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Good Long-term Results Following Simultaneous Pancreas-kidney Transplantation in a 69-y-old Recipient: A Case Report

Claudia Bösmüller, MD,¹ Felix Krendl, MD,¹ Franka Messner, MD, PhD,¹ Valeria Berchtold, MD,¹ Katrin Kienzl-Wagner, MD,¹ Stefan Scheidl, MD,¹ Rupert Oberhuber, PhD,¹ Dietmar Öfner, MAS, MSc, MD,¹ Stefan Schneeberger, MD,¹ and Christian Margreiter, MD¹

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.

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¹ Department of Transplant Surgery, Medical University of Innsbruck, Innsbruck, Austria.

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Correspondence: Claudia Bösmüller, MD, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Austria, Anichstr. 35, A 6020 Innsbruck, Austria. (claudia.boesmueller@tirol-kliniken.at).

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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 somotoric 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 05:49h for the pancreas and 07:30h for the kidney. Both grafts were implanted according to standard techniques (exocrine pancreatic drainage by duodeno jejunostomy). According to center protocol, immunosuppression consisted of thymoglobulin 4mg/KG/BW, mycophenolate mofetil (MMF) 2g daily, steroids with gradual tapering to 5mg, and tacrolimus (TAC) with a targeted trough level of 12 to 14ng/mL in the first month posttransplant, 6 to 8ng/mL from month 6 to 12, and 5 to 7ng/mL after month 12.

Perioperative antimicrobial prophylaxis consisted of piperacillin-tazobactam and micafungin. Prophylaxis against pneumocystis/CMV consisted of trimethoprim-sulfamethoxazole/valganciclovir. The regularly checked CMV-PCR was negative. Following perioperative IV heparin, oral anticoagulation consisted of acetylsalicylic acid. Regular long-term follow-up visits were made 2 to 3 times monthly. The annual physical checkup included chest radiograph, abdominal ultrasound, cardiological, angiological, dermatological, ophthalmological, and urological visits.

The patient's immunosuppression currently consists of TAC with a daily alternating dosage of 1.0/1.5 mg, whereby we aim for a trough level of 5 to 7 ng/mL, MMF 1000 mg, and prednisolone 5 mg. Antihypertensive medication consists of amlodipine, rilmenidine, and the gastritis prophylaxis ranitidine.

Statistical methods were descriptive, counts reported as percentages, continuous variables as median and range.

RESULTS

Both transplants showed good initial function without the need for dialysis or exogenous insulin; no rejection occurred. Summarizing complications, a wound-healing disorder (month 5) was successfully treated with a vacuum system, and 2 herpetic infections (stomatitis in month 1, nasal herpes in month 5) were reversed with valacyclovir. A mild increase in liver enzymes (month 1) was reversed by temporarily switching from pantoprazole to ranitidine for gastritis prophylaxis. Regarding necrosis of the second and third right toe, he benefited from CT-guided lumbar sympathectomy and peripheral blockade of the sciatic nerve (month 6) as he had oscillography-proven reduced perfusion of the toes but no signs of macroangiopathy in CT angiography and oscillography within a normal ankle-brachial index. Arterial hypertension (onset in month 7) was managed with amlodipine and rilmenidine after 6 mo of normotensive (even temporarily hypotensive) arterial blood pressure caused by a posttransplant total weight loss of 10 kg with initially negative fluid balances from high urine output and excretion of pancreatic juice. When he regained his pretransplant weight (80 kg) at month 7 including normal fluid balance, good oral alimentation, and maintenance steroids, his arterial hypertension recurred and he required the same 2 medications as pretransplant.

In postoperative month 38, he currently enjoys good quality of life with stable graft function proven by the following laboratory values: serum creatinine 1.5 mg/dL, HbA1c 5.5 g% (37 mmol/mol), fasting blood glucose 75 mg/dL, serum amylase 19 U/L, serum lipase 23 U/L, liver enzymes in normal range.

No malignancy or critical infectious disease occurred in the long-term follow-up. The regularly checked PCR for SARS-CoV-2 was negative. The patient has been vaccinated with an mRNA-based vaccine that was well tolerated.

DISCUSSION

Pancreas transplantation in elderly recipients is discussed controversially, whereby Freise et al experienced elderly patients as a risk group and Siskind et al demonstrated decreased patient and graft survival in this cohort, according to the UNOS database.^{3,4} In contrast, several centers reported 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).

CONCLUSION

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.

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