P-14.04
LIMITING WARM ISCHEMIA TIME IMPROVES ISLET CELL GRAFTS FROM DONOR PANCREASES AFTER CONTROLLED CIRCULATORY DEATH
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Introduction: Islet transplant programs are highly dependent on quality donor pancreases that lead to beta cell isolates containing a sufficiently large number of functional beta cells. Donors after controlled circulatory death (DCD III) are a valuable source for expanding the organ donor pool but they are considered at higher risk for graft dysfunction due to an initial period of warm ischemia. The present study examines whether DCD III impairs pancreatic islet isolation and investigates whether procurement and preservation limits can define a subgroup of DCD III organs equivalent to organs removed after brain death (DBD).

Materials and Methods: Pancreases retrieved by procurement teams affiliated to the Eurotransplant network and shipped to our Beta Cell Bank are retrospectively analysed for donor and procurement characteristics as well as quality control data of islet cell isolates (in particular beta cell yield and clinical transplantation utility). Organs from 141 DCD III and 609 DBD were included for comparative analysis.

Results and Discussion: In our cohort, beta cell yield per DCD III-organ was significantly lower than that per DBD-organ (58 x 10^6 beta cells versus 84 x 10^6 beta cells; p < 0.001), leading to a lower clinical utility rate (34% versus 42%) which can at least partially be attributed to an initial period of warm ischaemia. In the DCD III subgroup, both these outcome parameters are negatively correlated to the duration of acirculatory warm ischemia time (WIT), defined as the time elapsed from circulatory arrest to initiation of organ preservation (r = -0.197, p = 0.010), rather than to the duration of the agonal phase. When acirculatory WIT was limited to ten minutes (68/141), transplantation utility was similar to that in the DBD group (being 44%). When also restricting pancreaticectomy time (≤ 70min) and cold ischaemia time (≤ 9h), two parameters known to influence organ quality, DCD III organs (43/141) also yield the same amount of beta cells as DBD organs (75 x 10^6 beta cells; p = 0.413).

Conclusion: Selecting DCD III organs for clinical islet cell graft preparation on their acirculatory WIT, pancreaticectomy time and CIT, helps to avoid wasting efforts and resources on excluded organs and leads to isolates that meet similar quality control data as those prepared from DBD.


P-14.05
TREATMENT OF RODENT PANCREATIC ISLETS WITH NECROSTATIN-1 DELAYS XENOGRAFT ISLET GRAFT REJECTION
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Introduction: Intense research is currently focused on preventing graft loss following islet xenotransplantation, a potential treatment for Type I diabetes (TID). The addition of Necrostatin-1 (Nec-1), a potent inhibitor of necroptosis, to pancreatic islet culture media could promote islet survival and potentially improve islet function during culture. We aim to assess whether short-term culture with Nec-1 could improve the recovery and insulin secretion behavior of isolated Sprague-Dawley (SD) rat islets, and whether it improves graft survival in streptozocin (STZ)-induced diabetic mouse model.

Methods: Islets were isolated from pancreas of 250-300g male SD rats and cultured for up to 3 days. Control islets were cultured with CMRL-1066 + 10% serum while experimental islets were cultured with the same media but supplemented with 100 uM of Nec-1 for a 3-day culture. Islet samples were collected at Day 1 and Day 3 of culture. For islet recovery, islets were counted using dithizone (DTZ) staining. Day 3 untreated/ treated counts were normalized to Day 1. Insulin function was assessed via Glucose Insulin Secretory Release (GISR) assay and displayed as Stimulation index (SI). To assess in vivo engraftment, 500 rat islet equivalent (IE) were encapsulated in single-layer ultra-pure low viscosity high guluronate (UPLVG) alginate and were transplanted into intraperitoneal cavity of STZ-diabetic C57BL/6 mice.

Results: After 3 days of culture the islet recovery was significantly higher for islets treated with Nec-1 compared with untreated (Figure 1).

Fig. 1.

A significant reduction in insulin SI was observed between Day 3 control and Day 3 Nec-1 treated (Figure 2A) and a reduction in SI values was observed between Day 1 untreated and Day 3 untreated (Figure 2B) which not observed between Day 1 untreated and Day 3 untreated.