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Second Annual Analysis of the Collaborative Islet Transplant Registry

N. Close, R. Alejandro, B. Hering, and M. Appel for the CITR Investigators

ABSTRACT

In September 2001, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) founded the Collaborative Islet Transplant Registry (CITR). Each year, CITR produces a complete set of analyses available to the public. In its second year, CITR represents the efforts of 19 North American islet transplant programs reporting information on 138 islet transplant recipients (1999–2004), 256 processed pancreata that led to infusion, and 266 infusion procedures. This analysis focuses on recipients of islet-alone procedures. Median age of the recipient is 41.6 years (range, 23.1–64.4 years), duration of diabetes is 29 years (range, 4–50 years), and over 66% are female. Median weight of the recipient is 65 kg (range, 47–97 kg) and median body mass index (BMI) is 23.1 kg/m^2 (range, 18.8–31.6). Examining outcomes at 6 months following the recipient's last infusion, 67.0% are insulin independent, and at 12 months this percentage decreases to 58.0%. There is a striking decrease in the occurrence of severe hypoglycemic events subsequent to the first infusion. Over 82% of all recipients experience one or more severe hypoglycemic events in the year prior to their first infusion. However, only two recipients (2%) experience one or more severe hypoglycemic events between 30 days and 12 months postinfusion, but both of these recipients were on insulin replacement therapy and one had experienced a complete islet graft failure. The information provided in this analysis and subsequent analyses of CITR provides current and comprehensive information on outcome measures in islet transplantation.

THE number of transplant centers performing clinical islet transplantation continues to increase, as do the number of centers participating and reporting to the Collaborative Islet Transplant Registry (CITR). The data compilation and analysis providing the basis of this second CITR Annual Report was made to facilitate the identification of both critical risk factors and key determinants for successful clinical islet/beta-cell transplantation. These insights may then provide guidance to transplant centers in developing and refining protocols as islet/beta-cell transplantation continues to evolve as a therapy option for the treatment of labile type 1 diabetes. This report represents a larger collaboration between islet transplant programs in North America with CITR using a more comprehensive database.

METHODS

Both the charter of CITR and results from the inaugural year of the Registry are reported elsewhere in detail.[1,2] This analysis represents a 60% increase in the number of islet recipients, a 48% increase in the number of pancreas donors, and a 68% increase in the number of infusion procedures over the number reported in the first report of the Registry. With increased cumulative data, greater precision in understanding comparative outcomes may be achieved across time.

The CITR adheres to strict quality control and assurance procedures. All data submitted are reviewed through several quality review processes. Islet transplant recipient data for this analysis reflect data entered by the islet transplant centers on recipients from January 1, 1999, to December 31, 2004. The cumulative data were subject to analyses.

These data were reviewed by the Coordinating Center for quality assurance, errors, and data outliers. Any missing follow-up data on these recipients were identified and conveyed back to the site for verification and correction. Any questions concerning specific data elements were also sent to the islet transplant centers for review and correction, if necessary. All islet transplant centers were provided ample time for resolving issues of discrepant data. The database was then updated and closed for analysis on April 1, 2005.

From the EMMES Corp., Rockville, Maryland.

Address reprint requests to Nicole C. Close, MS, MeRITS PMO, 504 Scott Street, Bldg 503, Ft. Detrick MD 21702. E-mail: nicole.close@amedd.army.mil

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Table 1. Summary of North American Islet Transplant Activity, 1999–2004

All Islet Transplant Programs in North America	Number of Human Islet Infusion Procedures Conducted	Number of Patients Receiving Their First Infusion
Total	475	257
1999	18	10
2000	33	22
2001	65	45
2002	142	82
2003	106	45
2004	111	53

At this time, 138 recipients had been registered for CITR and were eligible for analysis.

The CITR also collects basic information annually from all islet transplant centers in North America, regardless of their participation with CITR (number of pancreata processed and used for islet transplant and number of patients infused). Thirty-eight islet transplant programs were sent a questionnaire requesting this information. All 38 programs responded, and 27 of the 38 programs had been active between 1999 and 2004, transplanting at least one patient. The remaining programs either had not transplanted yet or were in the process of setting up their islet transplant program. This information provides the basis for determining the completeness of CITR and to summarize current activity of islet transplantation in North America.

Table 1 displays the data collected from the 27 active islet transplant programs in North America for 1999 to 2004, which is inclusive of all active islet transplant programs in North America. The analyses reported herein represent 53.7% of all islet transplant recipients in North America and 56.0% of all islet infusion procedures conducted.

RESULTS

Nineteen North American islet transplant programs have contributed to this annual analysis. Programs submitted information on 118 islet transplant-alone recipients, 19 islet after kidney recipients, and one autograft transplant recipient (N = 138). The median age of islet transplant-alone recipients (ITA) was 41.6 years (range, 23.1–64.4 years) and the median duration of diabetes was 29 years (range, 4–50 years). More than 66% of the recipients were female. The median recipient weight was 65 kg (range, 47–97 kg) and median body mass index (BMI) was 23.1 kg/m^2 (range, 18.8–31.6). All recipients were diagnosed with type 1 diabetes. Table 2 shows recipient insulin requirement status prior to first infusion, fasting plasma glucose, and hemoglobin A_{1c}. On average, recipients required 36.6 units (SD 12.9) of insulin per day prior to their first infusion, their fasting plasma glucose was 169.8 mg/dL (SD 105.3), and their hemoglobin A_{1c} was 7.6% (SD 1.3).

Table 2. Recipient Summary Measures Prior to First Infusion

	Overall		
	N	Mean	SD
Daily insulin requirement prior to infusion (units)	116	36.6	12.9
Duration of intensive therapy (yrs)	77	15.1	11.1
Fasting plasma glucose (mg/dL)	109	169.8	105.3
HbA_{1c} (%)	112	7.6	1.3

Table 3. Immunosuppression Regimen at Time of First Infusion

	Overall	
	N	%
Total	118	100.0
Sirolimus + tacrolimus + daclizumab	73	61.9
Sirolimus + tacrolimus + daclizumab + infliximab	12	10.2
Sirolimus + tacrolimus + basiliximab + etanercept	5	4.2
Sirolimus + tacrolimus + MMF + methylprednisolone + anti-thymocyte globulin + daclizumab + infliximab + etanercept	5	4.2
Sirolimus + tacrolimus + 15-deoxyspergualin + daclizumab	5	4.2
Sirolimus + tacrolimus + hOKT3γ-1(Ala-Ala)	3	2.5
Sirolimus + tacrolimus + MMF + daclizumab	2	1.7
Sirolimus + tacrolimus + MMF + methylprednisolone + anti-thymocyte globulin + daclizumab + etanercept	2	1.7
Neoral cyclosporine + methylprednisolone + everolimus + anti-thymocyte globulin + infliximab + etanercept	2	1.7
Sirolimus + MMF + anti-thymocyte globulin + daclizumab	1	0.8
Neoral cyclosporine + methylprednisolone + anti-thymocyte globulin + etanercept	1	0.8
Missing information on immunosuppression	7	5.9

The median age of the deceased donor for ITA recipients was 44 years (range, 8–65 years) and body mass index was 28.3 kg/m^2 (range, 13.3–59.8). Fifty-three percent of the donors were male, and approximately 66% were white. The median serum creatinine of the donors was 1.1 mg/dL, total bilirubin 0.7 mg/dL, AST 39.0 IU/L, ALT 31.0 IU/L, serum lipase 28.0 IU/L, and serum amylase 68.5 IU/L. Median time from cross clamp to pancreas recovery was 28 minutes (range, 0–127 minutes) while duration of cold ischemia was 7 hours (range, 1.5–27.0 hours). University of Wisconsin (UW), two-layer and UW followed by two-layer preservation were used for pancreas cold storage, and Liberase HI was used for collagenase digestion in 199 of 200 of the reported islet isolation procedures. All of the processing facilities used a density gradient for islet purification, and 45.5% of the islet products incorporated islet cell culture incubation.

The majority of the islet-alone recipients received daclizumab for induction and sirolimus combined with tacrolimus for maintenance immunosuppression. Table 3 includes a listing of all reported immunosuppression regimens used at the time of the recipient's first infusion.

One hundred and twelve islet-alone recipients have completed at least one follow-up evaluation after their last