Long-Term Outcomes of Clinical Transplantation of Pancreatic Islets With Uncontrolled Donors After Cardiac Death: A Multicenter Experience in Japan

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ABSTRACT

Background. Pancreatic islet transplantation has emerged as an effective treatment for type 1 diabetes mellitus, but its use is limited due to an insufficient supply of cadaveric pancreata. In Japan, uncontrolled donors after cardiac death (DCD) are not deemed to be suitable for whole-organ pancreatic transplantation, and can provide a source of pancreas for islet transplantation. However, the long-term outcomes and utility of uncontrolled DCD in the clinical setting remain controversial. Here, we summarize the long-term outcomes of islet transplantation employing uncontrolled DCD as reported to the Japan Islet Transplantation Registry.

Methods. Sixty-four isolations and 34 transplantations of pancreatic islets were conducted in 18 subjects with type 1 diabetes mellitus under the cover of immunosuppression with basiliximab, sirolimus, and tacrolimus. All donors were uncontrolled DCD at the time of harvesting. The mean follow-up time was 76 months.

Results. Of the 18 recipients, 8, 4, and 6 recipients received 1, 2, and 3 islet infusions, respectively. Overall graft survivals (defined as a C-peptide level $\geq$0.3 ng/mL) were 72.2%, 44.4%, and 22.2% at 1, 2, and 5 years, respectively, whereas the corresponding graft survivals after multiple infusions were 90.0%, 70.0%, and 30.0%, respectively. Three of these recipients achieved insulin independence in 14, 79, and 215 days. Hb_{A1c} levels and the requirement of exogenous insulin were improved before loss of graft function. All recipients became free of severe hypoglycemia unawareness, however, at least 5 of 14 patients who had graft failure experienced recurrence of severe hypoglycemia after the loss of graft function.

Conclusions. Islet transplantation from DCD can relieve glucose instability and problems with hypoglycemia when the graft is functioning. However, islets from uncontrolled DCD may be associated with reduced long-term graft survival. Further improvements in the clinical outcome by modification of islet isolation/transplantation protocols are necessary to establish islet transplantation using DCD.

PANCREATIC islet transplantation has emerged as an effective treatment for type 1 diabetes mellitus (T1DM), but its use is limited due to an insufficient supply of cadaveric pancreata. Pancreatic islets are obtained from donors after brain death (DBD) all over the world, but access to DBD in Japan is quite rare. Also, pancreatic islet

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transplantation is categorized as tissue transplantation in Japan, which is operated with the use of special guidelines. Therefore, pancreata for islet transplantation have usually been obtained from donors after cardiac death (DCD).

DCD are a heterogeneous population, and the duration of cardiac death differs between subjects. A longer warm ischemia time (which may lead to organ damage) is a major concern with DCD. In Japan, most DCD suffer unexpected cardiac death. They are cannulated and perfused with cold preservation fluid within minutes after death to maintain organ viability, and are termed uncontrolled DCD. It has been reported that normally functioning pancreatic islets can be successfully isolated from pancreata from controlled DCD, and that they should be suitable for clinical isolation [1,2].

Previously, we reported that pancreatic islet transplantation from uncontrolled DCD ameliorated episodes of severe hypoglycemia, decreased levels of glycated hemoglobin (Hb_{A1c}), and sustained significant levels of C-peptide after a mean follow-up time of 41 months [3]. However, long-term outcomes and the utility of uncontrolled DCD in the clinical setting remain controversial.

Here, as a subsequent report from the Japan Islet Transplantation Registry, we summarize the outcomes from a mean follow-up of 76 months after pancreatic islet transplantations from uncontrolled DCD.

METHODS

Study Design

From September 2003 to March 2007, 64 isolations of pancreatic islets and 34 transplantations of pancreatic islets were performed in 18 T1DM patients (including 2 patients who had prior kidney transplantation). According to Maastricht donor categories, all DCD were considered to be uncontrolled and category V [4] at the time of harvesting. Six transplantation centers (Tohoku, Fukushima, Chiba, Kyoto, Kobe, and Fukuoka) were enrolled in this study for the isolation and transplantation of pancreatic islets. The Ethics Committee at each participating institution approved the study protocols. Each recipient was allowed up to 3 islet transplantations until achievement of insulin independence. Recipients were selected at each participating center based on regional priority, blood type, history of previous islet transplantation with a potential for insulin independence, and a long waiting period.

Isolation and Transplantation of Pancreatic Islets

Donors were cannulated and perfused with cold preservation fluid (in situ preservation) within minutes after death to prevent warm ischemia damage to the pancreas. Harvested pancreata were transported in chilled University of Wisconsin solution or in ET-Kyoto solution (Otsuka Pharmaceuticals, Tokyo, Japan). A 2-layer method with perfluorocarbon during transportation has been recommended [5]. Pancreatic islets were isolated locally at each facility, with each institution maintaining good practice guidelines. The method of isolation of pancreatic islets has been reported previously [6–8]. The pancreas specimen was digested with the use of Liberase HI (Roche Molecular Biochemicals, Indianapolis, Indiana). The release criteria were identical to those of the Edmonton protocol [6].

The fresh islet preparation without culture was infused into the portal vein. Two or 3 consecutive infusions of >5,000 islet equivalents (IEQ)/kg were planned for each recipient to achieve insulin independence.

The immunosuppression regimen comprised basiliximab induction and sirolimus/tacrolimus maintenance or the use of continuous immunosuppressive regimen in case of islet after kidney recipients, with basiliximab induction at the time of islet transplantation [3,6]. Sirolimus was replaced with mycophenolate mofetil in some cases.

Assessment of Islet Engraftment

Insulin independence was defined as freedom from the need to take exogenous insulin with adequate glycemic control. Partial graft function was defined as a C-peptide level $\geq$0.3 ng/mL and a requirement for insulin. Graft loss was defined as an initial increase in the C-peptide level but a decrease to <0.3 ng/mL. Severe hypoglycemia unawareness was defined as an episode of neuroglycopenia with unawareness severe enough for the subject to require assistance [9].

Flow Panel Reactive Antibodies (PRAs)

Alloantibodies were detected by means of flow cytometric methods with the use of the fluorescent signal for each HLA-coated bead and normalized to the signal of negative control serum [10].

Statistical Analyses

Values are expressed as mean $\pm$ standard error. Outcome measures for the overall data and strata-defined variables were estimated from Kaplan-Meier curves and compared with the use of logistic regression analyses. Statistical calculations were done with the use of Statistical Product and Services Solutions v15.0 (SPSS, Chicago, Illinois). A P value of <.05 was considered to be statistically significant.

RESULTS

Among 64 isolations of pancreatic islets, 34 isolations (53.1%) met the release criteria. Previously, we reported that the factors associated with islet isolation were analyzed by a logistic regression univariate analysis. We found that duration of hypotension before cardiac arrest, length of cold ischemia time, and use of ET-Kyoto solution for preservation were significant factors for islet release. According to multivariate analyses, use of ET-Kyoto solution was the only significant factor among these factors [3].

Thirty-four transplantations of pancreatic islets were performed in 18 T1DM patients under the cover of immunosuppression with basiliximab, sirolimus, and tacrolimus. Of the 18 recipients, 8, 4, and 6 recipients received 1, 2, and 3 islet infusions, respectively. Among the 10 patients who received 2 or 3 transplantations, the intervals between transplantations ranged from 0 to 954 days. The follow-up time ranged from 58.7 months to 94.1 months, and the mean follow-up time was 76.4 $\pm$ 3.3 months. Overall graft survivals (defined as the C-peptide level) were 72.2%, 44.4%, and 22.2% at 1, 2, and 5 years, respectively (Fig 1A). When recipients were divided into 2 groups (one group who had 1 islet infusion, and the other group who had 2 or 3 islet infusions), we found that recipients receiving multiple islet infusions had significantly prolonged survival of islet grafts

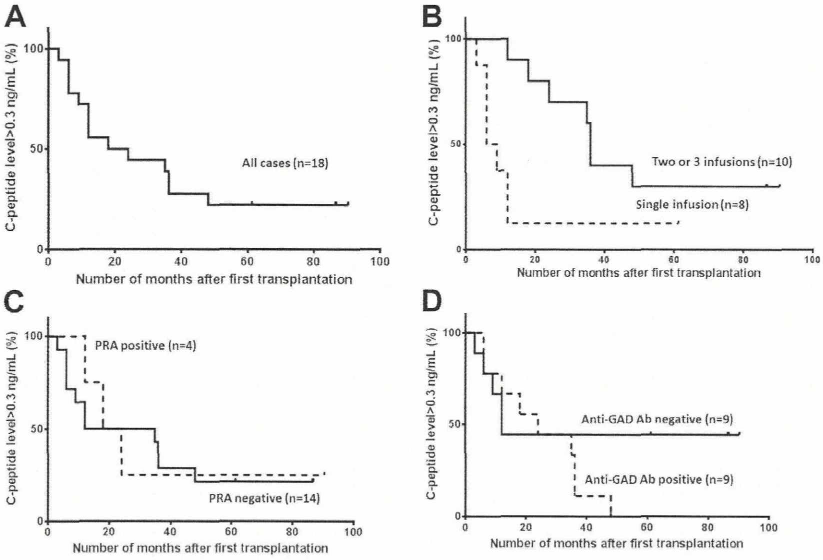

Fig 1. Islet graft survival according to Kaplan-Meier estimation. **(A)** Overall graft survival after islet transplantation from uncontrolled donors after cardiac death. Graft survivals (defined according to the C-peptide level) were 72.2%, 44.4%, and 22.2% at 1, 2, and 5 years, respectively. **(B)** Graft survival according to the number of islet infusions. Graft survivals of multiple infusions were 90.0%, 70.0%, and 30.0% at 1, 2, and 5 years, respectively, whereas the corresponding graft survival after a single infusion were 37.5%, 12.5%, and 12.5%, respectively. Multiple islet infusions significantly prolonged islet graft survival compared with a single infusion ($P = .017$). **(C)** Panel reactive antibody (PRA) positivity did not correlate with islet graft survival ($P = .85$). **(D)** Anti-glutamate decarboxylase (GAD) antibody positivity also did not correlate with islet graft survival ($P = .23$). The follow-up time ranged from 58.7 months to 94.1 months, and the mean follow-up time was 76.4 ± 3.3 months.

compared with those receiving a single infusion ($P = .017$). The graft survivals of multiple infusions were 90.0%, 70.0%, and 30.0% at 1, 2, and 5 years, respectively, whereas the corresponding graft survivals after a single infusion were 37.5%, 12.5%, and 12.5% (Fig 1B). Three of these recipients achieved insulin independence transiently after the 2nd transplantation for 215 days and after a 3rd transplantation for 14 days and 79 days.

Donor-specific alloantibodies were examined using flow PRA. Among these, 4 patients developed detectable levels of donor-specific alloantibodies. PRA positivity did not correlate with islet graft survival. Graft survivals for PRA-positive patients were 75.0%, 50.0%, and 25.0% at 1, 2, and 5 years, respectively, whereas the corresponding graft survivals for PRA-negative patients were 50.0%, 50.0%, and 21.4%, respectively (Fig 1C). Nine patients were positive for anti-glutamate decarboxylase (GAD) antibody. Being positive for anti-GAD antibodies also did not correlate with islet graft survival. The graft survivals of anti-GAD antibody–positive subjects were 66.7%, 44.4%, and 0% at 1, 2, and 5 years, respectively, whereas the corresponding graft survivals of anti-GAD antibody–negative subjects were 66.7%, 44.4%, and 44.4%, respectively (Fig 1D).

Hb_{A1c} levels and a requirement of exogenous insulin were improved before loss of graft function, but gradually worsened after the loss of graft function (Fig 2A). Serum creatinine levels were maintained even after the loss of graft function (Fig 2B).

All recipients became free of severe hypoglycemia unawareness, but at least 5 of 14 patients who had graft failure experienced recurrence of severe hypoglycemia after the loss of graft function.

DISCUSSION

Previously, we reported that pancreatic islet transplants from uncontrolled DCD sustained significant levels of C-peptide after a mean follow-up of 41 months [3]. The present report uses an extended follow-up from a multicenter study of outcomes after pancreatic islet transplantation from uncontrolled DCD.

Use of marginal-donor pancreata for islet isolation, such as DCD, is a way to alleviate donor shortages, particularly in countries such as Japan, where DBD are not readily available. According to the modified Maastricht classification [4], DCDs are classified into 5 categories; category I refers to subjects who are dead on arrival; category II is an unsuccessful resuscitation; category III (anticipated cardiac arrest) and category IV (cardiac arrest in a brainstem-dead donor) are described as controlled DCD; and category V (unexpected cardiac arrest in a patient in the intensive care unit) is described as uncontrolled DCD. Zhao et al reported that they isolated more viable islets from controlled DCD with short warm ischemia times than from pancreata from DBD, and that the islets from DCD were fully biofunctional [2]. Markmann et al reported that islets transplantation

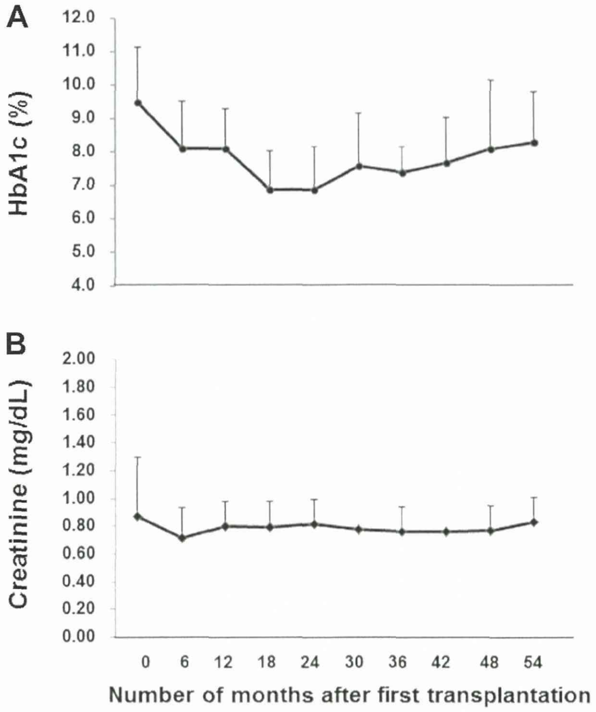

Fig 2. Changes in **(A)** Hb_{A1c} levels and **(B)** serum creatinine levels. Hb_{A1c} levels and the requirement of exogenous insulin were improved before loss of graft function, but gradually worsened after the loss of graft function. Serum creatinine levels were maintained even after the loss of graft function.

isolated from a single controlled DCD reversed diabetes of a T1DM recipient [1]. However, reports series of islet transplantations from DCD are limited. DCD are still not deemed to be suitable for donation.

In our series, all donors were considered to be uncontrolled DCD and category V of the modified Maastricht classification. Uncontrolled DCD have been used for kidney transplantation [11] and liver transplantation [12]. Islets are more likely to be damaged by warm ischemia in uncontrolled DCD. Damaged islets can be readily influenced by graft ischemia and/or instant blood-mediated inflammatory reactions [13]. Also, it has been suggested that DCD islets have lower contents of adenosine triphosphate and guanosine triphosphate, which could indicate energy loss [2]. The survival of transplanted islet grafts in our series reached only 22.2% at 5 years when >10,000 IEQ/kg were transplanted. However, in a publication from the Collaborative Islet Transplant Registry [14], the survival of transplanted islets from DBD after 5 years was 74%. Development of HLA antibodies against class I and/or II antigens can be associated with subsequent loss of islet grafts [15]. In our series, PRA-positive samples were detected less often, and a definitive association with graft survival could not be determined. Autoantibodies at the time of transplantation has been associated with reduced survival of islet grafts [16,17]. The presence of autoantibodies did not significantly affect graft survival in our series. However, 5-year graft survival was not observed in the anti-GAD antibody–positive group (though this could have been due to the small study cohort in our series). Overall, the reason for lower graft survival at 5 years in our series is not known, but could reflect the adverse effect of long intervals between transplantations [3] or may be associated with energy depletion within grafts.

In conclusion, islet transplantation from uncontrolled DCD can relieve glucose instability and problems with hypoglycemia while the graft is functioning. However, islets from DCD may be associated with reduced long-term graft survival. Further improvements in outcome by modification of the protocols for the isolation and transplantation of islets are necessary to establish islet transplantation from DCD. Recently, the β-cell secretory reserve of engrafted islets was shown to be improved markedly with the use of a protocol involving induction of antithymocyte globulin (ATG) and inhibition of tumor necrosis factor (TNF) [18]. We have started a phase II clinical trial in T1DM patients for islet transplantation from DBD and DCD to evaluate a protocol involving induction of ATG and inhibition of TNF (UMIN-CTR: 000003977). This trial could play a critical part in establishing islet transplantation in Japan.

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報告

本邦膵移植症例登録報告（2014）

日本膵・膵島移植研究会膵臓移植班

The Registry of Japanese Pancreas and Islet Transplantation 2014

The Japanese Pancreas and Islet Transplantation Association

【Summary】

Two hundred and eight cases of pancreas transplantation from deceased, non-heart beating and living-related donors have been performed in 14 institutions in Japan until the end of 2013 since April, 2000. The following donor- and recipient-related factors were analyzed; i.e., age and gender of donor and recipient, cause of death, histories of diabetes and dialysis, waiting period, total cold ischemic time, operative procedure, immunosuppression and survival rates of patient and graft.

In spite of donor poor conditions which were mostly marginal in Japan, the outcome of pancreas transplants was considered to be comparable to that of the US and Europe.

Keywords: simultaneous pancreas and kidney transplantation (SPK), pancreas after kidney transplantation (PAK), pancreas transplantation alone (PTA), deceased donors, non-heartbeating donors, living-related donors, marginal donor, bladder drainage, enteric drainage, tacrolimus, anti IL-2 receptor monoclonal antibody, mycophenolate mofetil (MMF)

Ⅰ. はじめに

膵・膵島移植研究会では，2007年以降，膵臓移植登録委員会において，毎年1回，本邦膵臓移植の現状ならびにその成績を報告している[1-7]。

1997年，「臓器の移植に関する法律」が実施されて以降，2013年末までに，本邦で実施された脳死下，心停止下での膵臓移植ならびに生体膵臓移植の全症例について，解析結果を報告する。

Ⅱ. 対象と方法

「臓器の移植に関する法律」実施後，2000年4月に第1例目の膵腎同時移植が行われてから，2013年末までに，本邦で実施された脳死下，心停止下での膵臓移植181例，ならびに生体膵臓移植27例，計208症例につき，患者数の推移，ドナー・レシピエント関連因子（ドナーの性と年齢，ドナーの死亡原因，レシピエントの性と年齢，透析歴と糖尿病歴，待機期間，総冷阻血時間，手術術式，免疫抑制法），移植成績（生存率，移植膵・移植腎生着率）を解析し治療成績を検討した。なお，累積生存率，膵および腎の生着率はKaplan-Meier法で算出した。

1. 膵臓移植認定施設

現在，認定施設は北海道大学（7），東北大学（7），福島県立医科大学（3），獨協医科大学（0），新潟大学（1＋2*），東京女子医科大学（27），東京医科大学八王子医療センター（0），国立病院機構千葉東病院（16＋18*），名古屋第二赤十字病院（7），藤田保健衛生大学（28＋2*），京都府立医科大学（8），京都大学（0），大阪大学（34＋1*），神戸大学（6），広島大学（5），香川大学（2），九州大学（30＋4*），以上，計17施設である。括弧内は2013年末までの実施移植数で，*は生体膵臓移植数である。

2. 膵臓移植実施体制

本邦における膵臓移植は中央調整委員会の下に，認定17施設の代表からなる実務者委員会が組織され，そこで作成された実施のためのガイドライン『膵臓移植に関する実施要綱，2010年版』（12月，改訂）に従って運用されている[8]。とりわけ，膵臓移植の特徴は，他の臓器と異なり，移植施設が近隣の経験の多い認定

施設と連携をとりながら，手術ならびに術後管理に対応している点が挙げられる。

3. レシピエントカテゴリーと登録システムとレシピエントの選択基準

膵臓移植には3つのレシピエントカテゴリーがあり，腎不全がある場合には膵臓と腎臓を同時に移植する膵腎同時移植（simultaneous pancreas and kidney transplantation：SPK）と先に腎臓移植を先行させ，後に膵臓移植を行う腎移植後膵移植（pancreas after kidney transplantation：PAK）とがあり，さらに腎不全のない場合には膵単独移植（pancreas transplantation alone：PTA）がある。

膵臓移植の適応基準に従い，レシピエント候補者の主治医が地域の膵臓移植適応評価委員会にデータを添えて申請して，その結果が中央調整委員会へ送付される。最終的に中央調整委員会から移植施設に対して，移植可能の是非が確認され，日本臓器移植ネットワークへ登録となる。

ドナー（脳死下，心停止下）発生時には，登録されたレシピエントの中から，選択基準に従って選択される。

Ⅲ. 結果と考察

1. 膵移植新規登録患者数

膵移植の日本臓器移植ネットワークへの登録は1999年10月より開始され，それ以降の新規登録患者数の推移を**図1**に示した。2013年末までに，日本臓器移植ネットワークに新規登録された患者数は計462名であった。2001年以降は毎年30名程度の新規患者が登録されていたが，臓器移植法改正後，2010年は42例，2011年は65例と急増し，2012年，2013年はおのおの39名，38名となっている。なお，登録後，糖尿病性合併症などの理由により41名が死亡し，47名が登録を抹消した。

2013年12月末日の時点で，移植後，死亡および取り消しを除いた登録待機中の患者188名について，性別，年齢ならびに待機期間につき検討した。性別では121例（約64%）が女性で，年齢では40歳代が89例（47%），次いで50歳代が44例（23%），30歳代が43例（23%）であった（**図2**）。

待機期間では，法改正後，新規症例は増えているとはいえ，3年以上待機例が44.7%と長く，とりわけ5年以上が29.3%と長期待機例が依然多い状態が続いている（**図3**）。

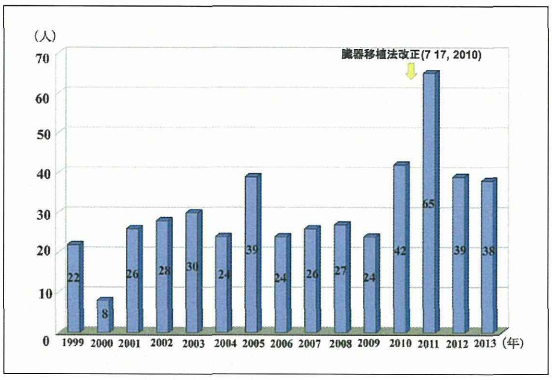

図1　膵移植新規登録患者数の年次推移

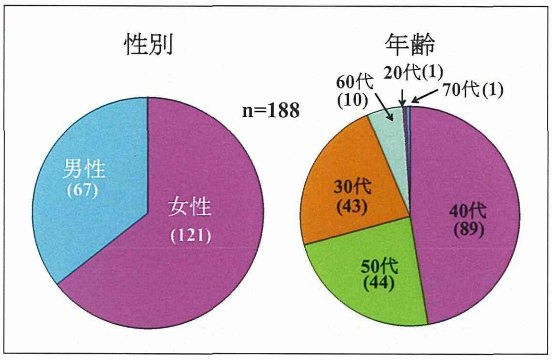

図2　膵臓移植待機登録者の性別と年齢（〜2013年12月）

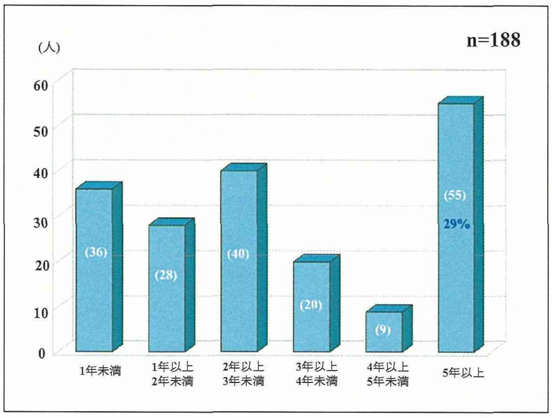

図3　膵臓移植登録者の待機期間（〜2013年12月）

2. 膵移植症例数

1997年10月「臓器の移植に関する法律」の施行後，2013年末までの脳死下での臓器提供の承諾は251例

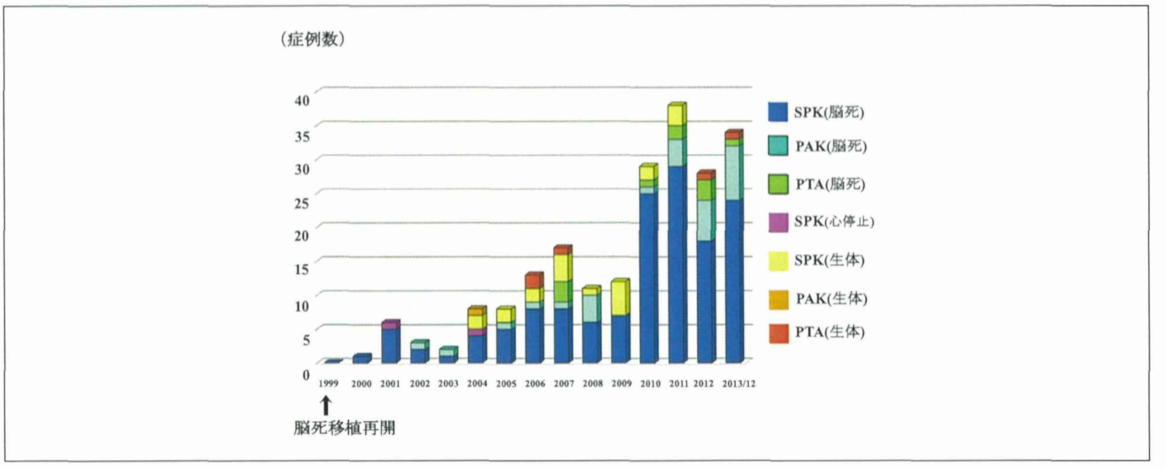

図4　膵移植症例数の年次推移

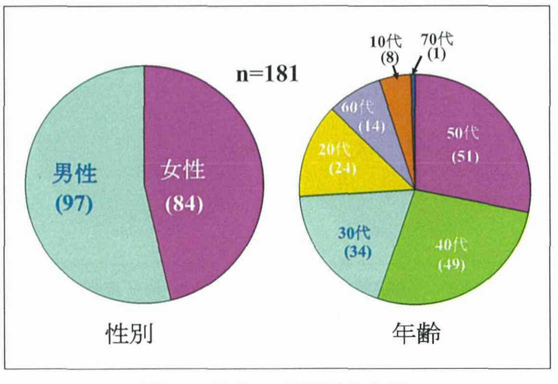

図5　ドナーの性別と年齢

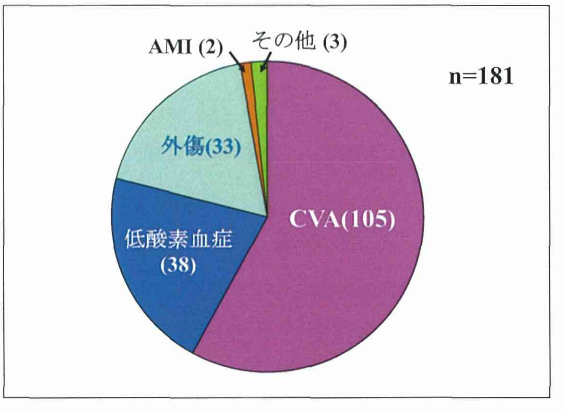

図6　ドナーの死亡原因

あり，そのうち，膵臓が提供に至ったのは179例（71.3%）であった。その内訳はSPKが141例，PAKが28例，およびPTAが10例であった。なお，提供されなかった72例の内訳は医学的理由が60例，未登録時期（～1999年9月）での提供が4例，意思表示カード上での未承諾が4例，適合者不在が3例，クロスマッチ陽性が1例であった。また，同期間中に2例の心停止下での膵臓移植（SPK）が行われた。さらに，生体ドナーからの膵臓移植も27例行われた。移植症例数の年次推移が示されている（**図4**）。

3. ドナー・レシピエント関連因子（脳死下・心停止下）

脳死・心停止下で行われた膵臓移植症例181例のドナーならびにレシピエントの関連因子について，解析した。

1）ドナー性・年齢

男女比は97：84と男性（53.6%）がやや多く，年令は50歳代が51名と最も多く，40歳代の49名に続き，30歳代，20歳代，60歳代がそれぞれ，34名，24名，14名であり，10歳代が8例，70歳代も1名みられた（**図5**）。本邦では40歳以上のドナーが100名と55.2%を占めていた。

2）ドナーの死亡原因

死因は脳血管障害が105名（58.0%）と最も多く，こうしたドナーにはなんらかの動脈硬化性変化が否定できない。他に，低酸素血症が38名，外傷が33名，心筋梗塞が2名，その他が3名であった（**図6**）。

3）レシピエント年齢・性差

男女比は70：111で女性（61.3%）に多く，年齢は40歳代が78名（43.1%）と最も多く，ついで30歳代が63名（34.8%）で50歳代が30名，20歳代，60歳代がともに5名であった（**図7**）。

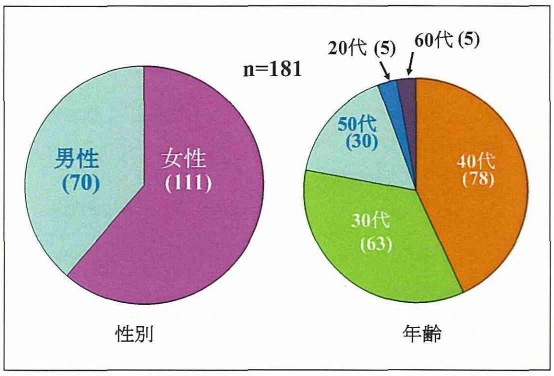

図7　レシピエントの性別と年齢

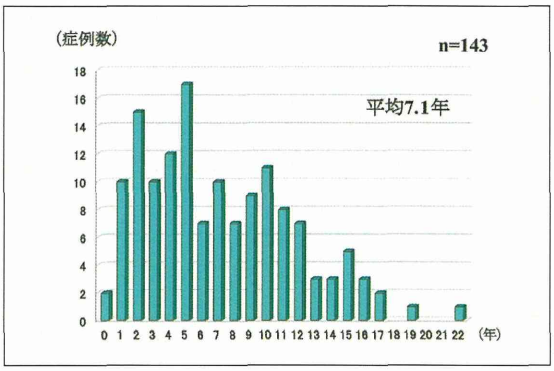

図8　レシピエントの透析歴

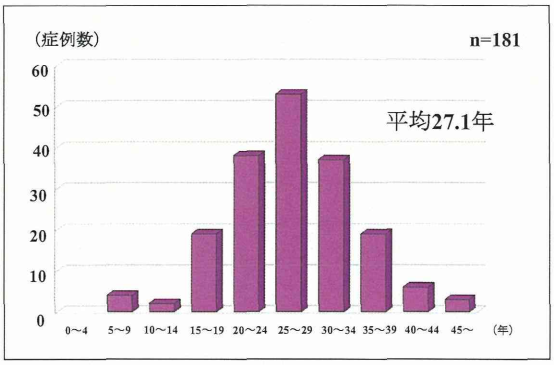

図9　レシピエントの糖尿病歴

4) 透析歴と糖尿病歴

透析歴は平均 7.1 (0〜22) 年で，糖尿病歴は平均 27.1 (9〜48) 年であった（**図 8，9**）。

5) 待機期間

移植を受けたレシピエントの平均待機期間は 1,305 (45〜4,722) 日と年々増加しており，約 3 年半であっ

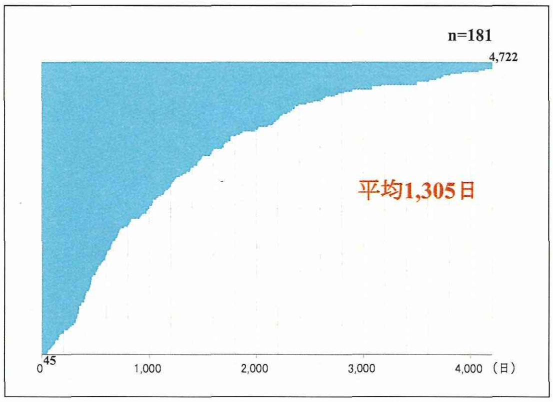

図10　レシピエントの登録後待機期間

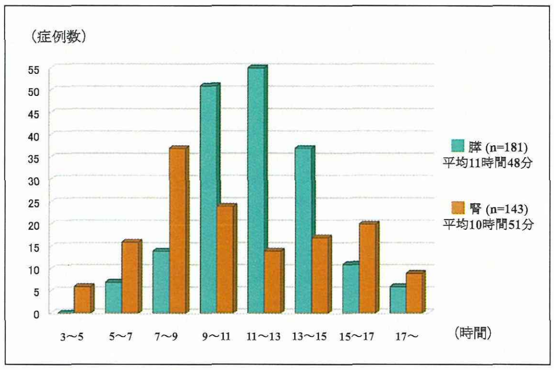

図11　移植膵・腎の総冷阻血時間

た（**図 10**）。

6) 総冷阻血時間（TCIT）

膵の TCIT は平均 11 時間 48 分であった。腎（SPK）の TCIT は平均 10 時間 51 分であり，2 峰性を示した。両臓器ともに十分許容範囲であった。これは SPK の場合，腎移植を先行させる場合と膵移植を先行させる場合があることによると考えられた（**図 11**）。なお，臓器搬送に要する時間は平均 3 時間 51 分であった。

7) HLA ミスマッチ

HLA ミスマッチ数は平均 2.60 であった（**図 12**）。

8) 移植術式（膵液ドレナージ）

脳死下（DD）での SPK 141 例では当初は安全性，尿中アミラーゼモニターを考慮して，膀胱ドレナージ（bladder drainage：BD）が行われたが，最近ではもっぱら腸管ドレナージ（enteric drainage：ED）が 118 例（83.7%）と大半を占めている。なお，BD 23 例のうち，尿路感染症や逆行性グラフト膵炎などの理由で 8 例は enteric conversion（EC）となった。また，心停止

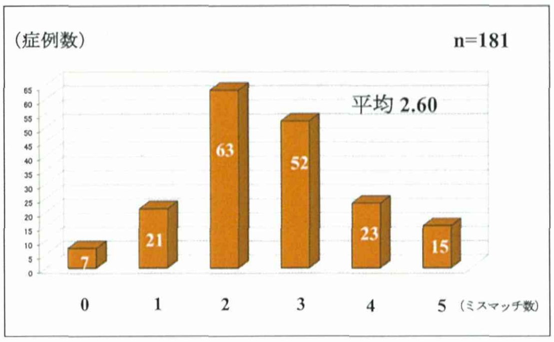

図 12　HLA ミスマッチ数

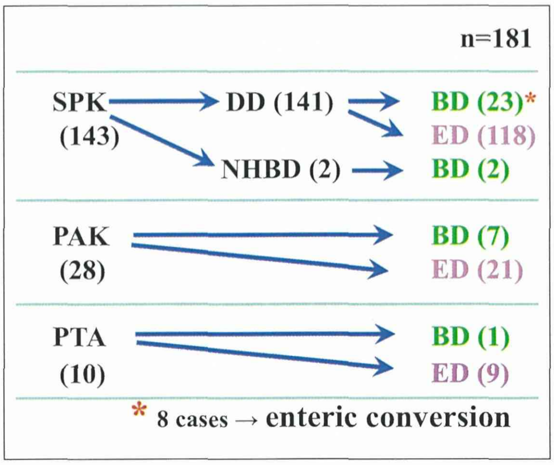

図 13　移植術式（膵液ドレナージ）

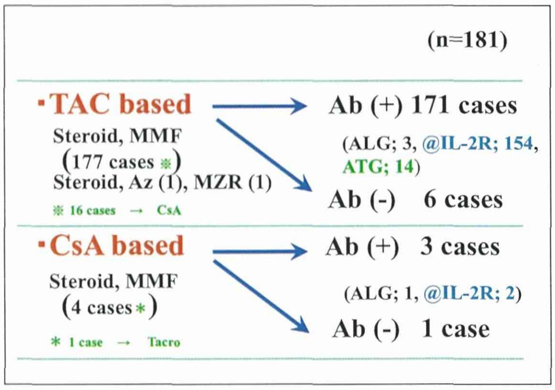

図 14　免疫抑制法

下（NHBD）での場合や PAK や PTA 症例ではグラフトの膵液をモニターする必要性から，40 例中 10 例（25.0%）に BD が用いられた（**図 13**）。なお，全例を通じて，5 例に膵再移植が行われた。

9）免疫抑制法

Tacrolimus（TAC）をベースとして，ステロイド，mycophenolate mofetil（MMF），抗 IL-2R 抗体（basiliximab）の 4 剤併用療法が 154 例（85.1%）と最も多く用いられている。うち，16 例が毒性のため TAC から cyclosporin（CsA）へ変更となっている。また，最近では，抗 IL-2R 抗体の代わりに，ATG（抗ヒト胸腺細胞ウサギ免疫グロブリン）が膵単独移植や二次（再）移植などの症例（14 例，7.7%）で使われている。一方，CsA をベースとして，4 剤併用療法が 3 例に行われ，うち 1 例は TAC へ変更となった（**図 14**）。

10）移植成績

本邦の膵臓移植はマージナルドナー（marginal donor）が多いことが特徴である。Kapur らによる marginal donor の定義［①45 歳以上，②不安定な血行動態（高用量のカテコラミンの使用），③心停止下での提供］[9] によると，生体を除く 181 例中 127 例（70.2%）が marginal case であった。

脳死・心停止下での膵臓移植症例 181 例のうち 8 例（すべて SPK）が死亡した。3 例は敗血症にて，3 例は心原性にて，さらに 1 例は GVHD にて死亡した。また，1 例は順調に経過していた症例であったが，7 年 10 カ月目に突然，脳出血をきたし死亡した。1 年，3 年，5 年生存率はいずれも 95.8% であった。なお，marginality の有無では差異を認めなかった。

移植膵の生着については，移植後急性期に 11 例が血栓症にて急性期に移植膵が摘出され，1 例は門脈血栓症が引き金となり 6 カ月後にインスリン再導入となった。移植後 2 年目に 1 例がイレウスからグラフト十二指腸穿孔により摘出された。他に，1 例がグラフト十二指腸からの出血（POD；45 日）で，また 1 例が超急性拒絶（POD；3）で，2 例が急性拒絶（POD；45，53 日）でおのおの摘出された。1 例は 1 型糖尿病の再燃，1 例はグラフト膵炎，14 例が慢性拒絶反応などの理由で，インスリン再導入となった。従って，死亡例を除き，計 34 例が移植膵の機能喪失となった。1 年，3 年，5 年生着率はそれぞれ 84.9%，78.0%，69.9% であった（**図 15**）。合併症に関して，マージナルドナーで多い傾向は認めたが，移植膵の生着率に差異を認めなかった。

今回，移植膵の生着率について，SPK と PAK/PTA で比較したところ，欧米での報告同様に前者が後者より統計学的に良好であった（**図 16**）。