INTRODUCTION

In contrast to well-published data with acceptable long-term results in large cohorts of single renal transplant recipients aged >65 y (lit.), combined pancreas-kidney transplantation in recipients >50 y is discussed controversially. Some groups have identified older recipients as a high-risk group, demonstrating decreased patient and graft survival in this population.1-4 Nevertheless, several centers have reported results for pancreatic transplantation in older patients as being comparable to those for younger recipients with the age cutoff ranging from 50 to 60 y.5-10

At our center, we have long-term experience with a total of 655 pancreas transplants performed between 1979 and August 2020, whereby 21 recipients were over 60 y of age; the oldest was age 69 and in remarkably good general condition with good mental adherence and a strong wish to undergo simultaneous kidney-pancreas transplantation (SPK). We retrospectively analyzed patient, pancreas, and kidney graft survival, graft function, and complications at month 38 posttransplant.

MATERIALS AND METHODS

Case Description

A 69-y-old type 1 diabetic (c-peptide negative: <0.003 pmol/mL) predialytic male patient with a BMI of 25.8 m² underwent SPK at our center. With his long-term diabetic history since the age of 32 y and a daily requirement of about 45 to 50 units of insulin, he suffered from strongly oscillating blood glucose levels despite a strict diet and regular physical exercise. As he also developed progressive diabetic nephropathy (GFR < 13.8 mL/min.), SPK was indicated. Pretransplant HbA1c was 6.5 g% (48 mmol/mol). His medical history included other secondary diabetic complications, such as peripheral arterial angiopathy and the amputation of a toe as well as peripheral sensomotoric neuropathy. Additionally, other comorbidities comprised chronic atrial fibrillation, arterial hypertension, and a traumatic fracture of the right leg.

The clinical findings made in the preoperative clinical evaluation were as follows:

Carotid arteries had a normal flow that was proven sonographically. Critical iliac vessel stenosis was excluded by a CT scan. Being predialytic, his daily urine output was balanced, bladder function, and prostate volume were normal. As coronary heart disease was excluded by a coronary CT and myocardial scan, a coronary angiography was not performed to avoid potential nephrotoxicity, probably requiring dialysis of iodine contrast load. Spirometry results were normal. Compliance was expected to be good as his younger brother had already successfully undergone SPK 7 y earlier.

Time from entering the waiting list until SPK was 16 d because he was the only candidate with a negative lymphocytotoxic crossmatch.

As a cytomegalovirus (CMV) antibody-negative recipient, he received the organs of a 27-y-old CMV-negative female donor with an HLA mismatch 2/2/2 and a cold ischemia time of 05:49 h for the pancreas and 07:30 h for the kidney. Both grafts were implanted according to standard techniques (exocrine pancreatic drainage by duodeno jejunoscopy). According to center protocol, immunosuppression consisted of thymoglobulin 4 mg/KG/BW, mycophenolate mofetil (MMF) 2 g daily, steroids with gradual tapering to 5 mg, and tacrolimus (TAC) with a targeted trough level of 12 to 14 ng/mL in the first month posttransplant, 6 to 8 ng/mL from month 6 to 12, and 5 to 7 ng/mL after month 12.
Pancreatic transplantation results in elderly patients as being comparable to those in younger recipients, with recipient cut-off age ranging from 50 to 55 y.3,8

Concerning the criteria for “old” pancreatic graft recipients, Arenas-Bonilla et al reported excellent long-term graft and patient survival following SPK from younger donors when defining “older” pancreatic recipients as above 40 y of age and focusing on their diabetic comorbidities.11

Regarding transplantation in an aging society, Viebahn et al analyzed their center experience with a distinctly older group of donors and recipients by comparing their pancreatic and patient survival to Eurotransplant data.12 They found a non-significant influence of donor and recipient age on the survival curves. Mittal et al and Shah et al reported on the feasibility of pancreas transplantation even in patients over 60 y.9,10

A recipient aged 69 y is to be critically viewed in the light of comorbidities based on advanced age and long-term diabetic disease. Therefore, a cautious pretransplant evaluation is of the utmost importance, especially concerning cardiac risk factors, and should include noninvasive and invasive testing methods depending on coronary status and clinical symptoms, followed by regular checkups during the waiting period.13,14 Our study patient with good mental adherence underwent precise pretransplant evaluation that excluded significant coronary stenosis and included an assessment of the iliac vessels.

At 16 d, his time on the waiting list was extremely short given the current mean waiting time of 192 d for first SPK (mean: 305.4 d for all pancreatic transplant candidates) and a current waiting list total of 8 patients.

Implantation of young donor organs with a short cold ischemia time seems to have contributed to good primary graft function.

Long-term immunosuppression consisted of prednisolone, MMF, and prolonged-release TAC with regular controls and cautious adaptation to avoid immunological, infective, oncological complications and to minimize side effects. In this balance, an exactly obtained therapeutic TAC level in the long-term follow-up was a major contributing fact.

The TAC trough level of 5 to 7 ng/mL aimed for after month 12 was sufficiently maintained with stable digestion and uncomplicated TAC metabolism: The patient expressed no fast TAC metabolism (defined as a ratio of TAC concentration/dosage <1.05; the optional cytochrome P genotyping was not performed for logistic reasons), which is an important factor in the dose adaptation of TAC formulations and is probably challenging in SPK recipients who have a higher immunological risk.15,16

This successful individual course in a patient with good general condition and stable pancreas and kidney function at month 38 is a noteworthy center experience in a total cohort of 21 patients over 60 y of age (median age 62 y; STD 2.3 y) with a median patient/kidney/pancreas survival of 72.0 mo (STD 57.1)/52.0 mo (STD 54.3)/47.0 mo (STD 58.0), respectively. Median donor age was 30.0 y (STD 11.3).

We conclude that, in this carefully selected patient, SPK was successful, as he was in good general condition with good mental adherence, had been precisely evaluated before transplantation, and received young donor organs with a short cold ischemia time. Cautious long-term immunosuppression with regular follow-up visits, including the management of
comorbidities, contributed to successful clinical results, which is probably good for the expansion of pancreas transplantation in physically and mentally well patients.

REFERENCES

1. Frei U, Noeldeke J, Machold-Fabrizi V, et al. Prospective age-matching in elderly kidney transplant recipients–a 5-year analysis of the Eurotransplant Senior Program. Am J Transplant. 2008;8:50–57.
2. Dreyer GJ, Hermke AC, Reinders ME, et al. Transplanting the elderly: balancing aging with histocompatibility. Transplant Rev (Orlando). 2015;29:205–211.
3. Freise CE, Stock PG, Melzer JS. Increased morbidity and mortality of simultaneous pancreas-renal transplantation in patients over 49 years of age. Transplant Proc. 1998;30:292.
4. Siskind E, Maloney C, Akerman M, et al. An analysis of pancreas transplantation outcomes based on age groupings–an update of the UNOS database. Clin Transplant. 2014;28:990–994.
5. Laurence J, Marquez M, Seal J, et al. The effect of recipient age on outcome after pancreas transplantation. Transplantation. 2014;99:e13–e14.
6. Schenker P, Vonend O, Krüger B, et al. Long-term results of pancreas transplantation in patients older than 50 years. Transpl Int. 2011;24:136–142.
7. Ablorsu E, Ghazanfar A, Mehra S, et al. Outcome of pancreas transplantation in recipients older than 50 years: a single-centre experience. Transplantation. 2008;86:1511–1514.
8. Afaneh C, Rich BS, Aull MJ, et al. Pancreas transplantation: does age increase morbidity? J Transplant. 2011;2011:596801.
9. Mittal S, Smilevska R, Franklin R, et al. An analysis of the association between older recipient age and outcomes after whole-organ pancreas transplantation - a single-centre, retrospective study. Transpl Int. 2020;33:529–535.
10. Shah AP, Mangus RS, Powelson JA, et al. Impact of recipient age on whole organ pancreas transplantation. Clin Transplant. 2013;27:E49–E55.
11. Arenas-Bonilla AJ, Campos-Hernández JP, Carrasco-Valiente J, et al. Influence of donor and recipient ages in survival of simultaneous pancreas-kidney transplantation. Transplant Proc. 2016;48:3033–3036.
12. Viebahn R, Klein H, Kraemer B, et al. Is pancreas transplantation getting old? Single-center experience in an aging society. Clin Transpl. 2009:165–169.
13. Eschertzhuber S, Hohlrieder M, Boesmueller C, et al. Incidence of coronary heart disease and cardiac events in patients undergoing kidney and pancreatic transplantation. Transplant Proc. 2005;37:1297–1300.
14. St Michel D, Donnelly T, Jackson T, et al. Assessing pancreas transplant candidate cardiac disease: preoperative protocol development at a rapidly growing transplant program. Methods Protoc. 2019;2:E82.
15. Torabi J, Konicki A, Rocca JP, et al. The use of LCP-tacrolimus (envarsus XR) in simultaneous pancreas and kidney (SPK) transplant recipients. Am J Surg. 2020;219:583–586.
16. Bösmüller C, Krendl F, Messner F, et al. LCPT in tacrolimus fast-metabolizing pancreas recipients compared to high-dose prolonged release tacrolimus versus non-fast metabolizers: a single-center experience. AJBSR. 2020;9:35–42.