TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Organ donation: when should we consider intestinal donation

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Keywords
deceased donor, intestinal donor profile, intestinal transplantation, multivisceral transplantation, small bowel transplantation.

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Conflicts of Interest
The authors disclose no commercial association that may pose a conflict of interest in connection with the submitted manuscript.

Received: 7 March 2012
Revision requested: 3 May 2012
Accepted: 8 August 2012
Published online: 21 September 2012

doi:10.1111/j.1432-2277.2012.01556.x

Summary

Although more than 2300 intestinal transplantations (IT) have been performed worldwide, a description of intestinal donor criteria is still missing. This causes confusion among transplant coordinators, OPOs, physicians at intensive care unit and transplant surgeons. A Med-line search looking for publications about donor criteria or donor selection in human IT was performed in December 2011. Retrospective analysis of 39 deceased donors from whom, in the period January 2006–December 2011, 20 isolated intestinal grafts and 19 multivisceral grafts were recovered and successfully transplanted. Review of the Literature: Among 3504 publications about IT, no study reported specifically about intestinal donor profile. The most commonly cited donor criterion was age, while all other criteria were inconsistently discussed. Based on the collected data, we suggest following inclusion criteria for donation of IT grafts: age 0–50 years, ICU-stay <1 week, no blunt abdominal trauma, most recent Sodium <155 mmol/l, no severe ongoing transfusion requirements, standard donor therapy including early enteral nutrition and a compatible donor–recipient size match. By providing simple criteria for intestinal donation from deceased donor, we may help to properly utilize the limited donor pool.

Introduction

Intestinal transplantation (IT) in the form of isolated intestinal (IIT) or multivisceral transplantation (MVT) represents nowadays a clinical reality utilized for many indications with more than 50% of the recipients being children [1–3]. Between 2000 and 2011, 74 ITs have been performed in Germany at 10 centres.

Although more than 2300 ITs have been performed worldwide, the field of transplantation still lacks a description of intestinal donor criteria. Only single-centre experiences and personal communications have been reported until now [2,4–13]. A simple definition of 'inclusion-criteria' to be considered during donor evaluation would be an indispensable tool for all members of the medical community involved: coordinators, organ procurement organizations (OPO), physicians at the intensive care unit (ICU) and transplant surgeons.

The aim of our study was to address this deficiency through a retrospective analysis of donor-evaluation of 39 deceased ITT/MVT donors in Germany whose organs were successfully transplanted during the last 6 years and

to compare these results with the ones reported internationally through a systematic review of the literature.

Patients and methods

Review of the literature

Med-line search using the key-words 'intestinal', 'transplantation', 'small bowel', 'donor', 'criteria', 'selection', was performed in December 2011. Publications about IT in humans were reviewed for investigating donor criteria or donor selection.

Personal experience

We performed a retrospective analysis of 39 deceased donors from whom, in Germany, in the period January 2006–December 2011, 20 isolated intestinal (II) grafts and 19 multivisceral (MV) grafts were recovered and successfully transplanted. II grafts were defined as including the small bowel with or without a colon-segment; while MV grafts included the II graft with other abdominal organs (e.g. intestine + liver (*en bloc* or separated) or intestine + liver + pancreas + stomach + duodenum *en bloc* or intestine + pancreas + stomach + duodenum *en bloc*).

Data were extracted from the anonymized database of the German OPO–Deutsche Stiftung Organtransplantation (DSO)–according to the donor information form as suggested by the European Committee of Experts on Organ Transplantation [14]. Data were analysed for every donor including recipient demographics and initial graft function (at 30 days and 1 year).

Continuous variables were presented as median and range (minimum–maximum) and ordinal variables as absolute number and percentage. Graft function rates were calculated according to the Kaplan–Maier method.

Results

Review of the literature

Among 3504 publications about IT (keywords 'intestine' 'donor'), only 32 reported about human IT matching the keywords 'intestinal', 'transplantation', 'donor', 'criteria', 'selection' and 'small bowel'.

There was no detailed study specifically aimed at defining an intestinal donor profile. The intestinal donor criteria extracted from our analysis of the international literature are outlined in Table 1.

Only 4 centres reported about their own large series (i.e. Pittsburgh $n = 500$, Miami $n = 141$, Washington $n = 67$ and Indianapolis $n = 57$) and mentioned about donor issue in different kinds of recipients [4, 9, 11, 27, 41–44].

The Pittsburgh group reported for the first time in 1997 about donor's risk factors affecting the early outcome in 72 patients who received 77 intestinal grafts. They showed that high vasopressor, prolonged cold ischaemia time, and high sodium affected the early graft survival and intestinal graft injury [42]. This was the first paper correlating donor data with outcome. As the same group in 2009 reported about 500 cases of intestinal and MVT, the only donor's variables reported but not further discussed were a young age (mean age of 16.6 years) and ABO-blood type identity.

In the Miami series with 141 paediatric intestinal and MVT, only the following donor's parameters were described, but nowhere discussed or correlated with outcome (neither early nor late) : a median donor age of 1.67 years, a median donor/recipient body weight ratio range of 1.04. HLA match was not considered a relevant factor [9].

The Washington group analysed their own series of 67 ITs and compared the outcome of 12 grafts from donors who underwent cardiopulmonary resuscitation versus 55 who did not. The authors concluded that a donor history of cardiac arrest and consequent CPR should not automatically exclude the use of the intestine graft for transplantation [11].

The Group from Indianapolis analysed the outcome of IT and MVT in correlation with the solution used to perfuse the grafts (i.e. UW-Solution in 22 vs. HTK-Solution in 35 cases). The authors showed no difference in patient and graft survival at POD 30 and POD 90 after transplantation. Additionally, no differences was noted in initial function, endoscopic appearance, rejection episodes or transplant pancreatitis in case of MVT [27].

In summary, the various reports of individual donor series revealed a total of 8 different donor criteria [i.e. (i) age, (ii) body weight or donor/recipient body weight ratio, (iii) ICU-stay, (iv) cause of death, (v) cardiac arrest or CPR, (vi) hypernatraemia, (vii) blood group identity and (viii) HLA-match). No more than 4 criteria were considered in any single report. The most commonly cited donor criterion was age, while all other criteria were inconsistently discussed.

Personal experience

Detailed donor data are reported in Table 2. All donors (15 male and 24 female) were heart-beating brain-dead deceased donors. The median age was 21 years. (8 months–51 years.), height 170 cm (78–195), weight 63 kg (11–85) and body mass index (BMI) 21 kg/m^2 (14–25). Most of the recipients (90%) were older than 18 years of age.

Table 1. Review of the literature containing specific data about donor inclusion criteria for intestinal procurement.

	Donor age	Size match	ICU-stay	Cause of death	Vasopressors, cardiac arrest	Laboratory parameters	Other findings
§Todo *et al.* [44] 1994							Donor criteria equivalent to liver donor in 1994
§Furukawa *et al.* [42] 1997 and Casavilla *et al.* [41] 1993, (*n* = 77)	range 0–48 years	NR	range 1–21 days	NR	High-dose vasopressor at recovery detrimental, no comment on cardiac resuscitation (10 of 77 cases)	hypernatraemia detrimental	prolonged ischaemia times detrimental
§Abu-Elmagd *et al.* [43] 2001, (*n* = 165)							All AB0 identical except 1: HLA-match at random; CMV D+ accepted in MVT or Liver-IT
§Abu-Elmagd *et al.* [4] 2009, largest single-centre report of IIT/MVT (*n* = 500)	16.6 ± 13.6 years (range 0.01–54 years)	NR	NR	NR	NR	NR	6 AB0 compatible, 494 AB0 identical 440 UW, 60 HTK: with HTK risk for graft pancreatitis in MVT
Farmer [6] 2008	13.3 ± 8.4 years	donor < recipient weight ratio: (0.95 ± 0.5)	NR	NR	no significant down-time, cardiac arrest, inotropic support	NR	NR
Gondolesi *et al.* [7] 2008 (review of other studies)	NR	donor 50–75% of recipient	NR	NR	DCD not preferred	NR	NR
Jan, Renz [8] 2005 (review of other studies)	NR	donor <50–75% of recipient	NR	NR	NR	NR	procurement quality important
Kato *et al.* [9] 2006, IIT/MVT in children (*n* = 141)	range 0–59 years	donor weight: 11 (2.7–67) kg	NR	NR	NR	NR	Graft size reduction and AB0 compatible IIT/MVT for overcoming mismatch; HLA-match at random; CMV D+ accepted
Mangus *et al.* [27] 2008 : UW (*n* = 22) vs. HTK (*n* = 35)	0–18 years *n* = 41, >18 years *n* = 16	donor weight <25 kg *n* = 16	NR	60% traumatic	NR	NR	No difference in outcome; no pancreatitis in MVT with HTK or UW
Matsumoto *et al.* [11] 2008: donors with CPR (*n* = 12) vs. donors without CPR (*n* = 55)	CPR: 7.7 ± 12.6 years (6 weeks–44 years) without CPR: 10.4 ± 12.7 years	NR	CPR 115 ± 62 hrs (>1 week) without CPR 97 ± 86 h	CPR: 50% hypoxia without CPR: 75% traumatic	CPR 19 ± 13 (1–52) min	CPR: Na 146 ± 12*, terminal ASAT/ALAT <100‡ without CPR: Na 144 ± 10*l	2 nonsurvivors with 15/25 min CPR and ICU stay 55/16 h

Table 1. continued

	Donor age	Size match	ICU-stay	Cause of death	Vasopressors, cardiac arrest	Laboratory parameters	Other findings
Mazariegos *et al.* [34] 2010: realized IIT/MVT donors, (*n* = 1347, 1998–2008, USA)	0–50 years	NR	NR	NR	<3 vasopressors at cross-clamp, CPR <15 min after brain death, no DCD	Na <170*, ASAT/ALAT <500‡, Creatinine <2†	NR
Nieuwenhuijs *et al.* [12] 2008 (review of other studies)	<50 years	donor < recipient	NR	NR	No prolonged haemodynamic instability, no-minimal inotropic support	NR	Brain death causes SIRS and organ dysfunction: requires donor therapy
Platz, Mueller [45] 2005, (*n* = 14)	<50 years	donor BMI < 25 kg/m^2	<7 days	NR	Stable donor	NR	enteral nutrition (50 ml/h) as immunonutrition
Yersiz *et al.* [13] 2003 (review of other studies)	NR	NR	NR	NR	No–minimal vasopressor requirement	Na < 160*‖	SDD, systemic antibiosis

CPR, cardio pulmonary resuscitation; NR, not reported; SDD, selective decontamination of the gut.
*mmol/l.
†mg/dl.
‡U/l.
§Series of single-centre reports regularly updated with inclusion of most recent experience in intestinal donor selection.

Table 2. Donor and recipient data.

Variable	Median (Range) or *n* (%)
Donor (*n* = 39)	
Female/Male	24 (62)/15 (38)
Age (years)	21 (0.6–51)
Donor <18 years	17 (44)
Height (cm)	170 (78–195)
Weight (kg)	63 (11–85)
BMI (kg/m^2)	21.2 (13.9–25.4)
ICU-Stay (admission–cross-clamp h)	52.4 (20.9–242.3)
Brain death certified–cross-clamp (h)	14.1 (7.6–33.7)
Cause of death (*n* = 20)	
Trauma	17 (44)
Cerebrovascular accident	14 (36)
Ischaemic stroke	3 (8)
Anoxia	3 (8)
Meningitis (Neisseria)	1 (2)
Thrombosis of cerebral veins	1 (2)
Abdominal pathologies	
Hip fracture + retroperitoneal haematoma	1 (2)
VP-shunt for many years	1 (2)
Cardio-thoracic pathologies	
Thoracic trauma (inclusive lung contusion)	7 (18)
Aspiration/pneumonia	6 (15)
Pulmonary embolism	1 (2)
Asthma, recurrent pneumonias	1 (2)
Plaques in aorta ascendens	1 (2)
Cardiac arrest due to cardiac reasons	2 (6)
Poor cardiac output for cerebral reasons	7 (18)
Other pathologies (multiple counts)	
Intra-cerebral vascular malformation	2 (5)
Epilepsia/hydrocephalus since birth	1 (2)
Trauma to peripheral extremities	7 (18)
Vertebral fracture	2 (5)
Anti-HBc and anti-HBs reactive	1 (2)
Nonreactive HIV- and HCV-NAT (HRD-donor)	2 (5)
Arterial hypertension	3 (8)
Smoking	6 (15)
Alcohol abuse	1 (2)
Diabetes	0 (0)
Haemodynamic parameter	
Mean arterial pressure (mmHg, *n* = 39)	88 (65–115)
Diuresis (ml/kg BW/h, *n* = 39)	2.8 (1.2–12.3)
Central venous pressure (mmHg, *n* = 25)	3 (–7 to 15)
Laboratory data (most recent)	
Haemoglobin (g/dl, *n* = 39)	10.8 (7.6–15.5)
White blood cells (G/l, *n* = 39)	14.7 (6.2–47.7)
Platelets (G/l, *n* = 39)	156 (28–429)
Peak sodium last 24 h (mmol/l, *n* = 39)	150 (133–166)

Table 2. continued

Variable	Median (Range) or *n* (%)
Most recent sodium (mmol/l, *n* = 39)	148 (119–166)
Creatinine (mmol/l, *n* = 39)	61.9 (15.9–97.2)
CK (U/l, *n* = 33)	340 (14–7874)
CKMB (U/l, *n* = 30)	37 (2–664)
Troponine (ng/ml, *n* = 25)	0.1 (<0.01–6.0)
ASAT (U/l, *n* = 38)	42.5 (9–653)
ALAT (U/l, *n* = 39)	23 (8–318)
yGT (U/l, *n* = 38)	18 (8–116)
Bilirubine (μmol/l, *n* = 39)	9.6 (1.5–34.0)
Amylase (U/l, *n* = 31)	55 (17–504)
Lipase (U/l, *n* = 36)	19.5 (4–270)
PT (measured as Quick in %, *n* = 39)	71 (44-114)
CRP (mg/l, *n* = 37)	99 (18–284)
PaO_2/FIO_2 (mmHg, *n* = 39)	452 (88–586)
pH (*n* = 38)	7.40 (7.19–7.64)
HCO_3 (mmol/l, *n* = 37)	24.5 (20.0–33.0)
Base excess (mmol/l, *n* = 38)	−0.05 (−5.70 to 8.60)
Anti-CMV reactive (*n* = 39)	17 (44)
Anti-EBV-VCA-IgG reactive (*n* = 36)	34 (94)
Anti-toxoplasmose reactive (*n* = 38)	15 (40)
Echocardiography (*n* = 36)	
No pathology	23 (64)
Regional hypo-/akinesia	11 (31)
Plaques in aorta ascendens/hypertrophy	2 (7)
Bronchoscopy (*n* = 32)	
No pathology	18 (56)
Aspiration/blood/massive secretion	6 (19)
Inflammation	8 (25)
Recipient	
Female/male	13 (33)/26 (67)
Age (years)	44.5 (3–59)
Recipients <18 years	4 (11)
Donor–recipient weight and size match	
Donor/recipient weight ratio (kg/kg, *n* = 24)	0.88 (0.52–1.72)
Donor/recipient size ratio (cm/cm, *n* = 24)	0.96 (0.68–1.13)
Technical data	
Median ischaemia time (h, *n* = 33)	6.2 h (3.1–12.1)

Most of the donors had normal values of liver enzymes and serum sodium.

The donor–recipient weight ratio (DRWR) was 0.88 (0.52–1.71) and donor–recipient height ratio (DRHR) was 0.96 (0.68–1.13).

The causes of death were traumatic brain injuries in 17 cases (44%) (7 isolated and 10 polytrauma), atraumatic subarachnoid haemorrhage (SAH) in 9 (23%), spontaneous intra-cerebral bleeding (ICB) in 5 (13%), anoxic brain damage due to cardiac arrest in 3 (8%), ischaemic stroke in 3 (8%), Neisseria Meningitis in 1 (2%) and thrombosis of cerebral vessels in 1 (2%).

The average time interval from ICU admission until cross-clamping at the donor operation was 52 h (21–243), i.e. 2 days (1–10).

At the time of hospital admission, 12 (31%) patients (4 head trauma, 5 SAH, 3 anoxia) were hemodynamically unstable (defined as needing multiple transfusions and/or high-dose vasopressors). The 3 head trauma patients underwent an emergency craniectomy, which was associated with severe bleeding and cardio-circulatory complications due to extreme brain oedema. All of the 12 initially unstable donors recovered from their unstable condition within 24 h.

Prehospital cardiac resuscitation was performed in 9 donors (see Table 3 for details): in 3 cases for primary cardiac failure (duration: 15, 15 and 20 min each), in 5 cases secondary to SAH (duration: 1, 5, 10, 10 and 25 min each) and in 1 case secondary to poly-trauma (3 min).

None of the 10 donors with a polytrauma experienced identifiable blunt, direct or deceleration abdominal trauma. These polytrauma donors included pedestrians, motorcyclists and unrestrained motor vehicle passengers. One donor experienced a hip fracture and retroperitoneal haematoma.

Review of preprocurement donor management revealed that donors received the following medications:

1 Vasopressors or inotropic agents: During the 12 h prior to organ recovery, norepinephrine was administered in 25 donors (76%) at an average dosage of 0.08 (0.02–0.6) μg/kg/min and epinephrine in one paediatric donor (5%) at a dosage of 0.14 μg/kg/min. Another paediatric donor received dopamine (4 μg/kg/min) and dobutamine (4 μg/kg/min). Due to neurocardiac injury after SAH one donor received a combination of norepinephrine (0.08 μg/kg/min) and dobutamine (2.08 μg/kg/min).

2 Antibiotics: Treatment was initiated in 22 cases (56%) with therapeutic indication for pulmonary infection in 4, meningitis in 1 and neurosurgery in 4.

3 Steroids: Hydrocortisone or prednisolone were administered in 27 patients (69%).

4 Insulin: Insulin was used for keeping the blood glucose below 160 mg/dl in 15 cases (38%).

5 Desmopressin: Diabetes insipidus required administration of desmopressin in 26 cases (67%).

6 Transfusions: Following admission, blood products were administered in 15 donors (39%) with an average of 5 (2–25) units of erythrocyte concentrate and 3 (0–25) units of fresh frozen plasma.

7 Enteral nutrition: Feeding via the gastrointestinal tract was initiated within 24 h after admission in all cases. Selective intestinal decontamination was not performed.

Before organ recovery, all donors were stable: mean arterial pressure (MAP) 88 mmHg (65–115), pH 7.40

Table 3. Data of the nine donors with prehospital cardiac arrest.

Age (years)/ Gender	Cause of cardiac arrest	Duration of CPR (min)	Time from admission–crossclamp (h)	Norepinephirine* (μg/kg/min)	WBC* G/l	Na^+* mmol/l	ASAT* (U/l)	ALAT* (U/l)	γGT* (U/l)	Lipase* (U/l)	Bili* μmol/l
21 ♂	AR,†	15	105.6	0.1	10.4	138	653	318	116	16	21
7 ♂	AR,†	15	50.7	0.0	14.4	150	269	69	17	7	5
11 ♂	Hypoxia,‡	20	70.6	0.0	6.2	156	141	189	16	126	5.6
23 ♂	Trauma,§	3	57.8	0.036	12	149	111	59	20	20	26.7
36 ♀	SAH,§	1	40.2	0.03	16.3	148	27	20	40	167	14
40 ♀	SAH,§	5	57.2	0.062	17.6	142	30	27	24	39	3
31 ♀	SAH,¶	10	24.9	0.3	15.0	141	108	146	31	13	13
17 ♂	SAH,§	25	72.2	0.0	14.7	141	28	32	31	7	10
24 ♂	SAH,§	10	62.6	0.083	14.8	155	60	15	17	11	12

AR, Arrhythmia; Bili, total serum bilirubine; CPR, cardiopulmonary resuscitation; Na^+, serum sodium; SAH, subarachnoidal haemorrhage; WBC, white blood cell count.
Hypoxia: Cardiac arrest due to hypoxia after strangulation; Trauma: cardiac arrest due to trauma complication.
♂, Male.
♀, Female.
*Most recent data before procurement.
†Heart not considered suitable for transplantation.
‡Heart not allocatable finally.
§Heart used for transplantation.
¶Heart not used due to inferior pumping function intra-operatively.

(7.19–7.64), CVP was 7.0 mmHg (−3 to 15), temperature 36.2° C (35.1–38.8), heart rate 103.5 bpm (50–149) and diuresis 2.8 ml/kg BW (1.2–12.3).

Different scores for organ donors based on graft type were calculated:

1 The liver donor risk index (DRI) [15] was 1.38 (0.91–2.93): 85% of all donors scored above the threshold of 1.0 for an ideal liver donor.

2 Expanded donor criteria (EDC): One donor (3%) met 3 liver specific EDC according to the guidelines of the German Medical Association [16]; 4 patients met 2 criterion (10%), 5 patients met 1 criterion (13%) and 29 none (74%).

3 The pancreas PPASS-score [17] was 14 (10–19): 10% of the donors scored above the threshold of 17 for an ideal donor.

All procured intestinal grafts were transplanted: 20 IIT and 19 MVT. In four cases (2 in IIT and 2 in MVT), the intestinal graft included the ascending and transverse colon.

Abdominal organs were perfused with UW-solution (University of Wisconsin–Belzer Viaspan®; Bristol-Meyers Squibb GmbH, Munich, Germany) in 10 donors [70 ml/kgBW (42–200)] and with HTK-Solution (HTK Custodiol®; Dr Franz Köhler Chemie, Alsbach-Haehnlein, Germany) in 29 [143 ml/kgBW (92–204)].

The time frame from start of donor operation until cross-clamping lasted 133 min (33–241), from cross-clamping until removal of the intestinal graft 31 min (7–68) and from start of donor operation until closure of the body 230 min (149–330). Table 4 summarizes the other organs recovered.

Table 4. Other transplanted organs from the same donors.

Organ	Transplantations	Reason for grafts not transplanted/used
Heart	26 (66.7%)	*n* = 13: 2 arrhythmia, 9 poor function, 1 coronary heart disease, 1 no permission, 1 others
Lung	29* (69.7%)	*n* = 12: 3 trauma, 5 aspiration/ pneumonia, 1 asthma, 1 size mismatch, 2 others
Liver	45† (100%)	–
Pancreas	31 (79.5%)	*n* = 7: 4 SMA-SMV anatomy/lesion, 1 oedema, 3 others
Kidney	77 (98.7%)	*n* = 1:1 atherosclerotic plaque in a. renalis

The percentage in column Transplantations refers to conversion rate of possible grafts to be transplanted.
*25 double-lung and 4 single-lung grafts.
†6 grafts used for 12 split liver transplantations, in 3 cases, a split was intended.

Intestinal graft survival rate at 30 days was 97.4% ± 2.5% and at 1-year, 73.0% ± 7.4% (median follow up time 1.5 years. (0.04–4.2), (Fig. 1). Patient survival rates at 1 month and 1 year were 97.4% ± 2.5% and 75.6 ± 7.1% respectively.

Discussion

Until now, more than 2300 ITs have been performed worldwide and mainly only large single-centre series have

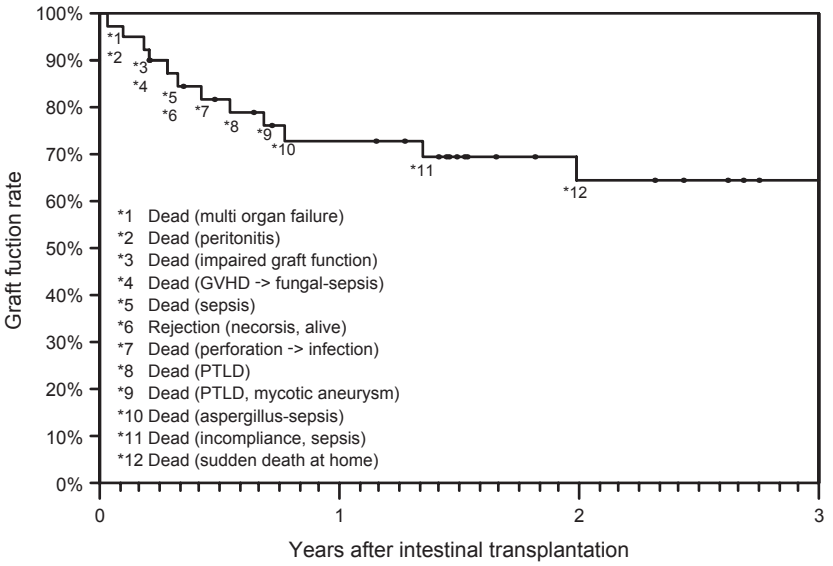

Figure 1 Intestinal graft survival rates from deceased donors procured in Germany between January 2006 and December 2011. The cause of graft loss is inserted in graph (marked with*). During the first year, they were in nine cases secondary to multiorgan failure, peritonitis, graft-versus-host disease (GVHD), sepsis due to various pathogens, rejection, PTLD and ischaemia due to ruptured mycotic arterial aneurysm as well as in one case without confirmed reason of death, but known impaired graft function.

been reported [4,9,18–21]. Interestingly, based on our review of the literature [5–13], no clear data about intestinal donor criteria (Table 1) with exception of donor age (<50 years) and donor–recipient size match (donor should be smaller than recipient) have been reported. This ambiguity and lack of guidance cause confusion for those involved in evaluating organ donors.

We therefore set out to provide the medical community, ICU staff, coordinators, OPOs and transplant surgeons with simple guidelines for intestinal donor 'inclusion-criteria'. To this end, we discuss the medical literature in the context of our intestinal donation experience in Germany during the past 5 years.

A detailed analysis of each key parameter follows:

Donor–recipient size match

The lack of intra-abdominal space represents a major problem for IIT and MVT, as the recipient's abdominal cavity is often small and retracted. Many authors addressed this issue [6,7,9,21–23], generally concluding that grafts from donors 25–50% smaller than the recipient are preferred without specific recommendations about height or weight. We postulated that the correctly measured donor's height and weight [24] may be useful this context. As the calculated DRWR and DRHR from our donor–recipient pairs were 0.88 (0.52–1.71) and 0.96 (0.68–1.13) respectively, most donors were approximately the same size as the recipient. However, as demonstrated by several authors, size reduction or adaptation of the graft may be possible to overcome the burden of donor–recipient size mismatch [7,25,26].

Therefore, we do not consider donor size mismatch to be an absolute exclusion criterion and cannot recommend a cut off for donor height and weight.

High BMI may correlate with high fat content in the mesenteric root causing obstacles during the implantation of the graft; however, neither the literature nor our data suggest a clear cut-off for donor BMI. On the basis of our personal experience, we suggest to consider IT-donation in donors with BMI <28.

ICU stay

The median ICU stay in our series was 2 days [1–10]. This was similar to the reported data in the literature [8–13,22,27]. There is consensus that intensive donor therapy improves the quality of organs [28].

Notwithstanding, an ICU-stay longer than 1 week should not exclude intestinal donation [11], if enteral nutrition is started as soon as possible after admission to the ICU, as recommended by guidelines for enteral nutrition [29]. This avoids disruption of the mucosa barrier and progression to luminal ileus, as well as stabilizes colon function and its flora if antibiotics are not added inappropriately [30]. Any available standard enteral nutrition has been shown to have a benefit over nothing [29], as long as it is not contaminated by microbes. Even

50 ml/h of unsweetened tea may preserve intestinal integrity in short-term.

Cause of death

The cause of the donor's death, in and of itself, does not represent an exclusion criterion *a priori* in our experience as also echoed by others [11]. Notwithstanding, in the case of a post-traumatic death, the mechanism of trauma and injury represents a major role in donor selection for intestinal donation: a direct abdominal trauma (blunt as well as open), a severe deceleration trauma with consequent potential laceration of the mesenteric root and bowel and cases of pancreatitis should represent contraindications to intestinal donation.

Other traumatic extra-abdominal lesions (i.e. thorax and extremities) should not represent a contraindication.

Vasopressors

In our series, 31% of the donors were haemodynamically unstable right after hospital admission, but subsequently recovered! Reasons for hypotension included polytrauma injuries, poor cardiac output after SAH/ICB and recovery following prehospital cardiac arrest with resuscitation. Initial hemodynamic instability was treated with vasopressors and inotropics, (e.g. norepinephrine >0.1 μg/kg/min supplemented by dobutamine >10 μg/kg/min), as well as transfusions as necessary until proper circulation was achieved. While there is concern that high doses of vasoactive medications may damage organs through visceral vasoconstriction, all unstable donors in our series recovered hemodynamically and subsequently their organ function recovered as well. In conclusion, short-term use of a high dosage of vasopressors in donors unstable upon hospital admission does not exclude intestinal donation.

In a similar way, Audibert and Mertens recommended the treatment of unphysiologic conditions in any patient to preserve the option of organ/heart-donation in patients without any chance of survival [31]. Their example is the treatment of complications of brain stem coning during the period of autonomic storm (e.g. antihypertensive therapy by esmolol or urapidil) as well as the poor cardiac output and hypotension right afterwards (e.g. by norepinephrine and dobutamine) for potential cardiac donors.

In our study population, intestinal donors with a poor cardiac output due to SAH-associated heart insufficiency required higher doses of catecholamines. The question of which catecholamine dosage and which agents are detrimental in organ procurement remains unanswered.

Cardiac arrest and cardio-pulmonary resuscitation

Cardiac arrest should not automatically preclude subsequent donation of an intestinal graft. To this end, Matsumoto *et al.* observed no inferior outcome in IIT and MVT when comparing grafts retrieved from donors with and without cardiac arrest [11]. Mean duration of cardiac arrest and subsequent cardio-pulmonary-resucitation (CPR) was 19.3 ± 12.7 min (range 1–52 min) with a time interval lasting from admission until cross clamp of 115 ± 61.7 h in a young donor population (7.66 ± 12.57 years). Compared with donors without CPR, no differences in terminal laboratory values as well as outcome parameters of the recipients were observed [11]. These results were confirmed by our data, with no differences in graft function. In our series, the donors with CPR were older when compared with the population of Matsumoto *et al.* (median 23 years, range 7–40 years), the duration of CPR was shorter (median 10 min, range 1–25 min) as was the time from admission until cross clamp (median 58 h, range 25–106 h), while terminal laboratory data had a wide variation (see Table 3).

In our series, the brain–heart connection related to cardiac failure after severe SAH [32] was responsible for cardiac arrest in all donors with SAH needing prehospital CPR. Echocardiography in these donors showed regional wall-motion-abnormalities or poor left ventricular output associated with the SAH, known as stress cardiomyopathy [33]. This entity and the potential for full hemodynamic recovery must be considered during donor selection.

Our data are in direct contrast to previous reports, which state that intestinal donors should not have any significant history of cardiac arrest or hemodynamic instability [6,7,12,21–23].

Age

The literature suggests that ideal intestinal donor should be younger than 50 years [5,6,8–13,27,34]. Although donors older than 50 years have been used successfully [9,34], our results were similar to those reported in the literature with most donors being younger than 18 years and only one over 50 years of age.

Laboratory values

Abnormal laboratory data require a case-by-case decision.

Sodium level (and its trend over time) represented the most important parameter influencing the acceptance of intestinal grafts. In our series, median peak sodium was 150 mmol/l and median sodium before procurement was 148 mmol/l. The sodium should be kept within normal range [13,28,34,35] for avoiding adverse events.

In the series investigated, the last liver enzyme values showed a wide range, even higher than in other studies [11].

After periods with a risk of intestinal ischaemia, it is important to know the trend of liver enzymes, bilirubin and creatinine. Decreasing values back towards normal range indicate a recovery, while increasing values need a careful evaluation.

Liver enzymes (ASAT, ALAT) twice above the reference range as well as creatinine and bilirubin in the reference range following CPR (and presumed significant intestinal ischaemia) had no impact on the outcome of IIT or MVT according to the study of Matsumoto *et al.* [11].

Inflammation markers were elevated in the study population, which was a frequent observation in donors due to brain tissue destruction and the SIRS associated with it [14,35]. Lactate and ph were not explicitly documented in most of studies, but we assume that these parameters were usually within normal range.

Medications

Diabetes insipidus should be treated by application of antidiuretic hormone [35].

Insulin therapy was required in many donors due to the target value of keeping the blood glucose below 160–200 mg/dl. Therefore, insulin use in donors simply reflected the quality of intensive care provided to the donor. Insulin application is also part of successful protocols of hormonal resuscitation in organ donors [28,36].

Treatment with steroids has a catecholamine-sparing effect, decreases the complications of the brain death-induced SIRS [35,37], offers a beneficial side effect of immune-modulation and an improvement of lung function [35]. Steroids are part of protocols of hormonal resuscitation in organ donors [28,36].

Donor risk scores

The application of different donor risk scores for predicting organ quality [15–17,38] appeared at first glance to be helpful. But, after a critical review, we concluded that their use would have merely resulted in the inappropriate exclusion of grafts, which were transplanted successfully, e.g. DRI for the liver was out of the ideal range in 82% of the cases.

Blood group

Previous publications have stated that identical AB0 blood group is preferred [6,21]. This limits the pool of available donors for a recipient. In our cohort, one AB0 compatible IIT- and one MVT were performed without impact on outcome. All others were AB0 identical.

Preservation solution

In a recent review about small bowel preservation for IT, Roskott *et al.* reported that UW solution is suboptimal for the intestinal graft despite good results for other organs and that extracellular solutions like HTK should be preferred [39].

In our series, 10 grafts had been preserved with UW-solution and 29 with HTK -solution. All grafts had primary function and an ischaemia time below 12 h. No differences in 1-year graft function rates were detected. The same results were obtained in a larger group investigated by Mangus *et al.* [27] with 22 grafts preserved in UW and 37 in HTK. In MVT-grafts, they did not observe complications related to the pancreas when comparing the solutions. From our data, it can be concluded that HTK was equivalent to UW for preservation of an intestinal graft for ischaemia times below 12 h. In contrast, Abu-Elmagd *et al.* [4] reported additional pancreatic complications in MVT grafts perfused with HTK compared with UW. HTK will be suitable for all intestinal grafts perhaps except for MVT grafts containing the pancreas due to the elevated risk of pancreatic complications.

Another risk factor to be taken into serious consideration is the use of an inappropriate flush volume with any solution if it is not weight-adjusted according to the manufacturer's instructions.

Other factors

The procurement of an IIT- or a MVT-graft requires the preservation of structures not routinely considered important in nonintestinal donors. This is especially true when including the colon with the intestinal graft or when the intestinal recipient has other individual anatomic needs to consider. Therefore, the surgeon experienced in intestinal procurement (usually coming from the transplant centre accepting the intestinal graft) must be present from the start of donor operation until the end.

Analysis of outcome

All transplanted intestinal grafts, but one in our series, were functioning after 30 days. In fact, one recipient died within 30 days not due to graft-related complications. A 1-year graft function rate of 73.0 ± 7.4% is comparable to the results reported in the cited literature. Survival rate and the reasons for graft failures within the first years are shown in Fig. 1. No correlation between the reason for

graft loss and donor variables could be identified beyond the factors discussed.

Conclusion

While our study focuses on the 39 German donors from whom intestinal grafts were successfully transplanted, we believe that the number of potential donor candidates who were not utilized is even more relevant. Although difficult to quantify, a review of German data [40] suggests that many potentially suitable intestinal donors are turned down for unclear reasons: for example, of the 6426 realized donors between 2006 and 2010, 0.5% intestinal grafts were used for transplantation ($n = 33$) compared to 10.3% of the pancreas and 77.0% of the liver grafts. It is impossible to quantify the basis for declining a specific potential donor, but personal communications with colleagues reveal that many donors are refused simply because of an uncertainty about their suitability. We acknowledge that our study group is small and therefore the power of statistical analysis is limited, but we have no control over past utilization of intestinal donors. This should not be an obstacle for describing 'inclusion- criteria' to be used during donor evaluation. Only by seeking to provide clarity to the issue, we can expand the intestinal donor pool. As all grafts had initial function, someone might argue that the selection of donors had been conservative. Still the range of donor data was beyond the scope usually communicated without severe adverse events/reactions reported. Unfortunately, this experience provides no risk stratification into good or bad donor characteristics, but at least we know when it is safe to consider donation of IT-graft.

Table 5. Currently proposed standard inclusion criteria for intestinal and multivisceral donors.

Donor data	Range in an ideal donor
Age	0–50 years
Donor–recipient size match	DRWR and DRHR compatible
BMI	<28
ICU stay	<1 week
Enteral nutrition	Initiate within <24 h after admission
CPR	<10 min
Trauma mechanism	Absence of direct or blunt abdominal trauma
Sodium	Most recent <155 mmol/l peak (last 24 h) <165 mmol/l
Transfusions	No significant ongoing requirements at time of procurement
Medication	Standard donor therapy
Preservation solution	HTK or UW (HTK should be preferred)
Blood group	Identical or compatible

CPR, cardio pulmonary resuscitation; DRWR, donor–recipient weight ratio; DRHR, donor–recipient height ratio; ICU, intensive care unit.

On the basis of collected data, we suggest following inclusion criteria for donation of IT grafts (see also Table 5): donor age 0–50 years, ICU-stay <1 week, no blunt abdominal trauma, most recent Sodium <155 mmol/l, no severe ongoing transfusion requirements, standard donor therapy including enteral nutrition and a compatible donor–recipient size match. HTK-solution appeared to be safe for organ preservation if ischaemia time was kept below 12 h.

We believe that any donor meeting these criteria should be considered potentially suitable and no other parameters should be used as an excuse for excluding intestinal grafts without seeking input from intestinal transplant centres.

Authorship

CLFF: designed research, collected data, analysed data and wrote the manuscript. AK: contributed important data for research design. RS: contributed important data for research design and wrote the manuscript. FS: contributed important data for research design, collected data, and analysed data. JP and AP: contributed important data for research design and collected data. WS: contributed important data for research design. SN: contributed important data for research design, designed research, analysed data and wrote the manuscript.

Funding

The authors have declared no funding.

Acknowledgement

The authors want to thank all coordinators and donor hospitals for their huge and essential contribution in realizing IT as well as recipient centres in providing follow-up information on graft function and critical remarks (Innsbruck, Groningen, Leuven, Berlin, Frankfurt, Jena, Muenster, Munich, Tuebingen, Eurotransplant).

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