



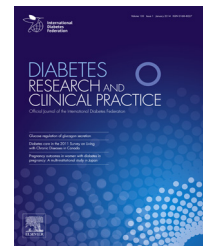
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Invited Review

Long-term outcomes after organ transplantation in diabetic end-stage renal disease

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ABSTRACT

Patients with type 1 diabetic end-stage renal disease (ESRD) may be offered single kidney transplantation from a live donor (LDK) or a deceased donor (DDK) to replace the lost kidney function. In the latter setting the patient may also receive a simultaneous pancreas together with a kidney from the same donor (SPK). Also in some cases a pancreas after kidney may be offered to those who have previously received a kidney alone (PAK). The obvious benefit of a successful SPK transplantation is that the patients not only recover from uremia but also obtain normal blood glucose control without use of insulin or other hypoglycemic agents. Accordingly, this combined procedure has become an established treatment for type 1 diabetic patients with ESRD. Adequate long-term blood glucose control may theoretically lead to reduced progression or even reversal of microvascular complications. Another potential beneficial effect may be improvement of patient and kidney graft survival. Development of diabetic complications usually takes a decade to develop and accordingly any potential benefits of a pancreas transplant will not easily be disclosed during the first decade after transplantation. The purpose of the review is to assess the present literature of outcomes after kidney transplantation in patients with diabetic ESRD, with or without a concomitant pancreas transplantation. The points of interest given in this review are microvascular complications, graft outcomes, cardiovascular outcomes and mortality.

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1. Introduction

The first pancreas transplantation ever was performed in Minnesota in 1966 by Kelly et al. [1]. Since then, the frequency of pancreas transplantation has increased as the results have improved over the last decades due to improvements in the surgical technique and also improvement in immunosuppressive regimens [2–7]. From December 16 through December 31, 2010, more than 37,000 pancreas transplantations have been reported to the International Pancreas Transplant Registry (IPTR), the majority of which were SPK transplantations [2]. Pancreas transplantation has become an established treatment option for patients with type 1 diabetes, especially those with additional end-stage renal disease (ESRD). In patients with diabetic ESRD, kidney transplantation increases survival compared with long-term dialysis treatment, with or without a concomitant pancreas transplant [8–10]. Transplant options for patients with type 1 diabetic end-stage nephropathy include simultaneous pancreas and kidney (SPK), live donor kidney (LDK) and deceased donor kidney (DDK) transplantation. Also in some cases a pancreas after kidney transplantation may be offered to those who have previously received a kidney alone (PAK). SPK transplantation relieves not only the patient's uremia, but also alleviates the hyperglycemic state of diabetes. Insulin independence after successful pancreas transplantation is also generally accepted to improve quality of life [3,11].

Large international patient registries suggest that the survival rate of SPK recipients is superior to that in diabetic patients receiving a single kidney graft only. However, such registries cannot fully account for differences in transplantation protocols and medication at different centers. Due to the increased operative risk of SPK transplantation the procedure has historically been offered to younger and physically healthier recipients while older diabetic recipients usually have received a kidney transplant only. It has therefore been difficult to prove superiority of additional pancreas transplantation.

2. Survival

2.1. Patient survival

Comparison of survival between patients on dialysis treatment and transplant recipients is hampered by selection bias. The healthiest patients and those of younger age are likely to be referred to transplantation whereas older patients and those with substantial comorbidity are referred to chronic dialysis treatment. To avoid the selection bias studies have been made among patients already accepted on the waiting list for transplantation comparing those who receive a transplant and those who remain listed assuming that the

two groups are otherwise at comparable risk. Given these limitations renal replacement therapy with kidney transplantation is associated with better patient survival long-term compared with chronic dialysis treatment [8–10]. It is well acknowledged that patients with diabetic ESRD are at particularly high risk of cardiovascular disease on dialysis therapy [8]. Patients with diabetes also have a higher mortality after kidney transplantation compared with patients without diabetes [12].

The survival rates of diabetic patients with ESRD who have received SPK transplants have steadily improved in the last decades. In SPK recipients, data from the IPTR show that 1 and 5 year unadjusted patient survival rates now reach more than 95% and 87%, respectively [2]. The patient survival rates in live donor kidney transplantation are 98% and 86% at 1 and 5 years, respectively, and in deceased donor kidney transplantation 95% and 77% at 1 and 5 years, respectively [13].

It is generally accepted that SPK recipients have improved survival compared with deceased donor kidney recipients [4,14–20]. However, studies to assess whether SPK transplantation is superior to that of live donor kidney transplantation alone in terms of improved patient survival are not consistent when observation time is less than 10 years after transplantation [3,15,18,21,22]. Some studies show equal patient survival rates in SPK recipients compared with LDK recipients [3,15,16,18]. Table 1 summarizes survival data of SPK versus LDK and DDK in studies with an observation time less than 10 years. Overall these studies demonstrate no survival benefit of SPK over LDK recipients.

Two recent major publications presented long-term outcomes in favor of better patient survival with SPK transplantation even when compared with LDK recipients. Data from the international Collaborative Transplant Study (CTS) showed that SPK recipients had superior survival beyond the 10th year post-transplant than those receiving a LDK or DDK kidney transplant alone [17]. A study from the Scientific Registry of Transplant Recipients (SRTR) in the US by Weiss et al. also showed superior patient survival among SPK recipients compared to both LDK and DDK recipients [21]. However, only SPK recipients with a functioning pancreas graft 1 year after transplantation were included in their analysis. These observations are in contrast to the findings of Young and colleagues, who analyzed Organ Procurement and Transplantation Network/United Network of Organ Sharing (OPTN/UNOS) database registry data [22]. On multivariate analysis, LDK transplantation was associated with lower adjusted risk over a period of 72 months follow-up with respect to patient death versus SPK transplantation. Table 2 summarizes survival data of SPK versus LDK and DDK in studies with an observation time of more than 10 years. Overall these studies demonstrate a survival benefit of SPK over LDK over DDK recipients.

Most single center publications originate in the US. Sollinger et al. [4] published a study including SPK recipients

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