Insulin therapy in pancreas donors as a predictor of subsequent transplant outcome

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Introduction

- Brain stem death causes high levels of systemic catecholamines and inflammation affecting all organs.
- Hyperglycaemia following brain death is common and is managed with insulin in about half of all donors.

Aim

- We hypothesised that donor insulin use (DIU) is a marker of irreversible pancreatic beta-cell death.
- We aimed to assess relationships of DIU to pancreas transplant outcome and function.

Methods

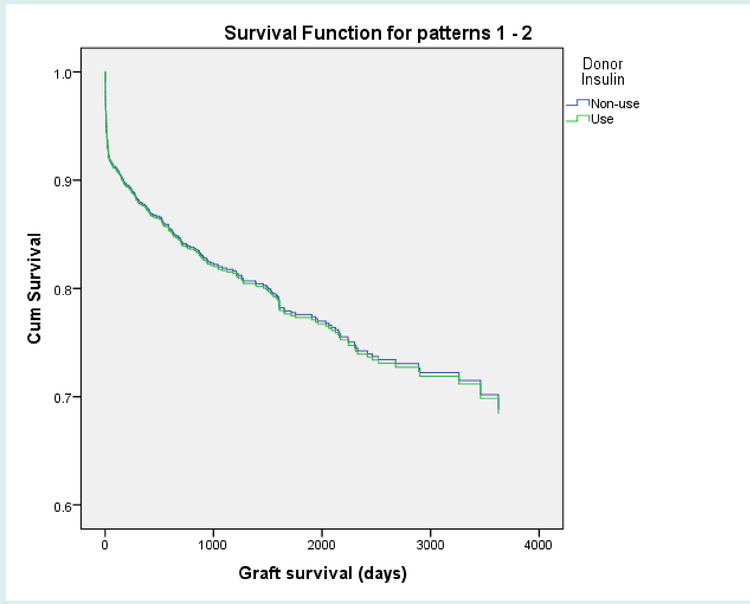
- National data from the UK Transplant registry (2004-2016) was reviewed retrospectively to determine donor variables associated with DIU and its relationship with graft survival.
- Early non-technical graft failure (transplant pancreatitis) was assessed from histology reports using our regional data.
- In a sub-group, we determined relationships between DIU and early c-peptide secretion.

Results

Table 1: Donor variables associated with insulin use in intensive care

	Donor insulin use in intensive care		p-value
	Yes (n= 1005)	No (n = 938)	(univariate)
Donor variables			
Age	**35.65 (SD 13.14)**	**34.17 (SD 13.85)**	**0.016**
Sex (male)	**460 (45.8%)**	**507 (54.1%)**	**<0.0001**
Ethnicity			
White	917 (93.5%)	875 (95.2%)	0.126
Asian	24 (2.4%)	14 (1.5%)	0.151
Black	16 (1.6%)	11 (1.2%)	0.577
Other	24 (2.4%)	19 (2.1%)	0.161
BMI	23.49 (SD 3.58)	23.77 (SD 3.57)	0.085
Smoking (Y/N)	496 (50.1%)	479 (52.1%)	0.391
Alcohol (Y/N)	69 (7.2%)	83 (9.3%)	0.088
Hypertension (Y/N)	74 (7.5%)	89 (9.7%)	0.083
Cardiac disease (Y/N)	34 (3.5%)	26 (2.9%)	0.474
Cardiac arrest (Y/N)	**275 (28.2%)**	**299 (33.4%)**	**0.015**
Creatinine	81.29 (SD 47.8)	82.04 (SD 51.87)	0.78
Peri-retrieval hypotension	**660 (67.0%)**	**542 (61.0%)**	**0.004**
Donor Type (DBD)	**909 (90.4%)**	**699 (74.5%)**	**<0.0001**
Cause of death			
Trauma	**140 (13.9%)**	**180 (19.2%)**	**0.002**
Meningitis	**35 (3.5%)**	**11 (11.7%)**	**0.0001**
Stroke (thrombo-embolic)	62 (6.2%)	47 (5.0%)	0.2579
Intracranial haemorrhage	516 (51.3%)	454 (48.4%)	0.1669
Hypoxic brain damage	**173 (17.2%)**	**195 (20.8%)**	**0.0049**
Brain tumour	14 (13.9%)	14 (1.5%)	0.86249
Other	58 (57.7%)	34 (3.6%)	0.0025

Figure 1: Donor-recipient variable adjusted survival plot according to donor insulin use or non-use

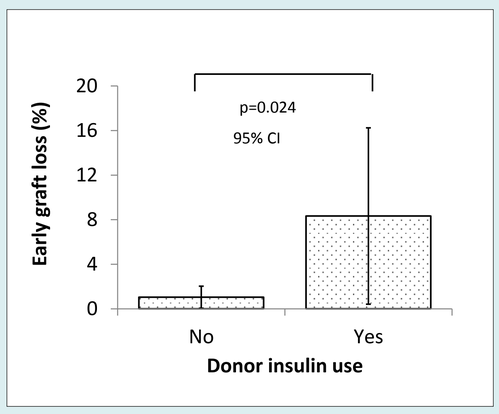


Insulin *vs.* non-insulin use (Cox Regression)

There was no difference in graft survival (median follow-up: 3 years) by DIU:

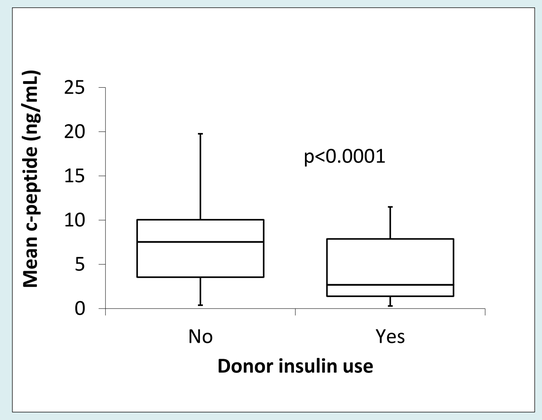
- donor variable-adjusted HR (95%CI), : 0.93 (0.76-1.14), p=0.684
- donor and recipient variable-adjusted HR 1.0, (0.77-1.29), p= 0.978

Figure 2 – Early non-technical graft loss according to donor insulin use



Proportion failing: with vs. without insulin: 6/72 (8.3%) *vs* 1/96 (1%) p=0.024).

Figure 3 – c-peptide at 72 hours post-transplant according to donor insulin use



In a sub-group (n=46), C-peptide levels in insulin *vs* no insulin donors: 4.3 vs. 7.5 ng/mL, p<0.001).

Conclusions

- DIU could be a useful clinical predictor of early pancreas graft outcome and function.
- Further understanding of the physiological processes causing hyperglycaemia in donors could improve donor selection and lead to better outcomes.