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LETTER TO THE EDITORS

Report of the first five DCDD pancreas transplants within the Eurotransplant region; excellent results with prolonged first warm ischemia times

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Dear Sirs,

The success of pancreas transplantation has led to an increased number of pancreas transplantations, which again has led to an increased need for suitable pancreas allografts. This initiated a search for alternative ways to increase the number of pancreas donors. Donation-after-circulatory-determination-of-death (DCDD) is such an alternative and is a recognized form of transplantation with regard to kidney, liver, and lung transplantation. However, there is limited experience with DCDD in pancreas transplantation [1–6]. A large study with Scientific Registry of Transplant Recipients (SRTR) data showed DCDD-status to have a marginally significant risk (HR 1.39; $P = 0.10$) compared with a donation-after-brain-death (DBD)-donor [1]. Nevertheless, similar patient survival and graft survival rates between DBD and DCDD-groups at 1-year, 5-years [2,3,6], and even 10-years follow-up [5] have been reported. Results describe higher rate of renal complications such as delayed graft function (DGF) or urinary tract infections [2,3] after DCDD transplantation, however, there were no higher rates in pancreas-related complications [2,5]. Interestingly, these reports are always with rather short 1st warm ischemia times (WITs), ranging from 14 min [4] to 21 min [5].

Within the Eurotransplant region DCDD is only performed in Austria, Belgium, and The Netherlands. In February 2011, the first DCDD pancreas transplantation within the Eurotransplant region was performed in our center. Since then four more DCDD pancreas transplantations were performed.

All five allografts were procured from DCDD-donors in The Netherlands. Pancreas allografts were matched and offered via Eurotransplant. Donor, transplant, and recipient characteristics are shown in the Table 1. HTK perfusion-fluid was used in all procedures. All patients were treated with alemtuzumab (Campath) induction-therapy and maintained on duo therapy, consisting of tacrolimus and mycophenalate mofetil.

At 1-year follow-up all recipients are alive with optimally functioning pancreas and kidney allografts. There were no perioperative complications. Three pancreas allografts were enteric-drained and two were initially bladder-drained and converted to enteric drainage afterward, according to a two-step protocol [7]. All patients had immediate pancreas function, measured as peroperative lowering of the blood glucose levels, and, except for the fourth recipient, all SPK-patients had immediate kidney function, measured as peroperative diuresis.

There were a few long-term complications: the first patient developed moderate interstitial and vascular rejection after 3 months, which was treated with antirejection therapy consisting of methylprednisolone. The third recipient developed a hematoma near the pancreas allograft, for which he was reoperated twice. After 2 months this recipient developed acute kidney insufficiency because of a ureteral stricture caused by a renal BK-infection, for which he was reoperated and reinsertion of the ureter to the bladder was performed. After lowering the immunosuppressive therapy, this recipient developed an interstitial rejection episode of the kidney, which was treated with methylprednisolone. The fourth recipient had a DGF of the kidney, for which he was treated with dialysis on days 2, 3, 4, and 6 postoperatively. After 6 weeks, a CT-scan showed a distal, partial venous thrombosis in the splenic vein, for which anticoagulant therapy (coumarine) was started liberally. The fifth recipient showed acute respiratory insufficiency because of a rhinovirus-infection 2 days after the operation, for which he was shortly admitted to the intensive care unit (ICU). HbA1c-values at 3-months follow-up were normal (mean of 32.6 mmol/mol) and most recent values are still within the normal ranges for all patients.

Most of the postoperative complications our recipients experienced are not necessarily directly related to DCDD-allografts. Only DGF of the kidney in the fourth recipient is seen more often after DCDD transplantation [2,3,5]. Although DCDD pancreas transplantation is not a new concept worldwide, only few reports of pancreas transplantation using allografts from DCDD-donors have been published [1–5]. Within Europe, UK-Transplant has the largest series of DCDD pancreas transplantation [8], with

Table 1. Donor, transplant, and recipient characteristics of all five DCD pancreas transplants.

	Donor 1	Donor 2	Donor 3	Donor 4	Donor 5	Mean
Donor factor						
Age (years)	17	11	25	47	29	26
Gender	Male	Male	Male	Male	Male	n/a
BMI	21	18	25	25	22	22
COD	CVA	Trauma	Trauma	CVA	Meningitis	n/a
Cardiac arrest	+	+	–	–	–	n/a
Amylase (U/l)*	117	20	128	215	229	142
Creatinine (μmol/l)*	100	50	76	50	76	70
Sodium (mmol/l)*	153	152	143	150	140	148
Albumin (g/l)*	48	22	28	33	25	31
ICU-stay (days)	1.9	4.1	2.4	2.9	1.7	2.6
P-PASS	15	12	15	18	14	15
PDRI	1.26	1.31	1.23	2.45	1.37	1.5
Transplant factor						
Allocation	Regional	Regional	Regional	Regional	Regional	n/a
Pancreas CIT (h)	10	6	12	11	10	9.6
Kidney CIT (h)	9	6	11	10	n/a	9
1st WIT (min)†	19	11	19	15	10	15
1st WIT (min)‡	39	22	38	31	30	32
Transplant type	SPK	SPK	SPK	SPK	PAK	n/a
Exocrine drainage	Bladder	Enteric	Enteric	Bladder	Enteric	n/a
Recipient factor	Rec. 1	Rec. 2	Rec. 3	Rec. 4	Rec. 5	
Age (years)	54	39	39	36	41	42
Gender	Male	Female	Male	Female	Male	n/a
Cardiovascular history	–	–	–	–	–	n/a
Dialysis	Pre-emptive	Pre-emptive	HD >2 years	HD >1 year	PD >5 years	n/a
Time on waiting list (months)	16.8	15.1	19.5	18.5	17.3	17.4
Complications	Rejection (vascular and interstitial)	No	Hematoma and reoperation; BKI and urethral stricture; rejection (interstitial)	DGF; partial venous thrombosis	Rhinovirus upper airway infection	n/a
Hospital stay (days)	37	14	35	26	14	25
HbA1c (mmol/mol)§	35	33	30	33	32	33
Creatinine (μmol/l)§	101	71	105	103	179	112
eGFR (ml/min/1.73 m^2)§	>60	>60	>60	52	36	n/a
Anticoagulant therapy	–	–	–	+	–	n/a

BMI, body mass index; CIT, cold ischemia time; COD, cause of death; CVA, cerebrovascular accident; DCDD, donation-after-circulatory-determination-of-death; HD, hemodialysis; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; n/a, not available; P-PASS, preprocurement pancreas allocation suitability score; PDRI, pancreas donor risk index; SPK, simultaneous pancreas-kidney; WIT, warm ischemia times.

*Most recent lab value.

†According to Eurotransplant definition (time from cardiac death till start of cold perfusion).

‡As described in American literature (time from withdrawal of ventilatory support till start of cold perfusion).

§First known value after 3 months postoperative; lab values measured on same day.

17% of all pancreas transplantations in 2010 being from DCDD-donors [9]. In the Eurotransplant region, our center is the first to use DCDD pancreas allografts for (vascularized) pancreas transplantation.

The pancreas allografts described here, all originated from young donors (mean age 26 years), and were transplanted with rather short CITs (mean 9.6 h). As this was our first experience with DCDD pancreas transplantations, we only accepted allografts without known risk factors (e.g. high donor age or long CIT). In the future, it might be possible to extend these limits, as is currently also seen in DCDD liver transplantation.

One of the remarkable findings was the long 1st WIT of the donor allografts. Mean 1st WIT was 32 min (range 22–39) when calculated as time from withdrawal of ventilatory life support (WVS) to start of cold perfusion and 15 min

(range 10–19) when calculated as time from donor cardiac arrest to start of cold perfusion. Our results show that, even with longer WITs we had excellent post-transplantation results: 100% patient and graft survival, so far. Whereas in European literature 1st WIT is commonly defined as the period between cardiac arrest and cold perfusion, in American literature [10] the period from WVS to start of cold perfusion is used. When using this "American" definition, the mean WIT was almost twice as long as compared to the mean WITs in previous reports from the United States and Australia [2,4,5]. This longer WIT has most likely a logistical cause; such as extra time needed for transferring the donor from the ICU to the OR. Current practice in The Netherlands is that WVS occurs in the ICU and the donor is only transferred to the OR after circulatory death is confirmed.

Four allografts were procured by regional teams and one allograft was procured by our own team. This was actually the donor with the highest PDRI (2.45). Specifically this case supports our opinion that a donor allograft should never be declined beforehand, solely based on preprocurement factors or a risk model such as the P-PASS or PDRI. The ultimate decision lies with the accepting physician or transplant surgeon.

Based on these first results we are confident that DCDD pancreas transplantation has the potential to increase the number of available pancreas allografts and we will certainly continue to use DCDD pancreas allografts for transplantation, even with the longer 1st WITs that we usually face.

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