially affect insulin secretion positively (dobutamine) or negatively (noradrenaline).

Aim

- We hypothesised that some VaDs might induce beta-cell stress/death and be associated with adverse pancreas transplant outcomes.
- We aimed to assess relationships of VaD use to pancreas transplant graft survival.

Methods

- We used Cox-regression in UK Transplant registry data (2004-2016) to assess associations between use of five VaDs and covariate-adjusted pancreas graft survival (median follow-up: 3 years) before and after correction for multiple testing (p-value threshold: <0.01).

Results

- In 2271 pancreas transplant donors, VaDs were used in the following numbers (proportions): dobutamine 80 (3.5%), dopamine 87 (3.8%), adrenaline 167 (7.4%), noradrenaline 1657 (73.0%) and vasopressin 1273 (56.1%).
- Use of adrenaline, dopamine and vasopressin were not related to graft survival.

Noradrenaline use vs non-use

Noradrenaline use was associated with better graft survival after adjusting for:
- Donor variables HR (95%CI): 0.65 (0.43-0.98), p=0.004
- Donor and recipient variables - HR (95%CI): 1.35 (1.05-1.72), p=0.018
- Donor and recipient variables and cold ischaemic time - HR (95%CI): 1.30 (1.003-1.67), p= 0.048; (but not after correction for multiple testing)
- (Cox-regression analysis)

Dobutamine use vs non-use

Dobutamine use was associated with poorer graft survival after adjusting for:
- Donor variables HR (95%CI): 0.65 (0.43-0.98) p=0.039;
- But this relationship became non-significant after further adjustment for recipient variables and cold ischaemic time.
- (Cox-regression analysis)

Conclusions

- Noradrenaline use was associated with better graft survival in models adjusting for donor and recipient variables but not after correcting for multiple testing.
- Further research is required to replicate these findings and establish whether relationships are truly significant and causal before any change in practice is made.
- Better outcomes associated with noradrenaline use could be explained by inhibition of pancreatic insulin secretion thereby resting beta-cells at a time of high metabolic stress.