Regence

Medical Policy Manual Transplant, Policy No. 06

Pancreas Transplant

Effective: November 1, 2023

Next Review: August 2024
Last Review: September 2023

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Transplantation of a normal pancreas is a treatment method for patients with diabetes.

MEDICAL POLICY CRITERIA

Note: Islet cell transplantation is considered in a separate medical policy (see Cross References).

I. Pancreas transplant may be considered **medically necessary** when both of the following (A. and B.) are met:
   A. Candidates must meet both of the following general criteria:
      1. Adequate cardiopulmonary status; and
      2. Documentation of patient compliance with medical management.
   B. Transplant for any of the following indications:
      1. A combined pancreas-kidney transplant in diabetic patients with uremia; or
      2. Pancreas transplant after a prior kidney transplant in patients with insulin-dependent diabetes mellitus (IDDM); or

3. Pancreas transplant alone in patients with documentation of any of the following conditions, which persist despite optimal medical management:
    a. Severely disabling and potentially life-threatening hypoglycemia unawareness as evidenced by chart notes or emergency room visits; or
    b. Potentially life-threatening labile diabetes as evidenced by documentation of erratic blood glucose levels and hemoglobin A1c equal to or greater than 8% or hospitalization for diabetic ketoacidosis.

II. Pancreas retransplantation may be considered **medically necessary** after one failed primary pancreas transplant.

III. Pancreas transplantation that does not meet Criterion I. or II. is considered **not medically necessary.**

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

MULTIPLE TRANSPLANTS

Although there are no standard guidelines regarding multiple pancreas transplants, the following information may aid in case review:

- If there is early graft loss resulting from technical factors (e.g., venous thrombosis), a retransplant may generally be performed without substantial additional risk.
- Long-term graft losses may result from chronic rejection, which is associated with increased risk of infection following long-term immunosuppression, and sensitization, which increases the difficulty of finding a negative cross-match. Some transplant centers may wait to allow reconstitution of the immune system before initiating retransplant with an augmented immunosuppression protocol.

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Diagnosis and indication for transplant
- Pre-transplant evaluation including pulmonary status and pertinent co-morbidities and treatments
- Failed primary pancreas transplant

CROSS REFERENCES

1. Islet Cell Transplantation, Transplant, Policy No. 13

BACKGROUND

Pancreas transplantation can restore glucose control, and is intended to prevent, halt, or

reverse the secondary complications of insulin-dependent Type 1 diabetes mellitus (IDDM). Achievement of insulin independence with resultant decreased morbidity and increased quality of life is the primary health outcome of pancreas transplantation. While pancreas transplantation is generally not considered a life-saving treatment, in a small subset of patients who experience life-threatening complications from IDDM, pancreas transplantation could be considered lifesaving. In addition to the immune rejection issues common to all allograft transplants, autoimmune destruction of beta cells has been observed in the transplanted pancreas, presumably from the same mechanism responsible for type 1 diabetes.[1]

Pancreas transplantation occurs in several different scenarios such as:

1. Patient with type 1 diabetes with renal failure who may receive a cadaveric simultaneous pancreas/kidney transplant (SPK)
2. Patient with type 1 diabetes who may receive a cadaveric or living-related pancreas transplant after a kidney transplantation (pancreas after kidney, i.e., PAK)
3. Patient with non-uremic type 1 diabetes with specific severely disabling and potentially life-threatening diabetes related problems who may receive a pancreas transplant alone (PTA).

PTA has also been investigated in patients following total pancreatectomy for chronic pancreatitis. The experience with SPK transplants is more extensive than that of other transplant options.

The approach to retransplantation varies according to the cause of failure. Surgical/technical complications such as venous thrombosis are the leading cause of pancreatic graft loss among patients with diabetes. Graft loss from chronic rejection may result in sensitization, increasing both the difficulty of finding a cross-matched donor and the risk of rejection of a subsequent transplant. Each center has its own guidelines based on experience; some transplant centers may wait to allow reconstitution of the immune system before initiating retransplant with an augmented immunosuppression protocol.

EVIDENCE SUMMARY

SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT

The U.S.-based Organ Procurement and Transplant Network (OPTN) reported a one-year patient survival rate of 97.5% (95% confidence interval [CI] 96.9% to 98.0%) for primary simultaneous pancreas/kidney transplant (SPK) procedures performed between 2008 and 2015.[2] Three- and five-year patient survival rates were 94.8% (95% CI 93.9% to 95.5%) and 88.9% (95% CI 87.8% to 89.9%), respectively.

Martin-Gonzalez (2023) published a retrospective observational study was conducted in two cohorts of SPK recipient patients that underwent surgery between 2001 and 2021.[3] The two cohorts represented an initial protocol (cohort 1; n=32) and an updated protocol (cohort 2; n=23). Average survival was 2546 days (95% CI: 1902-3190) for cohort 1 and 2540 days (95% CI: 2100-3204) for cohort 2 ($p > 0.05$). Pancreatic graft failure-free survival had an average of 1705 days (95% CI: 1037-2373) in cohort 1, lower than the average in cohort 2 (2337 days; 95% CI: 1887-2788) ($p = 0.016$). Similarly, renal graft failure-free survival had an average of 2167 days (95% CI: 1485-2849) in cohort 1, lower than the average in cohort 2 (2583 days; 95% CI: 2159-3006) ($p = 0.017$).

Barlow (2017) analyzed U.K. registry data that compared outcomes in patients with type 1 diabetes and end-stage renal disease who had SPK transplants (n=1739) with live donor kidney transplants (n=370).[4] In multivariate analysis, there was not a significant association between type of transplant and patient survival (HR [hazard ratio] 0.71, 95% CI 0.47 to 1.06; p=0.095). SPK recipients with a functioning pancreas graft had significantly better overall survival than those with a living donor kidney transplant (p<0.001).

Pancreas transplant has been found to improve mortality in patients with type 1 diabetes. Van Dellen (2014) reported a retrospective analysis of data on 148 SPK patients and a wait-list control group of 120 patients.[5] The study also included 33 patients who had PAK and 11 PTA patients. All patients had uncomplicated type 1 (insulin dependent) diabetes. Overall mortality was 30% (30/120 patients) on the waiting list and patients who underwent transplantation had a mortality rate of 9% (20/193 patients); the difference between groups was statistically significant (p<0.001). One-year mortality was 13% (n=16) on the waiting list and 4% (n=8) in the transplant group (p<0.001).

There are some data on outcomes in patients with type 2 compared with type 1 diabetes. Sampaio (2011) published an analysis of data from the United Network for Organ Sharing (UNOS) database.[6] The investigators compared outcomes in 6,141 patients with type 1 diabetes and 582 patients with type 2 diabetes who underwent SPK between 2000 and 2007. In adjusted analyses, outcomes were similar in the two groups. After adjusting for other factors such as body weight; dialysis time; and cardiovascular comorbidities, type 2 diabetes was not associated with an increased risk of pancreas or kidney graft survival or mortality compared to type 1 diabetes.

Mora (2010) described the long-term outcome of 12 patients 15 years following SPK transplant.[7] Metabolic measures of glucose control were measured at 1, 5, 10, and 15 years following the procedure. Of this subset of patients, six (50%) had non-diabetic glucose challenge tests. Basal serum insulin levels declined over this period as well, from 24 mU/L to 16 mU/L at 1 and 15 years, respectively. The authors concluded that in a select group of patients whose pancreatic graft continued to function after 15 years, some glycemic control continued, albeit in a diminished fashion. It should be noted that this represented a small fraction of the 367 patients receiving the SPK transplant at this single center (12 of 367 SPK; 3.3%). The number of allograft survivals at five or more, and 10 or more years in this study was 43 (11.7%) and 28 (7.6%), respectively.

The improved glycemic control that may occur in SPK transplant patients, principally in those with labile disease while on medical therapy alone, is purported to reduce risk of complications from diabetes. Davenport (2009) published results of a registry review (n=58) on cardiovascular risk factors in an Irish study of SPK transplant recipients.[8] Glycosylated hemoglobin values fell from a mean of 8.1 to 5.2 (p<0.0001) from pre-transplant levels. Similar statistically significant declines were seen in total cholesterol, triglycerides, and creatinine. Systolic and diastolic blood pressures were likewise improved but with a greater range of pre- and post-transplant variability. These endpoints are commonly accepted as surrogates for cardiovascular risk. The authors compared both a surgical method (bladder vs. enteric drainage) and mode of immunosuppression (cyclosporine vs. tacrolimus) on changes to blood pressure and cholesterol. No significant differences were found in either measure based on surgical drainage method, nor did immunosuppressive therapy have an impact on blood pressure reduction. Cholesterol reduction was greater in the cyclosporine than the tacrolimus group (-1.3 to -0.2, respectively), favoring the less contemporary strategy. The authors noted

that this was in contrast to other recently published studies favoring both enteric drainage and tacrolimus. While this single arm study suggested beneficial cardiovascular effects from transplant, other factors such as rejection rates were more likely to influence the conditions under which transplantations took place.

PANCREAS AFTER KIDNEY TRANSPLANT[9]

Parajuli (2019) described a single center's experience with 635 pancreas and kidney transplant patients (611 SPK, 24 PAK).[10] Transplants were performed between 2000 and 2016. The mean length of time between kidney transplant and pancreas transplant was 23.8 months in the PAK group. Pancreas rejection rates at one-year post-transplant were 4% and 9% with PAK and SPK respectively. During the entire study period, PAK patients were more likely to experience pancreas rejection (38% vs. 16%; p=0.005). Kidney and pancreas graft survival rates did not differ between groups at one year or at last follow-up. Pancreas graft survival rates for PAK and SPK at one year were 100% and 89%, respectively (p=0.09). Death-censored pancreas graft failure rates for PAK and SPK at last follow-up were 13% and 25%, respectively (p=0.17). Patient survival at last follow-up was similar between groups (71% with PAK vs. 68% with SPK; p=0.79).

Gruessner (2016) reported updated patient survival rates for pancreas after kidney (PAK) transplants. According to UNOS and International Registry data, patient survival after PAK from 2010 to 2014 was 97.9% after one year and 94.5% after three years.[11] This compares with one-year and three-year patient survival rates for 2005 to 2009 of 96.4% and 93.1%, respectively.

PAK transplantation allows the uremic patient the benefits of a living-related kidney graft, if available, and the benefits of a subsequent pancreas transplant that is likely to result in improved quality of life compared to a kidney transplant alone. Uremic patients for whom a cadaveric kidney graft is available, but a pancreas graft is not simultaneously available benefit similarly from a later pancreas transplant. Based on international pancreas registry data, at five years post-transplant, the patient survival rate after PAK is 83%.[12]

Bazerbachi (2012) reviewed a single center’s experience with PAK and synchronous pancreas-kidney (SPK) transplantations.[13] Between 2002 and 2010, 172 pancreas transplants were performed in diabetic patients; 123 SPK and 49 PAK. The median length of time between kidney and pancreas transplantation in the PAK group was 4.8 years. Graft and patient survival rates were similar in the two groups. Death-censored pancreas graft survival rates for SPK and PAK were 94% and 90% at one year, 92% and 90% at three years, and 85% and 85% at five years (all respectively, p=0.93). Patient survival rates (calculated beginning at the time of pancreas transplantation) in the SPK versus PAK groups were 98.3% and 100% after one year, 96.4% and 100% after three years, and 94.2% and 100% after five years (all respectively, p=0.09).

Fridell (2009) reported a retrospective review (n=203) of a single center’s experience with PAK and SPK since 2003, when current induction/tacrolimus immunosuppressive strategies became standard.[14] Of the cases studied, 61 (30%) were PAK and 142 (70%) were SPK. One-year patient survival rates were 98% and 95% (PAK and SPK, respectively; p=0.44). Pancreas graft survival rates at one year were observed to be 95% and 90%, respectively (p=0.28). The authors conclude that in the modern immunosuppressive era, PAK should be considered as an acceptable alternative to SPK in candidates with an available living kidney donor.

Kleinclauss (2009) retrospectively examined data from diabetic kidney transplant recipients (n=307) from a single center and compared renal graft survival rates in those who subsequently received a pancreatic transplant to those who did not.[15] The comparative group was analyzed separately depending on whether they were medically eligible (KTA-E) for pancreas transplant, but chose not to proceed for financial or personal reasons, or were ineligible (KTA-I) for medical reasons. The KTA-I (n=57) group differed significantly at baseline from both the PAK group (n=175) and the KTA-E group (n=75) with respect to age, type of diabetes and dialysis experience; kidney graft survival rates were lower than either of the other groups, with 1-, 5-, and 10-year rates of 75%, 54%, and 22%, respectively ($p<0.0001$). The PAK and KTA-E groups were similar in age, race, type of diabetes, and dialysis experience. The authors compared 1-, 5-, and 10-year kidney graft survival rates in PAK patients with those in the KTA-E group: 98%, 82%, and 67% versus 100%, 84%, and 62%, respectively, and concluded that the subsequent transplant of a pancreas after a living donor kidney transplant did not adversely affect patient or kidney graft survival rates.

PANCREAS TRANSPLANT ALONE[9]

Boggi (2021) reported results of a single-center cohort study of 66 patients with type 1 diabetes who received PTA.[16] After 10 years of follow-up, patient survival was 92.4%. Of these patients surviving to 10 years, 57.4% had optimal graft function (defined as normoglycemia and insulin independence) and 3.2% had good graft function (defined as HbA1c <7%, no severe hypoglycemia, >50% reduction in insulin requirements, and restoration of clinically significant C-peptide production). Four patients (6.0%) developed end-stage renal failure (stage 5, estimated glomerular filtration rate [eGFR] < 15 ml/min/1.73 m2), and 2 additional patients (3.0%) showed stage 4 kidney failure (eGFR 15-30 ml/min/1.73 m2) at the 10-year posttransplant assessment.

Gruessner and Gruessner (2016) reported updated patient survival rates for PTA.[11] According to UNOS and the International Registry data, for the period of 2010 to 2014, patient survival after PTA was 96.3% after one year and 94.9% after three years. This compares with one-year and three-year patient survival rates of 97.5% and 93.3% for 2005 to 2009, respectively.

According to international registry data one-year graft function increased from 51.5% in 1987-1993 to 77.8% in 2006-2010 ($p<0.0001$).[12] One-year immunologic graft loss remains higher (6%) after PTA than PAK (3.7%) or SPK (1.8%). In carefully selected IDDM patients with severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and labile diabetes that persists despite optimal medical management, the benefits of PTA were judged to outweigh the risk of performing pancreas transplantation with subsequent immunosuppression. The majority of patients undergoing PTA are those with either hypoglycemic unawareness or labile diabetes. However, other exceptional circumstances may exist where non-uremic IDDM patients have significant morbidity risks due to secondary complications of diabetes (e.g., peripheral neuropathy) that exceed those of the transplant surgery and subsequent chronic immunosuppression. Because there is virtually no published evidence regarding outcomes of medical management in this very small group of exceptional diabetic patients, it is not possible to generalize about which circumstances represent appropriate indications for pancreas transplantation alone. Case-by-case consideration of each patient's clinical situation may be the best option for determining the balance of risks and benefits.

Noting that nephrotoxic immunosuppression may exacerbate diabetic renal injury after PTA,

Scalea (2008) reported a single institutional review of 123 patients who received 131 PTA for development of renal failure.[17] Mean graft survival was 3.3 years (range, 0 to 11.3), and 21 patients were lost to follow-up. Mean estimated glomerular filtration rate (eGFR) was 88.9 pre-transplantation versus 55.6 post-transplantation, with mean follow-up of 3.7 years. All but 16 patients had a decrease in eGFR, and mean decrement was 32.1 mg/min/1.73. Thirteen developed end-stage renal disease, which required kidney transplantation at a mean of 4.4 years. The authors suggested that patients should be made aware of the risk and only the most appropriate patients offered PTA. Future updates of this policy will continue to follow this clinical topic.

PANCREAS RETRANSPLANTATION[18]

Parajuli (2019) compared outcomes among SPK patients who did or did not receive pancreas retransplantation after isolated pancreas graft failure.[19] Among 109 SPK patients with pancreas graft failure, 25 underwent pancreas retransplantation and 84 did not. Mean follow-up time after pancreas graft failure was longer among patients who underwent pancreas retransplantation (7.6 years vs. 4.6 years). Rates of death-censored kidney graft failure at last follow-up were lower among patients who underwent pancreas retransplantation (24% vs. 48%; p=0.04). However, given the retrospective nature of the study, selection bias may have influenced the observed outcomes. Patient survival was not significantly different between groups. Among patients who underwent retransplantation, one-year pancreas graft survival was 84%.

Rudolph (2015) reported higher graft survival rates, but not patient survival rates, after primary transplant.[20] A total of 2145 pancreas transplants were performed, 415 (19%) of which were retransplants. Death-censored graft survival at one year was 88.2% in initial transplants and 75% in retransplants (p=0.06).

Fridell (2015) reported on 441 initial transplants and 20 late transplants.[21] One-year graft survival rates were 92% after initial transplant and 90% after retransplant (p=0.48). Similarly, one-year patient survival rates were 96% after initial transplants and 95% after retransplants (p=0.53).

Siskind (2015) published the largest comparative study to date which included long-term outcomes for 1149 retransplant patients and 19,705 primary transplant patients.[22] Patient data was collected from the UNOS database (1996-2012) and PAK, PTA, PWK and SPK patients were included in the analysis. Adjusted patient survival rates were compared at 1-, 3-, 5-, 10-, and 15-year follow-up. Analysis of 30-day retransplantation outcomes was not performed due to small sample size. Graft survival was significantly worse in the retransplant group compared to primary transplant at all follow-up points, for all transplant types:

Table 1: Graft Survival

Graft Survival	Primary Transplant, %	Retransplant, %	P
1 year	85.44	37.16	<0.0001
3 year	76.86	21.93	<0.0001
5 year	69.23	14.45	<0.0001
10 year	52.26	2.79	<0.0001
15 year	36.96	0.17	<0.0001

Table 2: Patient Survival

Patient Survival	Primary Transplant, %	Retransplant, %	P
1 year	94.83	98.99	<0.0001
3 year	90.20	96.67	<0.0001
5 year	85.41	93.19	<0.0001
10 year	71.85	79.80	<0.0001
15 year	58.86	54.93	<0.0001

Authors speculated that the improved survival rates in the retransplantation group could be attributed to retransplantation of the kidney with the pancreas versus pancreas alone; however, subgroup analysis did not support this hypothesis. These study findings significantly differ from previous nonrandomized comparative studies which have indicated pancreas retransplantation has comparable graft survival rates to primary transplant.

The OPTN has reported data on transplants performed between 2008 and 2015.[2] Patient survival rates after repeat transplants were similar to survival rates after primary transplants. For example, the one-year survival rate was 91.0% (95% CI, 88.7% to 92.8%) after a primary pancreas transplant and 96.4% (95% CI, 92.1% to 98.4%) after a repeat pancreas transplant. The numbers of patients transplanted were not reported, but OPTN data stated that 663 patients were alive one year after primary transplant and 154 after repeat transplants. The three-year patient survival rate was 87.5% (95% CI, 85.1% to 89.6%) after primary transplants and 91.2% (95% CI, 86.2% to 94.4%) after repeat transplants. The five-year patient survival rate was 79.9% (95% CI, 77.4% to 82.2%) after primary transplants and 83.7% (95% CI, 78.2% to 88.0%) after repeat transplants. The one-year graft survival rate was 81.8% (95% CI, 78.9% to 84.3%) after primary pancreas transplant and 77.7% (95% CI, 70.8% to 83.1%) after repeat transplant.

Data are similar for patients receiving SPK transplants, but follow-up data are only available on a small number of patients who had repeat SPK transplants, so estimates of survival rates in this group are imprecise. Three-year patient survival rate was 94.8% (95% CI, 93.9% to 95.5%) after primary SPK transplant and 87.9% (95% CI, 73.4% to 94.8%) after a repeat SPK transplant. The number of patients living 3 years after transplant was 2871 after a primary combined procedure and 36 after a repeat combined procedure.

Seal (2014) reported on 96 consecutive PTA patients treated at a single center in Canada; 78 were initial transplants, and 18 were retransplants.[23] Pancreas graft survival was similar for primary transplants and retransplants at one year (88% vs 100%, p=0.88) and three years (85% in both groups, p=0.99). Patient survival rates were also similar in the two groups at one year (96% and 100%, p=0.95) and three years (93% and 100%, p=0.93).

Buron (2013) reported on their experience with pancreas retransplantation in France and Geneva.[24] Between 1976 and 2008, 568 pancreas transplants were performed at two centers, including 37 repeat transplants. Patient survival after a repeat pancreas transplant was 100% after one year and 89% after five years. Graft survival was 64% at one year and 46% at five years. Among the 17 patients who underwent a second transplant in a later time period i.e., between 1995 and 2007, graft survival was 71% at one year and 59% at five years. In this more recently transplanted group, graft survival rates were similar to primary pancreas transplants which was 79% at one year and 69% at five years.

Studies for pancreatic retransplantation are limited to retrospective reviews and non-randomized feasibility studies. The evidence for graft and patient survival following the first retransplantation of the pancreas following PAK, PTA, or SPK transplantation has shown

outcomes similar to primary transplantation.[20, 25-29] No clinical trials were found that reported survival outcomes following more than one retransplantation.

HIV+ TRANSPLANT RECIPIENTS

The Organ Procurement Transfer Network (OPTN) permits HIV test positive patients as organ candidates if permitted by the transplant hospital.[25]

The American Society of Transplantation (2019) published a guideline on solid organ transplantation in HIV-infected patients.[30] For kidney-pancreas transplants, the following criteria for transplantation are suggested:

- Cluster of differentiation 4 count >200 cells/mL for at least 3 months (insufficient data to recommend for or against transplantation in patients with counts >100 cells/mL and no history of opportunistic infection)
- Undetectable HIV viral load while receiving antiretroviral therapy
- Documented compliance with a stable antiretroviral therapy regimen
- Absence of active opportunistic infection and malignancy
- Absence of chronic wasting or severe malnutrition
- Appropriate follow-up with providers experienced in HIV management and ready access to immunosuppressive medication therapeutic drug monitoring
- The guideline authors note that patients with a previous history of progressive multifocal leukoencephalopathy, chronic interstitial cryptosporidiosis, primary central nervous system lymphoma, or visceral Kaposi's sarcoma were excluded from studies of solid organ transplantation in HIV-infected patients. Patients with HIV and concomitant controlled hepatitis B infection may be considered for transplant. Caution is recommended in hepatitis C-coinfected patients who have not been initiated on direct acting antiviral therapy.

A retrospective analysis of all deceased donor pancreas transplants performed in the U.S. between 1988 and 1999 revealed that since the mid-1990’s allograft half-lives ranged from eight to nine years for PTA transplants to nearly 13 years for SPK transplants.[31] The data indicates that insulin-independence with functioning grafts can been achieved for longer than 20 years.

AGE

In the past 5 to 10 years, several analyses of outcomes by patient age group have been published and there is now general agreement among experts that age should not be a contraindication; however, age-related comorbidities are important to consider when selecting patients for transplantation.

Siskind (2014) used data from the United Network for Organ Sharing (UNOS) database to publish the largest study of pancreas outcomes by recipient age.[32] Investigators included all adult patients who received SPK or PTA between 1996 and 2012 (n=20,854). There were 3160 patients between the ages of 50 and 59 years, and 280 patients age 60 or older. Overall, Kaplan-Meier survival analysis found statistically significant differences in patient survival ($p<0.001$) and graft survival ($p<0.001$) among age categories. Graft survival was lowest in the 18- to-29 age group at 1, 5, and 10 years, which the authors noted might be due to early immunological graft rejection due to more robust immune responses. However, 10 and 15 year graft survival was lowest in the 60 and older age group. Patient survival rates decreased with increasing age, and the differential between survival in older and younger ages increased with

longer follow-up intervals. Lower survival rates in patients 50 and older could be due in part to comorbidities at the time of transplantation. Also, as patient age, they are more likely to die from other causes. Still, patient survival at 5 and 10 years was relatively high, as shown in Table 3.

Table 3: Patient Survival by Age Group[32]

	Age 18-29, %	Age 30-39, %	Age 40-49, %	Age 50-59, %	Age 60+, %
1 year	95.4	96.0	94.9	93.3	91.0
5 years	86.3	87.8	85.7	81.6	71.4
10 years	73.5	76.8	71.8	61.5	42.5

Shah (2013) reviewed data on 405 patients who underwent PTA between 2003 and 2011.[33] One-year patient survival was 100% for patients younger than age 30, 98% for patients age 30 to 39 years, 94% for patients 40 to 49 years, 95% for patients 50 to 59 years and 93% for patients age 60 or older. There was not a statistically significant difference in the rate of patient survival by age (p=0.38). Findings were similar for one-year graft survival; there was not a statistically significant difference in outcomes by age of the transplant recipients (p=0.10).

Afaneh (2011) reviewed data on 17 individuals at least 50-years-old and 119 individuals younger than 50 who had a pancreas transplant at a single institution in the U.S.[34] The two groups had similar rates of surgical complications, acute rejection and non-surgical infections. Overall patient survival was similar. Three- and five-year survival rates were 93% and 90% in the younger group and 92% and 82% in the older group.

Schenker (2011) in Germany compared outcomes in 69 individuals at least 50-years-old and 329 individuals younger than 50 years who had received a pancreas transplant.[35] Mean duration of follow-up was 7.7 years. One-, five-, and 10-year patient and graft survival rates were similar in the two groups. For example, the five-year patient survival rate was 89% in both groups. The five-year pancreas grant survival rate was 76% in the older group and 72% in the younger group. The authors of both studies, as well as the authors of a commentary accompanying the Schenker article,[36] agreed that individuals age 50 years and older are suitable candidates for pancreas transplantation.

PRACTICE GUIDELINE SUMMARY

AMERICAN DIABETES ASSOCIATION

The American Diabetes Association (ADA) Position Statement made the following recommendations on kidney and pancreas transplantation for patients with type 1 diabetes:[37]

- “Consider solid organ pancreas transplantation simultaneously with kidney transplantation in patients with type 1 diabetes who have an indication for kidney transplantation and are poorly controlled with large glycemic excursions. (B)”
- “Consider solid organ pancreas transplantation after kidney transplantation in adult patients with type 1 diabetes who have already received a kidney transplant. (C)”
- “Judiciously consider solid organ pancreas transplantation alone in adults with type 1 diabetes, unstable glucose control, hypoglycemia unawareness, and an increased risk of diabetes-related mortality, who have attempted all of the more traditional approaches to glycemic control and have remained unsuccessful, yet are judged responsible enough to manage the antirejection medication regimen, risks, and follow-up required with an organ transplant. (C)”

ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

The Board of Directors of the Organ Procurement and Transplantation Network (OPTN) issues an updated comprehensive list of transplant related policies regularly, most recently June 2023.[25]

Each candidate registered on the pancreas waiting list must meet *one* of the following requirements:

- Be diagnosed with diabetes
- Have pancreatic exocrine insufficiency
- Require the procurement or transplantation of a pancreas as part of a multiple organ transplant for technical reasons

Each candidate registered on the kidney-pancreas waiting list must meet *one* of the following requirements:

- Be diagnosed with diabetes
- Have pancreatic exocrine insufficiency, with renal insufficiency

In addition, waiting time criteria indicated that for kidney-pancreas transplant candidates 18 years and older, candidates must meet *all* of the following conditions:

1. The candidate is registered for a kidney-pancreas.
2. The candidate qualifies for kidney waiting time according to *Policy 8.4: Waiting Time*.
3. The candidate is on insulin.

The OPTN policy also delineated pancreas, kidney-pancreas, and islet allocation, classifications, and rankings.

SUMMARY

SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION (SPK)

There is enough research to show that simultaneous pancreas kidney (SPK) improves outcomes (e.g., normalizes insulin production and kidney function, improves quality of life, and improves diabetic complications) for patients with diabetes. Therefore, SPK transplantation for patients with diabetes may be medically necessary when policy criteria are met.

PANCREAS AFTER KIDNEY TRANSPLANT (PAK)

There is enough research to show that pancreas after kidney transplant (PAK) improves health outcomes for patients with diabetes. The International Pancreas Transplant Registry provides information that PAK improves health outcomes in some patients with diabetes who have previously received a successful kidney transplant. Therefore, PAK transplantation for patients with diabetes may be considered medically necessary when policy criteria are met.

PANCREAS TRANSPLANT ALONE (PTA)

There is enough research to show that pancreas transplantation improves health outcomes including quality of life and reduce short complications for patients with diabetes. Therefore,

pancreas transplantation for patients with diabetes that have conditions which persist after optimal medical management may be considered medically necessary when policy criteria are met.

RETRANSPLANTATION

There is enough research to show that the health outcomes for pancreas retransplantation recipients appear similar to those reported for initial transplants. Therefore, retransplantation after one failed primary pancreas transplant may be considered medically necessary when policy criteria are met.

There is not enough research to show that a third or subsequent pancreas transplant improves health outcomes and there are documented safety concerns. Therefore, a third or subsequent pancreas transplant including simultaneous kidney-pancreas transplant, pancreas after kidney transplant, or pancreas alone transplant are considered not medically necessary when policy criteria are not met.

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CODES

Codes	Number	Description
CPT	48550	Donor pancreatectomy (including cold preservation), with or without duodenal segment for transplantation
	48551	Backbench standard preparation of cadaver donor pancreas allograft prior to transplantation, including dissection of allograft from surrounding soft tissues, splenectomy, duodenotomy, ligation of bile duct, ligation of mesenteric vessels, and Y-graft arterial anastomosis from the iliac artery to superior mesenteric artery and to splenic artery
	48552	Backbench reconstruction of cadaver donor pancreas allograft prior to transplantation, venous anastomosis, each
	48554	Transplantation of pancreatic allograft
HCPCS	S2065	Simultaneous pancreas kidney transplantation
	S2152	Solid organs(s), complete or segmental, single organ or combination of organs; deceased or living donor(s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre- and post-transplant care in the global definition

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