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Chapter 11
ECD for Adult Liver Transplantation

Masahiko Taniguchi and Hiroyuki Furukawa

11.1 Introduction

Since Starzl [1] performed the world's first deceased-donor liver transplant in 1963, more than 6,000 deceased-donor liver transplants have been performed annually in the USA. There, as in other parts of the world, the biggest problem with liver transplants is the unequivocal shortage of donors. In response, countries mostly in Europe and the USA have explored extended criteria donors (ECD), which include elderly donors and donors with a fatty liver. This paper describes the current state of and problems with these ECD.

11.2 Definition

11.2.1 Donor Criteria for Deceased-Donor Liver Transplants

Selection of appropriate donors is essential to the success of a deceased-donor liver transplant. Aspects that must be considered when selecting a donor include age, body mass index (BMI), medication being taken, a history of drinking, the presence or lack of liver disease, a history of infection, and a history of malignancy. Moreover, causes of death and changes in hemodynamics and liver function must also be considered. Criteria for selection of an ideal donor include a donor age of 50 or younger, normal liver function and a lack of liver disease, stable hemodynamics, a lack of severe abdominal trauma, no systemic infection, a lack of malignancy, and normal kidney function [2].

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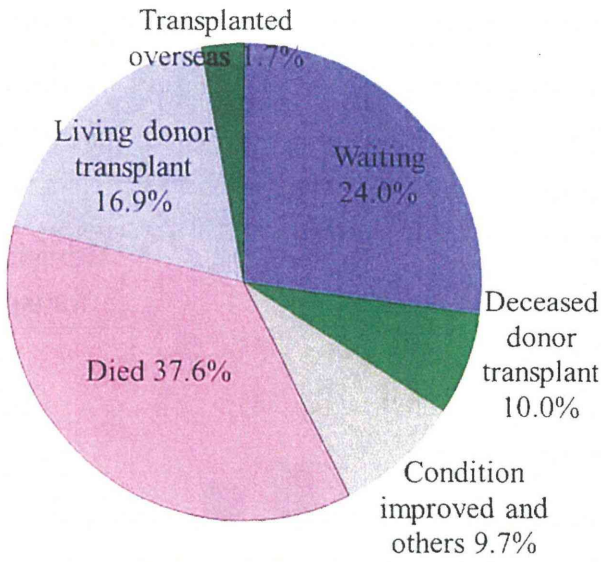

Fig. 11.1 Removal reasons (total 1,677 cases)

11.2.2 Definition of ECD

Procedures such as living-donor liver transplantation and split transplantation have been performed to cope with the shortage of donors, but these procedures have reached their limit. The reality is that surgeons must rely on liver transplants from marginal donors, i.e., liver transplants from ECD. Although there are no set criteria for ECD, there are tentative criteria. These include elderly donors, donors with a fatty liver, donors infected with HBV, donors infected with HCV, donors with hypernatremia, donors receiving prolonged respiratory care in the ICU, a liver that has been ischemic for some time as a result of cardiac arrest or low blood pressure, a donor with a high BMI, a donor using vasoactive drugs, and a liver that has been stored (both warm and cold) for a prolonged period [3, 4].

11.2.3 Outcome

In Japan, 402 individuals were registered with the Japan Organ Transport Network (http://www.jotnw.or.jp/) as candidates for a deceased-donor liver transplant as of December 2012. Since candidates for a deceased-donor liver transplant were first registered in October 1997, a total of 1,677 candidates registered prior to the end of December 2012 (Fig. 11.1). Of these patients, 168 (10.0 %) received a deceased-donor liver transplant and 284 (16.9 %) received a living-donor liver transplant in Japan, 29 (1.7 %) received a deceased-donor liver transplant overseas, and 631 (37.6 %) died. Changes in the number of liver transplant recipients since 1999 are shown in Fig. 11.2. More than 2 years has passed since the revision of the Organ Transplant Act. The number of candidates who received a deceased-donor liver transplant in Japan increased about 5 times a year compared to the number who

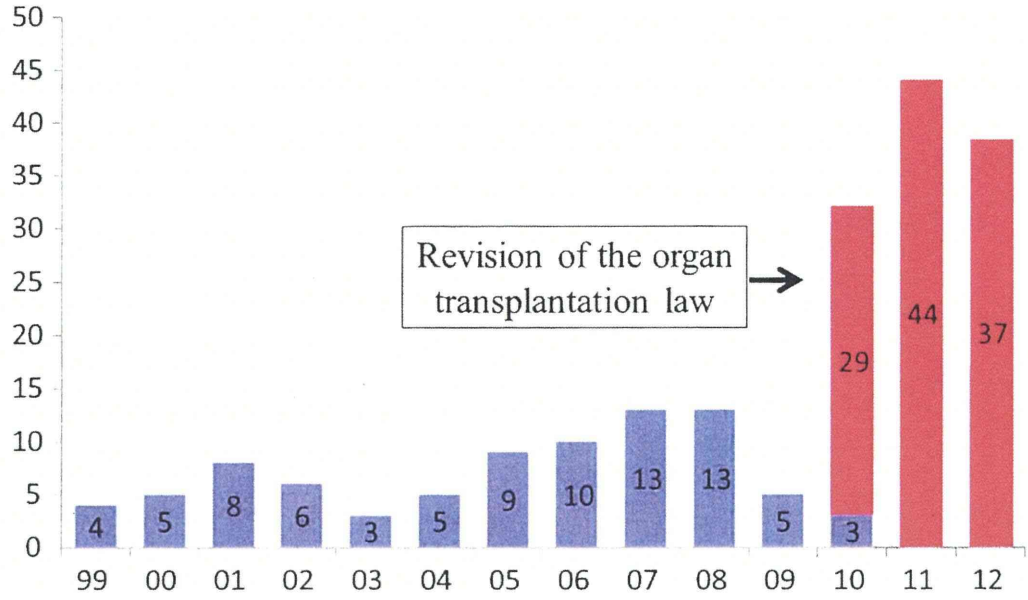

Fig. 11.2 Changes in the number of liver transplants in Japan

Table 11.1 Multivariate analysis for the 3-month patient survival

	Coefficient (SE)	Odds ratio (95 % CI)	*P*-value
MELD score ≥25	4.213 (1.387)	12.3 (1.7–90.3)	0.0133
Donor age ≥55 years	2.514 (1.015)	14.0 (1.6–119.5)	0.0159
CIT ≥600 min	2.639 (1.094)	67.6 (4.5–1024.9)	0.0024

(Quote from [5])

received a transplant before the act was revised. However, one in three individuals still die without receiving a liver transplant; so the stark reality is that there is an unequivocal shortage of donors in Japan as well.

Although the revision of the Organ Transplantation Law in July 2010 allowing organ procurement with family consent has increased the number of deceased donors, it remains insufficient. In this situation of a serious organ shortage, the use of ECD is inevitable. We analyzed ECD and recipient factors to determine which ones impacted early recipient outcomes [5]. From February 1999 to January 2011, 100 deceased-donor liver transplantations were performed in Japan, including 85 consecutive adult cases that were studied to evaluate whether 6 recipient and 16 donor factors affected the 3-month recipient survival. Upon univariate analysis, model for end-stage liver disease (MELD) score ≥25, donor age ≥55 years, and cold ischemia time (CIT) ≥10 h significantly reduced the 3-month survival. Multivariate analysis confirmed the independent contributions of three adverse factors including MELD score ≥25, donor age ≥55 years, and CIT ≥10 h (Table 11.1). Three-month recipient survivals with 0, 1, 2, and 3 positive factors were 100 %, 94.4 %, 53.8 %, and 0 %, respectively.

The importance of analyzing both donor and recipient factors simultaneously has been emphasized to match donors and recipients to compensate for their risks.

From this study, MELD score, CIT, and donor age were observed to independently impact the 3-month recipient survival rates. Subgroup analysis showed recipients with more RFs to have inferior 3-month survival; however, it was more than 66.7 % when CIT was maintained within 10 h. To minimize CIT, further efforts to reduce transportation time and to adjust donor and recipient operative times are mandatory. In the long term, we must promote deceased donation to reduce recipient MELD scores by shortening the waiting time and revise the allocation system to minimize CIT by giving priority to the local area.

11.3 Basic and Clinical Research

11.3.1 Elderly Donors

Problems with grafts from elderly donors are the presence of severe arteriosclerosis and problems with the liver parenchyma, e.g., fatty liver [6, 7]. These two conditions have a profound negative impact on the graft survival rate soon after transplantation [7]. Typically, a donor age of over 60 has a massive impact on the outcome of a transplant. However, the number of transplants of grafts from elderly donors has increased over the past few years as a way to cope with the shortage of donors. Surgeons in Spain in particular are actively performing transplants of grafts from elderly donors. Fewer than 15 % of potential donors in the USA are of age 60 or over, but in Spain more than 30 % of these potential donors are of age 60 or over. As a result, the number of donors in Spain increased 136 % compared with 33 % increase in the USA [8]. Nevertheless, there is no question that considering grafts from elderly donors increases the number of available grafts, thus reducing the number of patients who die while awaiting a transplant.

But what are the outcomes of transplant grafts from elderly donors? According to the Spanish Registry for Liver Transplantation, the 1-year survival rate is 76 % for a recipient of a graft from a donor ageing 60–69, while that for a recipient of a graft from a donor ageing 80–89 is 72 %. These figures differ a little from the 1-year survival rate of 80 % for a recipient of a graft from a donor ageing 15–60. Nevertheless, the 5-year survival rate for a recipient of a graft from a donor ageing 60–69 is 56 % and that for a recipient of a graft from a donor ageing 80–89 is 51 %, but that for a recipient of a graft from a donor ageing 15–60 is 66 %, so the difference in survival rates has increased. This is because elderly donors are obviously more susceptible to liver cancer, recurrence of hepatitis C, and recurrence of an underlying illness [9]. Currently, liver transplants from elderly donors have outcomes on par with liver transplants from younger donors, provided there are no other risks besides the donor's age [10]. This is because recipients are chosen in light of the condition of the graft and risk factors on the part of the recipient. A liver transplant from an elderly donor to a low-risk recipient will not affect the transplant's outcome. Thus, having an elderly donor is becoming less of a factor for a less satisfactory transplant outcome.

11.3.2 Fatty Liver

Thirteen to twenty-six percent of brain-dead donors have a fatty liver [11]. Fatty infiltration of the liver is classified as either macrovesicular or microvesicular steatosis. Microsteatosis is reversible, so it is not associated with the incidence of primary graft nonfunction or the recipient's survival rate [12, 13]. In contrast, the extent of macrovesicular steatosis is associated with the recipient's prognosis. Normally, severe macrovesicular steatosis of more than 60 % often leads to primary nonfunction, thus precluding the use of the liver [14]. A liver transplant from a donor with moderate (30–60 %) macrovesicular steatosis involves a high incidence of primary nonfunction compared to transplantation of a normal liver (13 % vs. 3 %) [15]. If the donor and recipient have no other risk factors, then a transplant from a donor with moderate macrovesicular steatosis results in a post-transplant outcome equivalent to a transplant from a normal donor [16]. Given the ever-increasing number of deaths of patients awaiting a transplant, efforts must be made to improve the outcomes of transplants from donors with moderate macrovesicular steatosis.

11.3.3 Donors After Cardiac Death

The particulars have taken up other section (DCD Liver).

11.3.4 HBV-Positive Donors

Liver transplantation from an HBcAb-positive donor to a recipient who is HBsAb-positive or HBcAb-positive results in few problems. However, hepatitis B often recurs when such a liver is transplanted to other recipients [17]. Thus, hepatitis B immunoglobulin and antivirals must be used after liver transplantation from an HBcAb-positive donor [18].

11.3.5 HCV-Positive Donors

There are few significant differences in the post-transplant survival rate when a liver from an HCV-positive donor is transplanted to a patient with HCV-related cirrhosis compared to a liver from an HCV-negative donor [19, 20]. However, a liver transplant from an elderly and HCV-positive donor exacerbates fibrosis more than a transplant from an elderly and HCV-negative donor and is more susceptible to graft failure [21]. Recipients in whom the donor strain of HCV became predominant after transplantation are known to have a longer relapse-free survival than recipients who

retained their own HCV strain [22]. A graft from an HCV-positive donor with fibrosis or inflammation is not suitable for transplantation, so a liver biopsy prior to transplantation is crucial.

11.3.6 Matching of ECD Grafts and Recipients

Use of ECD grafts has reduced the deaths of transplant candidates [23]. From 2000 to 2007, the number of liver transplants performed in the USA increased from 4,595 to 6,228 (a 26.2 % increase). Presumably this is the result of introducing a system of organ allocation based on the MELD score and encouraging the use of marginal donors.

Which patients should receive an ECD graft? A large-scale retrospective study of over 1,000 patients at UCLA [24] scored extended criteria based on a donor age of 55 and over, donor hospitalization for longer than 5 days, a cold ischemia time of more than 10 h, and a warm ischemia time of more than 40 min. According to the study, a higher ECD score (donor score, or DS) resulted in a higher post-transplantation mortality rate. In other words, a higher DS results in greater risk, so recipients in poor condition prior to transplantation (a high MELD score) are more likely to have a poorer outcome after transplantation. A DS of 2 or less means that a transplant is possible with little risk in many cases, but a DS of more than 2 means that a transplant should be avoided in risky cases, e.g., urgent cases. Similarly, a study of 650 patients in Spain found that an elderly donor, a fatty liver with 30 % of more steatosis, and cold ischemia time were extended criteria associated with primary graft dysfunction [25]. Matching a donor with a high ECD score and a recipient with a MELD score of 29 or higher is most likely to lead to graft failure.

According to data from the Organ Procurement and Transplantation Network (OPTN) and current conditions in the USA, 12,056 liver transplants were performed from June 2002 to June 2005. Of these, 2,873 (23.8 %) were transplants of a graft from an ECD. An ECD graft is most often (33 %) transplanted to a recipient with a MELD score of <15 [4]. Based on an analysis of data covering 20,023 liver transplants in the US Scientific Registry of Transplant Recipients, Feng et al. [26] calculated the donor risk index (DRI). ECD grafts from a donor age of 40 or older or a DCD donor or grafts that were a split/partial graft closely correlated graft failure. Feng et al. reported that grafts with an increased DRI have been preferentially transplanted into older candidates with moderate disease severity (nonstatus 1 with lower MELD scores) and without hepatitis C. Although the use of an ECD graft is a significant risk factor for graft failure, there is no correlation between the use of an ECD graft and the recipient's MELD score. The same group later conducted a follow-up of 28,165 recipients in the USA, and they found that patients with a low MELD score had a higher mortality rate from receipt of a high DRI graft than from waiting for a transplant. That said, patients with a MELD score of 20 or higher did receive some survival benefit even when they received a DRI graft. Based on these findings, recipients with a high MELD score benefit more from a high DRI graft

than recipients with a low MELD score. Matching a high DRI graft and a recipient with a low MELD score results in less of a survival benefit for the recipient and reduces the chances for a recipient with a high MELD score to receive a transplant, so such matches should be avoided [27].

11.4 Conclusion

This paper has described the use of ECD in liver transplants. As mentioned earlier, the unequivocal shortage of donors is a global problem. This is particularly true for Japan, where far fewer deceased-donor liver transplants are performed in comparison to Europe and the USA. Because there are so few deceased-donor liver transplants, organs must not be wasted and transplants should be successful so that the wishes of their donors can be satisfied. To that end, liver transplant surgeons must strive more than their counterparts in Europe and the USA to perform transplants from ECD and reduce the risk of ECD grafts.

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Chapter 19
ECD for Pancreas Transplantation

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19.1 Introduction

In terms of absolute shortages of donors, organ transplantation in Japan is in a more serious position than in Europe or the United States. In Japan, a law allowing organ transplantation from brain-dead donors finally came into force in October 1997. The first organ procurement after the enactment of this law was carried out from a deceased donor in February 1999. The heart, liver, and kidneys were successfully transplanted into four recipients. The first pancreas transplantation (PTx) after the law was successfully performed at Osaka University Hospital in April 2000. Since then, however, only 86 cases of procurement occurred over the approximately 13 years from the introduction of the law, because the law was very strict and limited for organ procurement to donors who provided prior written consent. The law was eventually revised to more closely resemble laws in Europe and the United States in July 2010. Since then, procurement numbers have rapidly increased to 118 in 2.5 years. After revision of the law, the number of donations has increased 7.1-fold. The number of PTx was 84 (33.6/year, as of December 31, 2012) after the revision, compared to 64 (5.0/year) before the revision.

Although the number of donors increased, donor shortages and severe environment surrounding donors as described later still exist in our country. Transplant outcomes, however, are comparable to those in Europe and the United States. Most organ transplantations except for small bowel transplantation have been covered by health insurance since April 2006. This is probably due to recognition of the high quality of organ transplantation in Japan.

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Unlike transplantations of lifesaving organs such as the heart, liver, and lung, PTx is recognized as a treatment mainly focused on quality of life. Recently, however, PTx, particularly simultaneous pancreas and kidney transplantation (SPK), has been reported to improve life expectancy in recipients [1]. With the passage of the waiting period after registration to the Japan Organ Transplant Network (JOTN), both deaths and serious cases of diabetic complications necessitating withdrawal of the registration have increased. Therefore, as potential solutions, so-called marginal donors as well as living donors have been considered in Japan.

This chapter examines the present status and problems of PTx in Japan from the perspective of "marginal donors."

19.2 Definition of a "Marginal Donor"

The term "marginal donor" has not yet been clearly defined but is considered almost equivalent to expanded or extended donors (ECD). According to a report regarding strategies to expand the donor pool by Kapur et al., "marginal donors" are defined as follows [2]: (1) >45 years old; (2) hemodynamically unstable at the time of harvest (usage of high-dose dopamine (>10 μg/kg/min) or at least two vasopressors); and (3) non-heart-beating status. In Kapur's series of PTx, 68 transplants were performed from non-marginal donors, while 69 transplants were from marginal donors according to these criteria. The overall rate of pancreas graft survival was 86 %, with a mean follow-up of 23 months. A total of 22 pancreas grafts were received from donors >45 years old (13 grafts; >50 years old). The actual graft survival rate of the >45-year-old donor group was 86 %. Fifty-one grafts were removed from hemodynamically unstable donors on high-dose vasopressors. The actual graft survival rate in the group was 86 %. Delayed graft function was observed significantly more often among recipients of grafts from donors on high-dose vasopressors, but no significant difference in graft survival was evident between recipients of pancreas grafts from marginal and non-marginal donors.

According to International Pancreas Transplant Registry (IPTR) data, the following variables are associated with increased risk of pancreas allograft thrombosis: (1) donor age over 40 years; (2) cardiovascular or cerebrovascular cause of brain death; and (3) pancreas preservation time more than 24 h [3].

Also, anecdotal experience suggests that (1) donor body weight (BW) >150 % of ideal BW or donor body mass index (BMI) >30 kg/m^2 may be associated with increased risk of pancreas graft loss due to thrombosis, pancreatitis, infection, or primary nonfunction; (2) donor liver biopsy showing greater than 25–30 % macrovesicular steatosis may be associated with a fatty pancreas, leading to increased risk of early graft loss; and (3) fatty infiltration of the pancreas may be associated with increased risk of early graft loss [4].

Donors under cardiac death will be discussed in another chapter.

19.3 Present Status of Donors for PTx in Japan

From October 1999 to the end of 2012, a total of 423 patients with type 1 diabetes (T1D) were registered with the JOTN and 148 cases of PTx were performed. Almost every donor was deceased, with the exception of two non-heart-beating donors. During the waiting period, however, 38 patients died and 33 were withdrawn from registration due to serious diabetic complications, such as cerebral hemorrhage and infarction and myocardial infarction. During the same period, another 26 pancreases were utilized with or without kidneys from living-related donors.

Donor characteristics are shown in Table 19.1. Three obvious differences in donor characteristics exist between Japan and the United States. One is regarding the age of donors, another is the cause of brain death, and the last is the waiting time from registration to transplantation. The mean age of donors was 25.5 years in the United States [5], compared with 43.4 years in Japan. In particular, the population >45 years old accounted for 50.0 % of donors in Japan (6.7 % in the United States), as shown in Fig. 19.1. Next, the most common cause of brain death in the United States was trauma (69.6 %), followed by cerebrovascular accident (CVA, 25.1 %), while the most common causes in Japan were CVA (58.9 %) followed by trauma (18.9 %) (Fig. 19.2). Organs from older donors who have died due to CVA might carry a higher risk of atherosclerotic changes, fatty degeneration, or diabetes. The last issue is about the waiting time until transplantation after registration. In the United States, 65.7 % of patients underwent transplant within 12 months, while most patients (61.5 %) in Japan

Table 19.1 Characteristics of 148 PTx donors

Donor's gender	
Men	80
Women	68
Age at PTx	
10s (%)	5 (3.4)
20s (%)	19 (12.8)
30s (%)	31 (20.9)
40s (%)	38 (25.7)
50s (%)	40 (27.0)
60s (%)	14 (9.5)
70s (%)	1 (0.7)
Cause of death	
CVA (%)	87 (58.8)
Injury (%)	28 (18.9)
Hypoxia (%)	28 (18.9)
AMI (%)	2 (1.4)
Others (%)	3 (2.0)
Resuscitation	
Yes (%)	62 (41.9)
No (%)	86 (58.1)
Marginality	
Yes (%)	108 (73.0)
No (%)	40 (27)

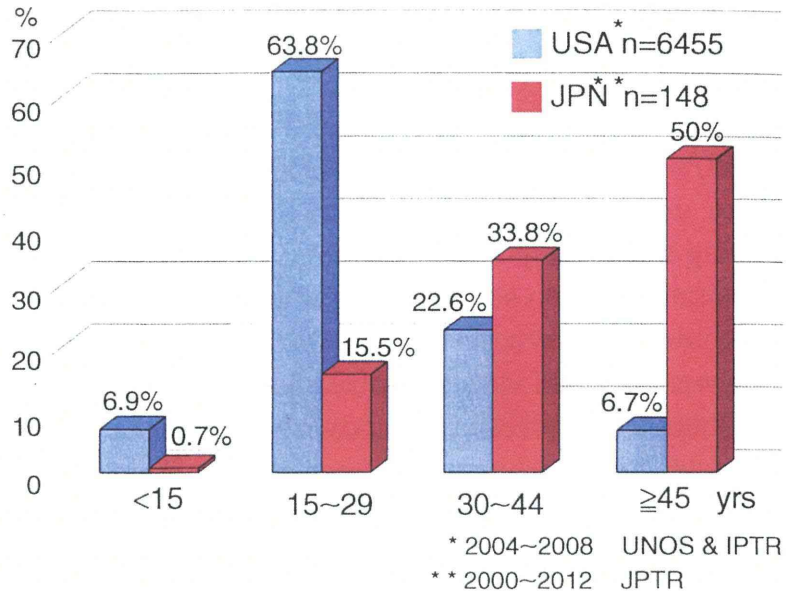


Fig. 19.1 Donor age between the United States and Japan

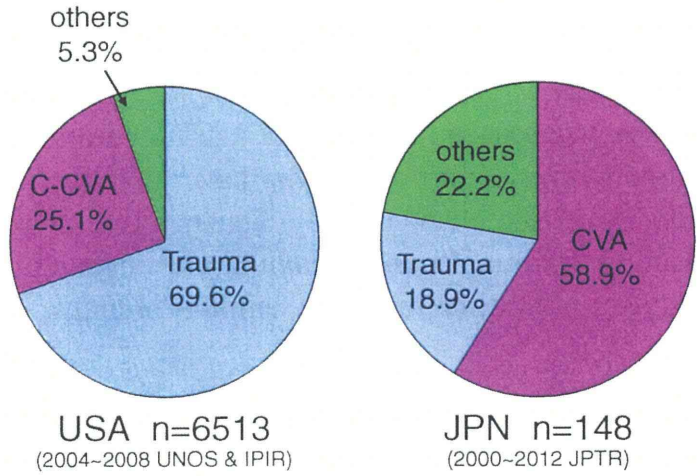


Fig. 19.2 Cause of death between the United States and Japan

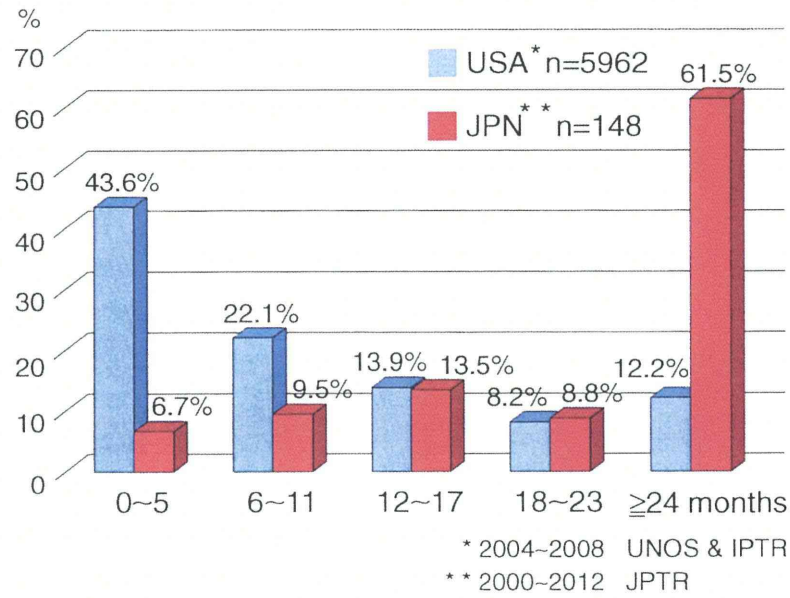


Fig. 19.3 Waiting period for PTx

have to wait >24 months (mean, 1,380 days; Fig. 19.3). Under such circumstances, we Japanese have no choice but to accept marginal donors.

In the present series, 108 donors (73.0 %) meeting at least one of the three conditions in Kapur's criteria were considered as marginal.

During the same period, 176 liver grafts were harvested in our country. Comparing the usage of liver grafts to that of pancreas grafts, the liver to pancreas ratio (L/P ratio) was 1.19. In contrast, ratios in main overseas organ procurement organizations (OPOs) and American OPOs were 7.18 and 3.26, respectively. Pancreas grafts were thus not actively harvested in the United States or other countries. However, there is one transplant center of the University of Wisconsin where selected, less-than-ideal donors are aggressively used, with an L/P ratio of 1.25 [6].

19.4 Outcomes of PTx in Japan

The first case of PTx under brain death was performed at Tsukuba University in 1984, before implementation of the laws regarding organ transplantation [7]. Because no consensus regarding brain death had been established in Japan at that time, 11 cases of PTx were subsequently performed under cardiac death, mainly at Tokyo Women's Medical University [8]. Unfortunately, the results were less than satisfactory. Survival rates for pancreas grafts were 55 %, 46 %, and 36 % for 1, 3, and 5 years, respectively. This was attributed to the viability of pancreatic grafts during the agonal stage prior to procurement.

A total of 148 PTx from 204 organ procurements had been performed as of the end of 2012 after the introduction of laws on organ transplantation. The percentage usage of pancreas grafts was 72.5 %. Characteristics of these transplantations are shown in Table 19.2, revealing similar findings to results from Europe and the United States. In terms of recipient sex, 92 (62.2 %) were females and 56 (37.8 %) were males. Recipient populations in their 40s, 30s, and 50s comprised 66 (44.6 %), 51 (34.5 %), and 23 patients (15.5 %), respectively. Mean duration of diabetes was 27.1 years (range, 6–48 years). However, the mean period of dialysis among SPK patients was relatively longer, at 7.9 years (range, 0–22 years). As described above, the problem is that the waiting time for recipients, which was 1,380 days (range, 45–4,722 days) as of the end of 2012, is getting longer and longer.

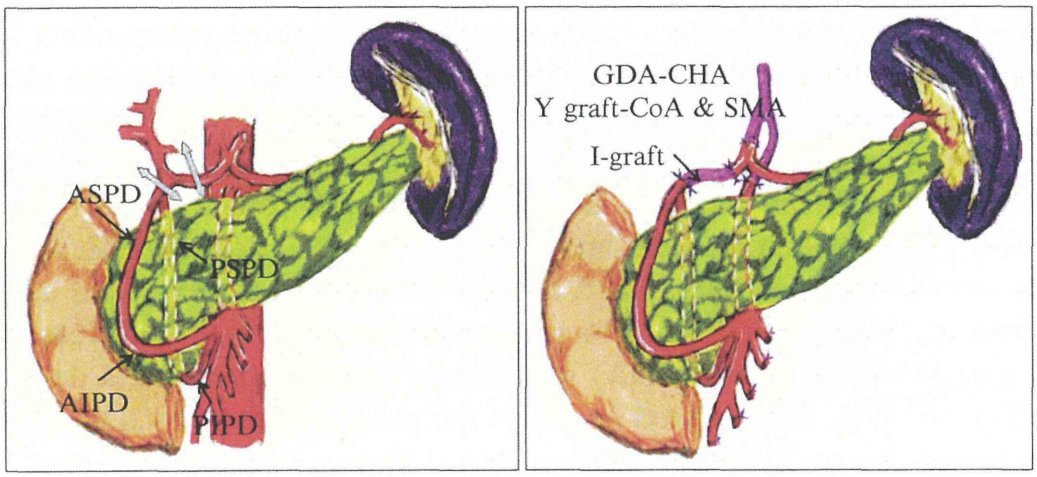
Recipients were classified into three categories: spontaneous pancreas and kidney transplantation (SPK); pancreas after kidney transplantation (PAK); and pancreas transplant alone (PTA). As of December 2012, totals of 119 SPK, 20 PAK, and 9 PTA had been performed. Mean total cold ischemic time (TCIT) of the pancreas was 11 h 43 min. Mean TCIT for kidney grafts in SPK patients was 11 h 8 min. Mean number of total HLA-A, -B, and -DR mismatches was 2.61 ± 1.18.

PTx was managed and performed under a cooperative system as an all-Japan team from the beginning in Japan. To increase blood supply to the pancreas head, a donor gastroduodenal artery (GDA) was usually reconstructed with a donor iliac artery (I-graft) (Fig. 19.4). Blood supply to the pancreas head via GDA is usually blocked if the liver is harvested, but if not, blood flow was usually preserved. There are two blood supplies to the pancreas head: one via the GDA from the celiac artery and the other via the inferior pancreaticoduodenal artery (IPD)—first jejunal artery from the superior mesenteric artery (SMA). According to a report by Donatini [9], the main blood flow is supplied from the anterosuperior pancreaticoduodenal artery

Table 19.2 Characteristics of 148 PTx recipients

Recipient's gender	
Men	56
Women	92
Age at PTx	
20s (%)	6 (4.1)
30s (%)	51 (34.5)
40s (%)	66 (44.6)
50s (%)	23 (15.5)
60s (%)	2 (1.3)
Mean duration of DM (years)	32.9 (6–47)
Mean duration of dialysis (years)	7.9 (0–22)
Mean waiting time (days)	1,380 (45–4,722)
TCIT	
Pancreas	11 h 43 min
Kidney	11 h 08 min
Recipient's category	
SPK (%)	119 (80.4)
PAK (%)	20 (13.5)
PTA (%)	9 (6.1)
Immunosuppression	
TAC + ST + MMF + Ab	
TAC + ST + MMF	
CsA + ST + MMF + Ab	
CsA + ST + MMF	
Others	
Tx procedure	
ED (%)	118 (79.7)
BD (%)	30 (20.3)
HLA mismatches	
Mean ± SD	2.61/1.18

TCIT total cold ischemic time, *TAC* tacrolimus, *CsA* ciclosporin, *ST* steroid, *MMF* mycophenolate mofetil, *Ab* antibody, *ED* enteric drainage, *BD* bladder drainage



GDA: gastroduodenal artery, CHA: common hepatic artery
A(P)SPD: antero- (postero-) superior pancreaticoduodenal artery
A(P)IPD: antero- (postero)- inferior pancreaticoduodenal artery

Fig. 19.4 Arterial reconstruction of pancreas graft

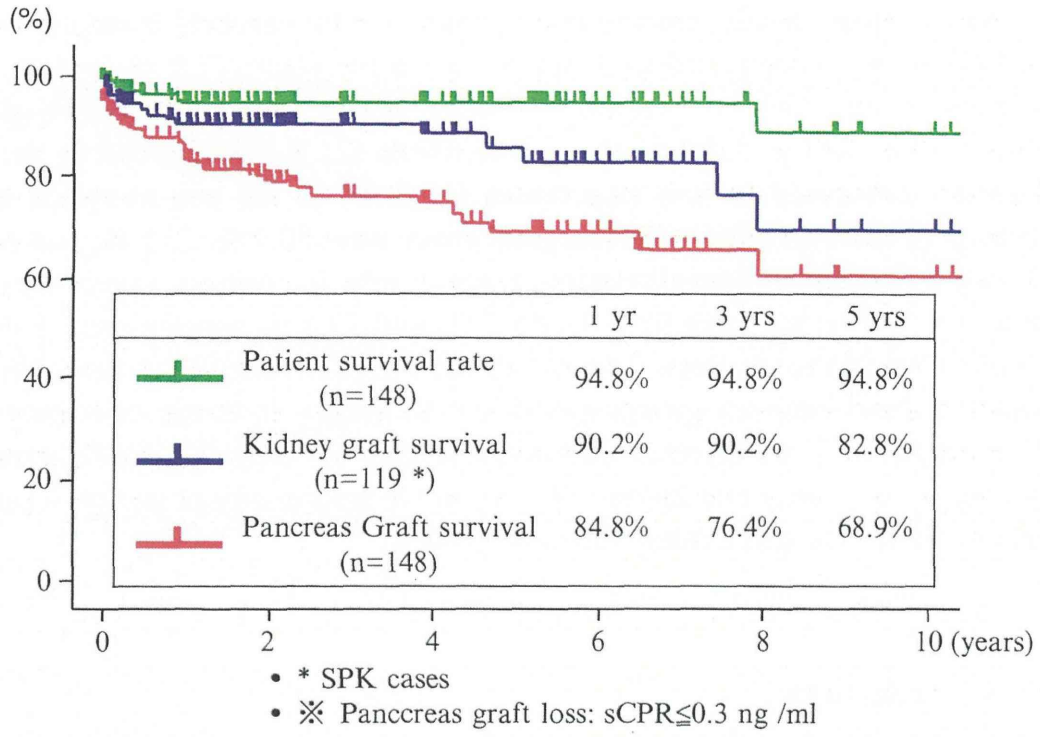


Fig. 19.5 Patient survival and graft survivals of PTx (until December 31, 2012)

(ASPD) via the GDA. Further, regarding communications between the superior and inferior branches of the pancreaticoduodenal artery (PD), there is reportedly communication of 25 % between the ASPD and anteroinferior PD (AIPD) and 75 % between the posterosuperior PD (PSPD) and posteroinferior PD (PIPD). The GDA reconstruction will be useful to increase blood flow to the pancreas, especially in PTx from a marginal donor.

Regarding drainage of pancreatic juice, enteric drainage (79.7 %) was more common than bladder drainage (20.3 %).

In most cases (91.9 %), the immunosuppressive regimen comprised tacrolimus-based quadruple induction therapy. Basiliximab directed against interleukin-2 receptor (CD25) was mostly used as an induction therapy. As an antimetabolite, mycophenolate mofetil was usually used.

Outcomes for 148 PTx are shown in Fig. 19.5. Eight recipients died, due to sepsis ($n=3$), cardiogenic events ($n=3$), graft-versus-host disease (GVHD) ($n=1$), and cerebral bleeding ($n=1$). The patient survival rate was 94.8 % at 1, 3, and 5 years. Nine pancreas grafts were removed in the acute phase, due to thrombus ($n=7$) and perforation ($n=1$) and bleeding ($n=1$) of duodenal grafts. Another 18 pancreases were lost, due to rejection ($n=15$), recurrence of T1D ($n=2$), or graft pancreatitis ($n=1$). Pancreas graft survival rates were 84.8 %, 76.4 %, and 68.9 % at 1, 3, and 5 years, respectively. Pancreas graft loss was defined as a serum C-peptide level <0.3 ng/ml according to high-sensitivity immunoassay. Among SPK recipients, eight kidney grafts were lost and the patients reintroduced onto dialysis due to chronic rejection ($n=7$) or primary nonfunction ($n=1$). Kidney graft survival rates were 90.2 %, 90.2 %, and 82.8 % at 1, 3, and 5 years, respectively.

Next, transplant results were analyzed between marginal cases ($n=108$) and non-marginal cases ($n=40$). Regarding mortality, five marginal recipients (4.6 %)

died, due to sepsis ($n=2$), cardiogenic events ($n=1$), cerebral bleeding ($n=1$), and GVHD ($n=1$), compared to 3 non-marginal recipients (7.5 %; sepsis, $n=1$; cardiogenic event, $n=1$). No significant difference was evident between groups. In terms of pancreas graft function, 23 pancreases (21.3 %) were lost in the marginal group, compared to four pancreases (10.0 %) in the non-marginal group. Pancreas graft survival rates in the marginal group were 80.9 %, 73.2 %, and 66.0 % at 1, 2, and 5 years post-transplantation, respectively. In contrast, survival rates in the non-marginal group were 92.5 %, 85.2 %, and 77.4 %, respectively. Pancreas graft failure tended to be more frequent in the marginal group, but no significant difference existed between groups ($p=0.35$). Similarly, in terms of kidney graft function among SPK recipients, eight kidneys (9.1 %) were lost in the marginal group compared to only one kidney (3.2 %) in the non-marginal group. Again, no significant difference was evident between groups.

19.5 Conclusion

In this study, 73 % of donors for PTx in Japan were marginal because of an absolute shortage of donors. However, transplant outcomes appear comparable to those in Europe and the United States. Pancreas and kidney graft functions in the marginal group tend to be inferior to those in the non-marginal group, but no significant differences are apparent.

Further investigations are necessary to clarify factors in marginal donors that contribute to better or worse outcomes.

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Chapter 23
ECD for Small Intestine Transplantation

Takehisa Ueno

23.1 Introduction

The prognosis of intestinal failure has improved dramatically owing to the development of parenteral nutrition (PN). However, PN-related complications, such as central venous catheter infection, venous access thrombosis, and intestinal failure associated with liver disorder, are still major causes of mortality in patients with intestinal failure. However, patients who develop life-threatening complications are considered for intestinal transplantation. Intestinal transplantation, which can significantly improve their prognosis and quality of life, has become an established treatment for intestinal failure [1]. More than 2,300 intestinal transplants have been performed worldwide [2].

Although there are relatively few candidates for intestinal transplantation, the waiting time is relatively long. For candidates wait-listed in 2010, the median time to transplant in the United States was 14.9 months for patients less than 18 years old and 2.8 months for those 18 years or older [3].

Since the intestine is very sensitive to ischemia, hemodynamically stable donors have been traditionally preferred. The shortage of organs has led centers to expand their criteria to accept marginal donors. A combination of multiple marginal factors seems to have an additive effect on graft quality. Clinical and new investigational strategies aimed at manipulating marginal donor organs to improve outcome will be covered, as well as approaches for marginal donor allocation.

In the past, intestinal transplant teams could be selective in choosing donor organs for two reasons; first, the supply of potential intestinal grafts far exceeded the comparatively low demand, and second, there were few if any criteria for defining

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