

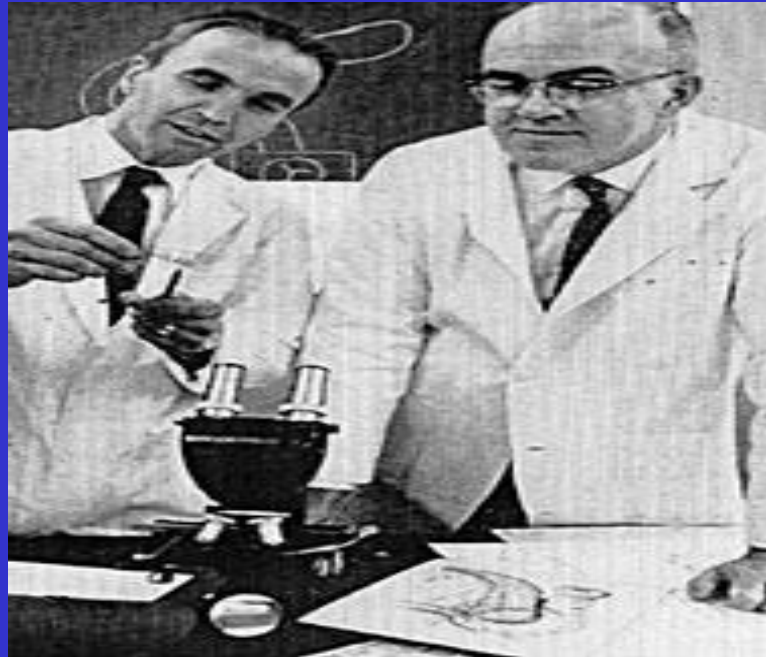
Pancreas Transplantation

Reza F. Saidi, MD, FICS, FACS

Outlines

- Origin
- Indications
- Surgery
- Immunosuppression
- Results

**Kelly WD, Lillehei RC, Merkel FK, Idezuki Y, Goetz FC
(1967). "Allotransplantation of the pancreas and
duodenum along with the kidney in diabetic
nephropathy". *Surgery* 61 (6): 827–37**



PURPOSE OF BETA CELL REPLACEMENT THERAPY

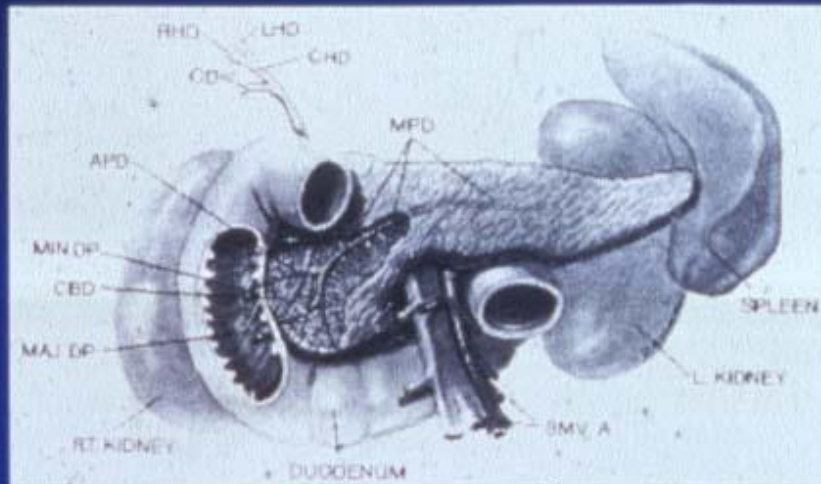
- **Improve quality of life by establishing insulin-independent, normoglycemic state**
- **Prevent/ameliorate secondary complications of diabetes**

Options for Replacement of Pancreatic Endocrine Function

Transplantation



Whole Organ Pancreas



Islets of Langerhans

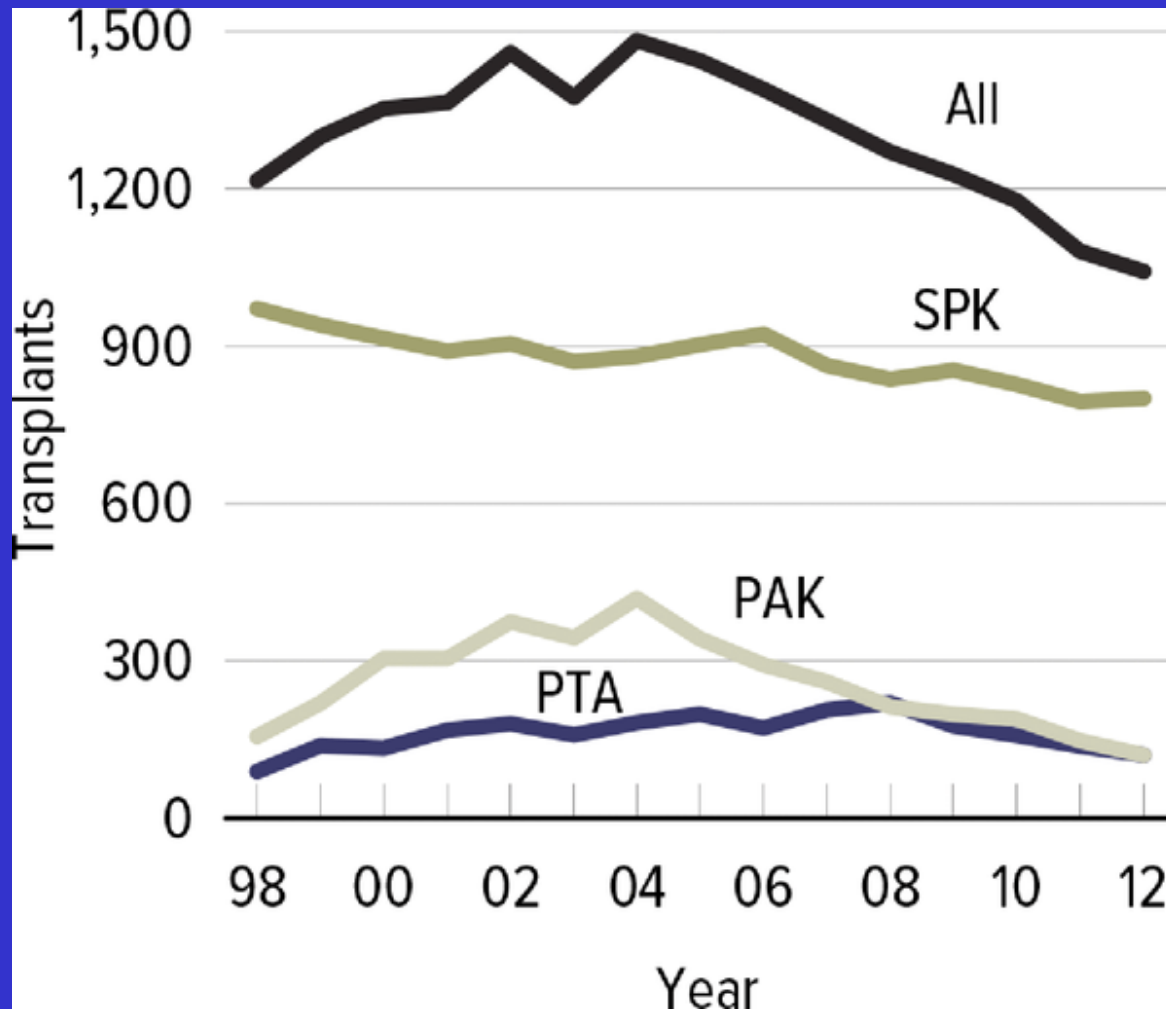
THREE CATEGORIES OF B- CELL REPLACEMENT PANCREAS(P) or ISLET(I) TRANSPLANT RECIPIENTS

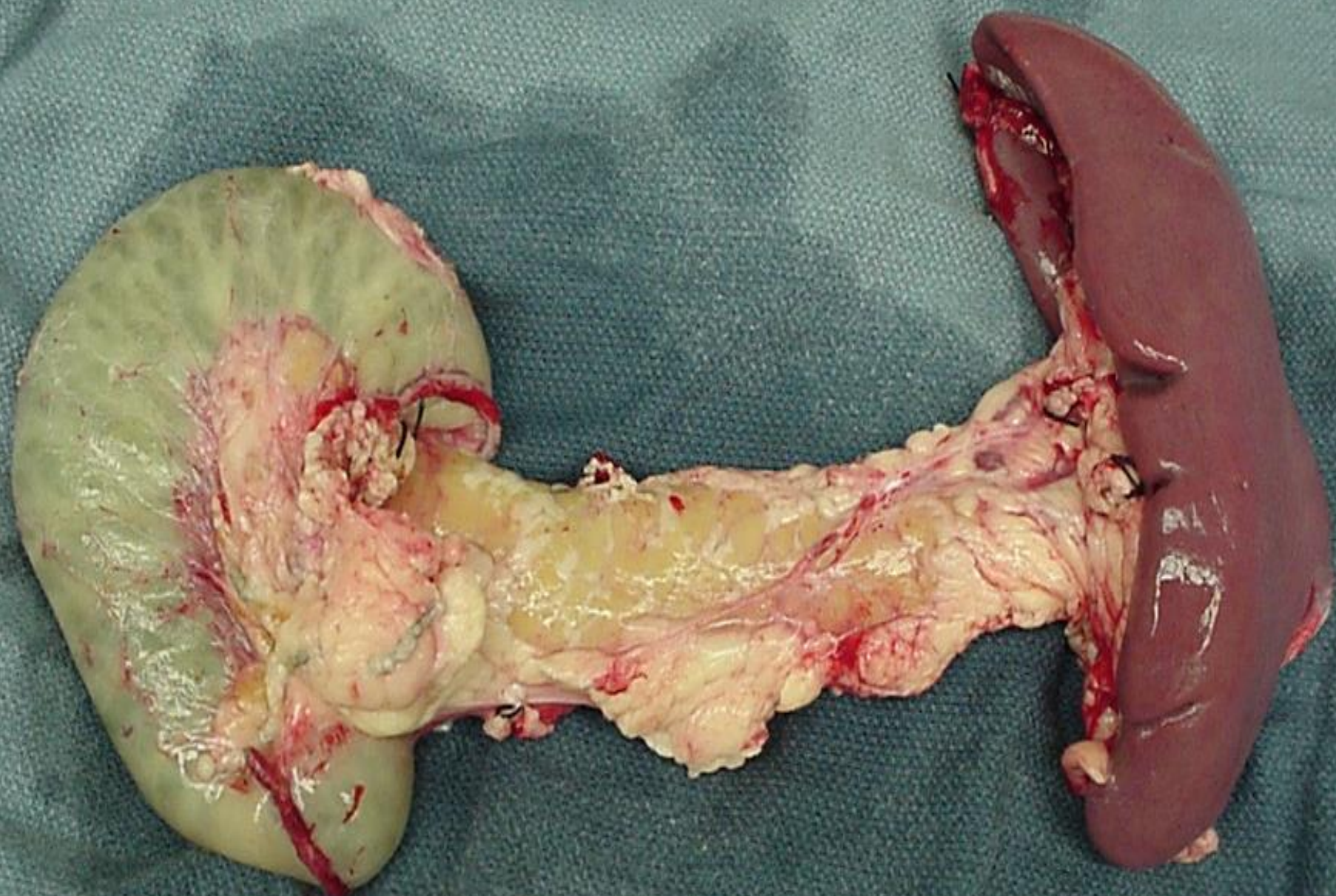
Simultaneous kidney transplant
(SPK or SIK)

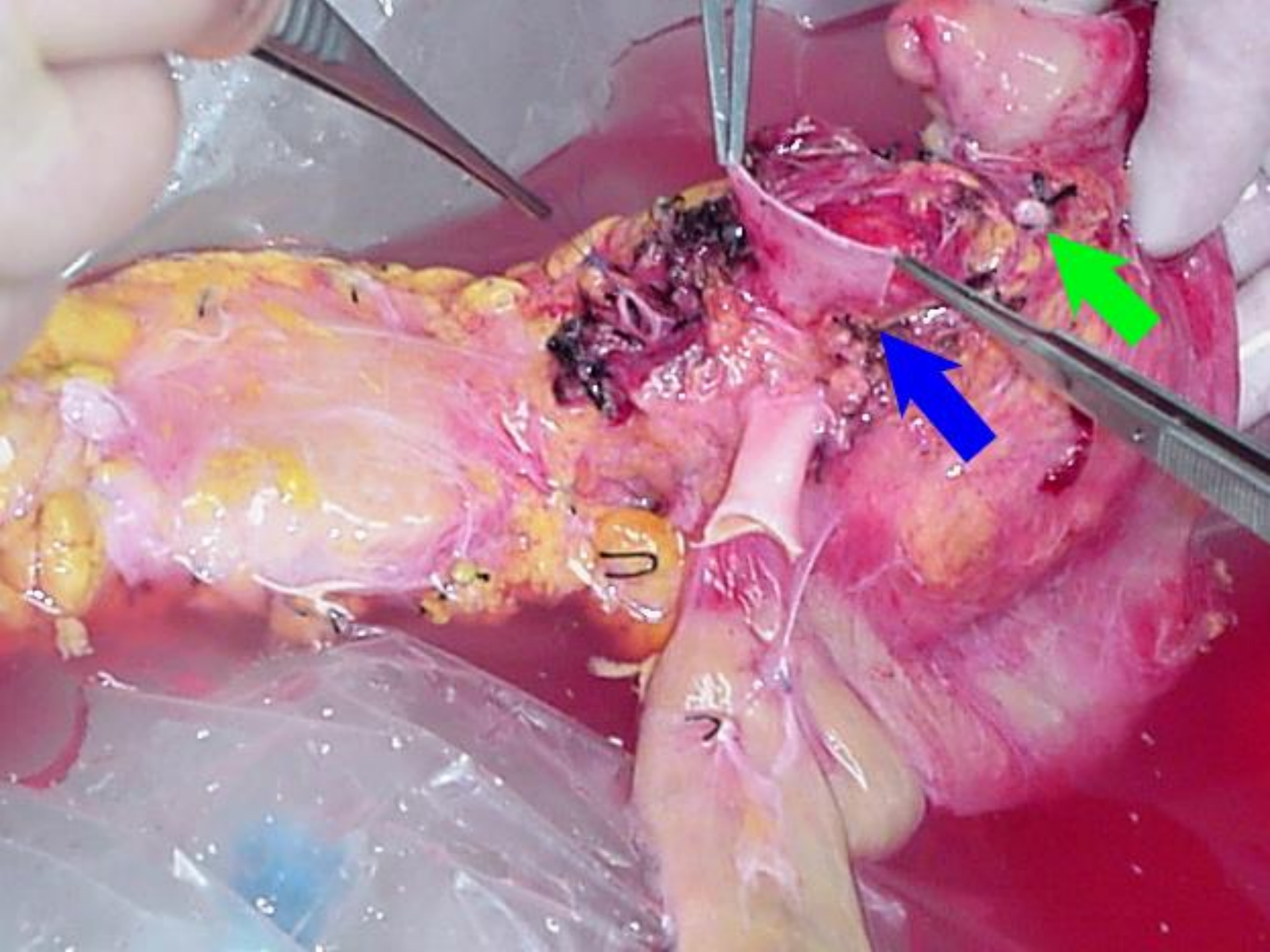
After kidney transplant (PAK or
IAK)

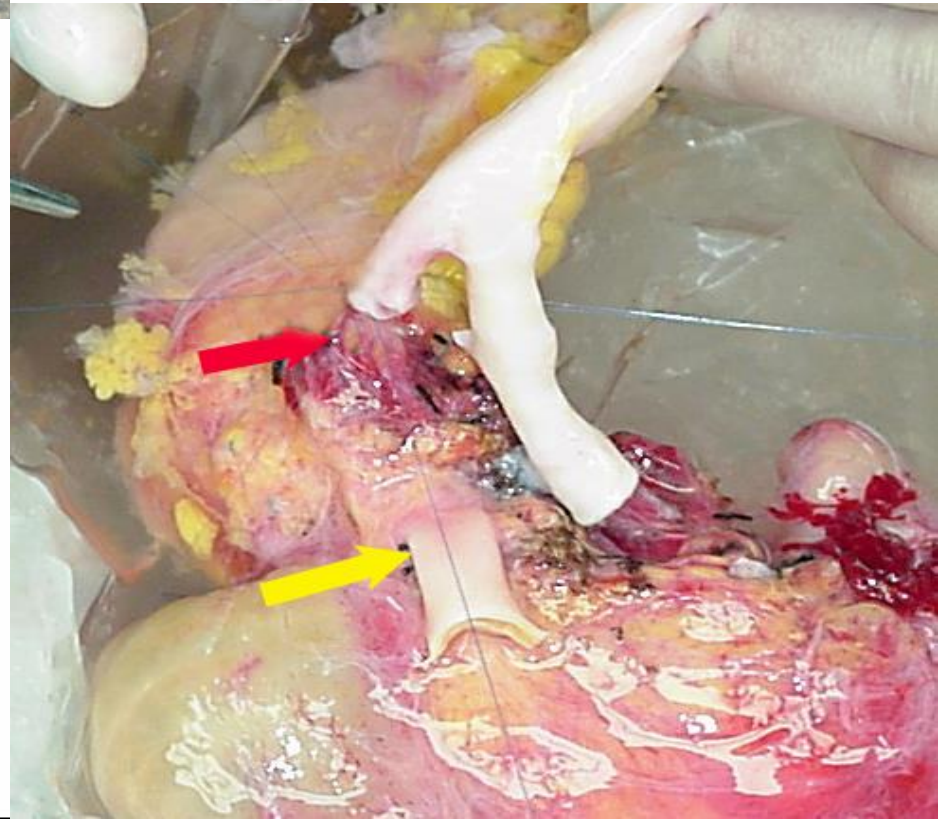
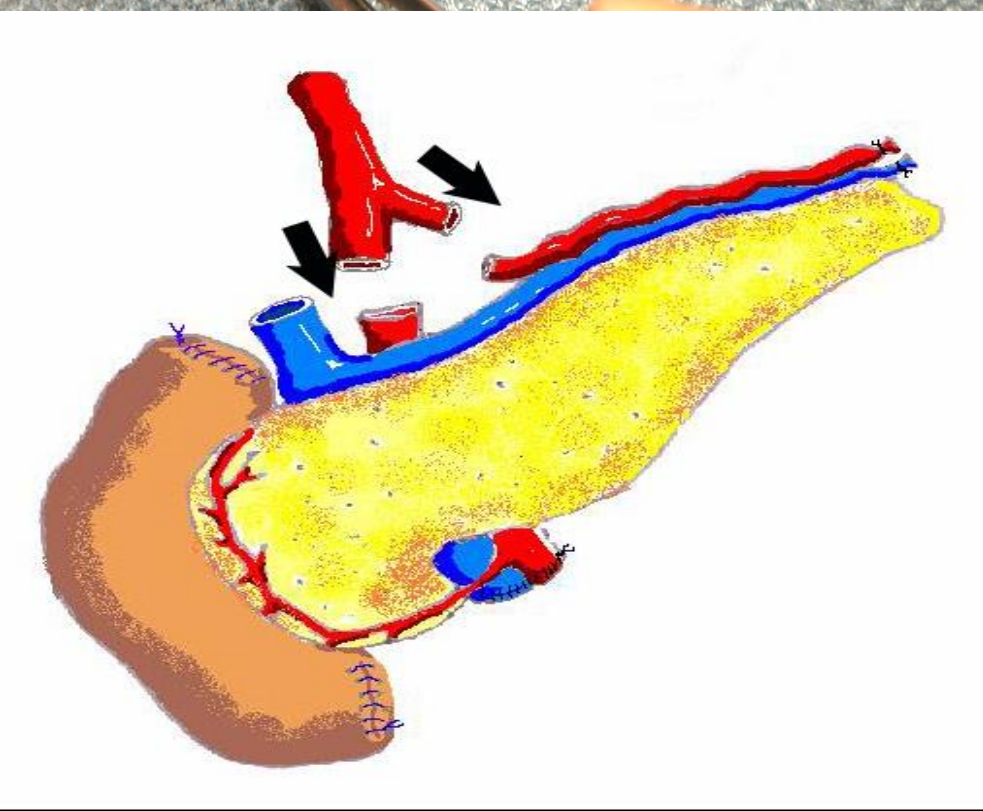
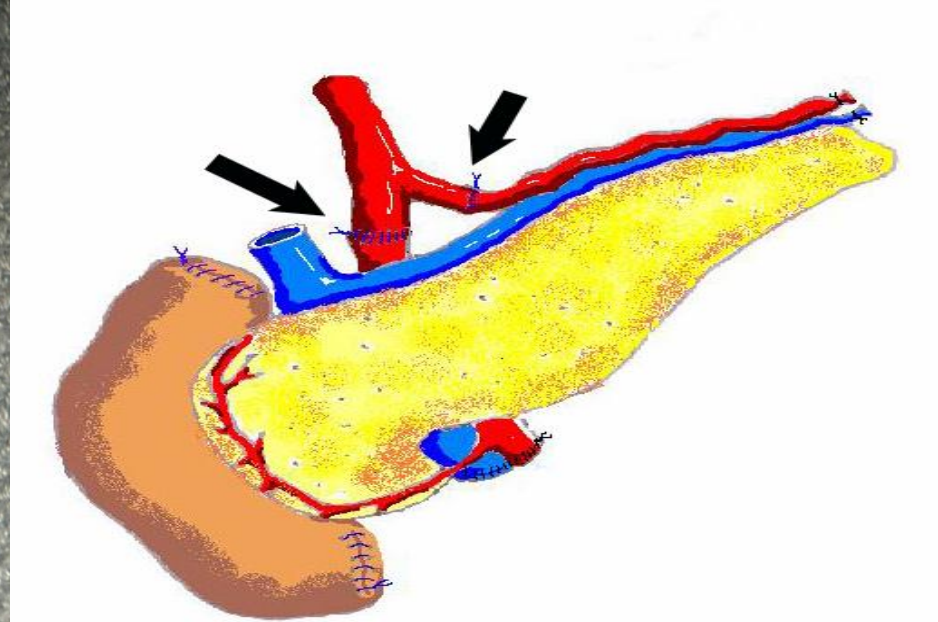
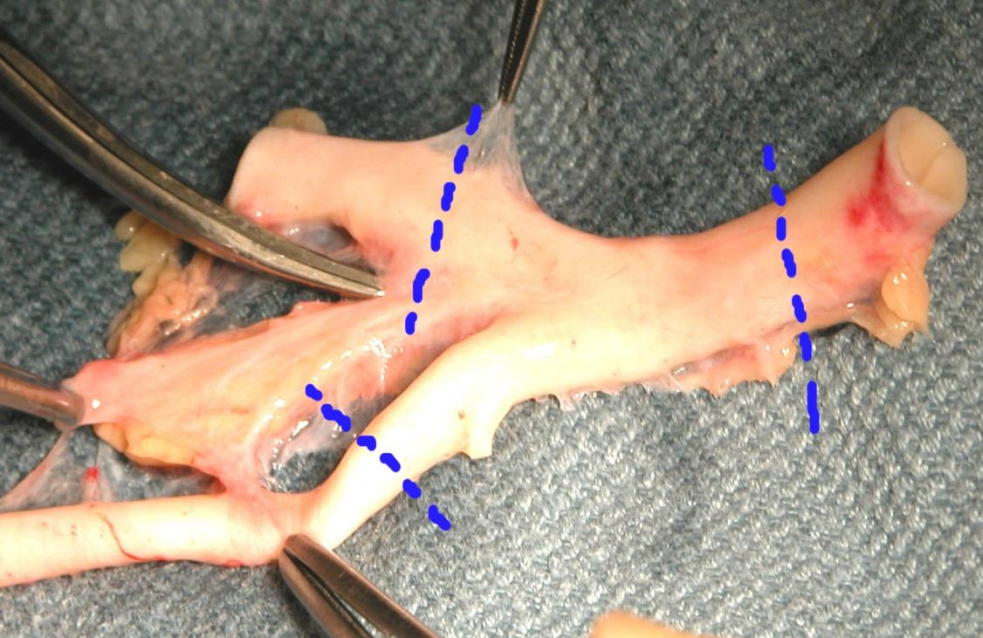
B-cell transplant alone (PTA or
ITA)

Pancreas Transplants in the U.S. 1988-2012





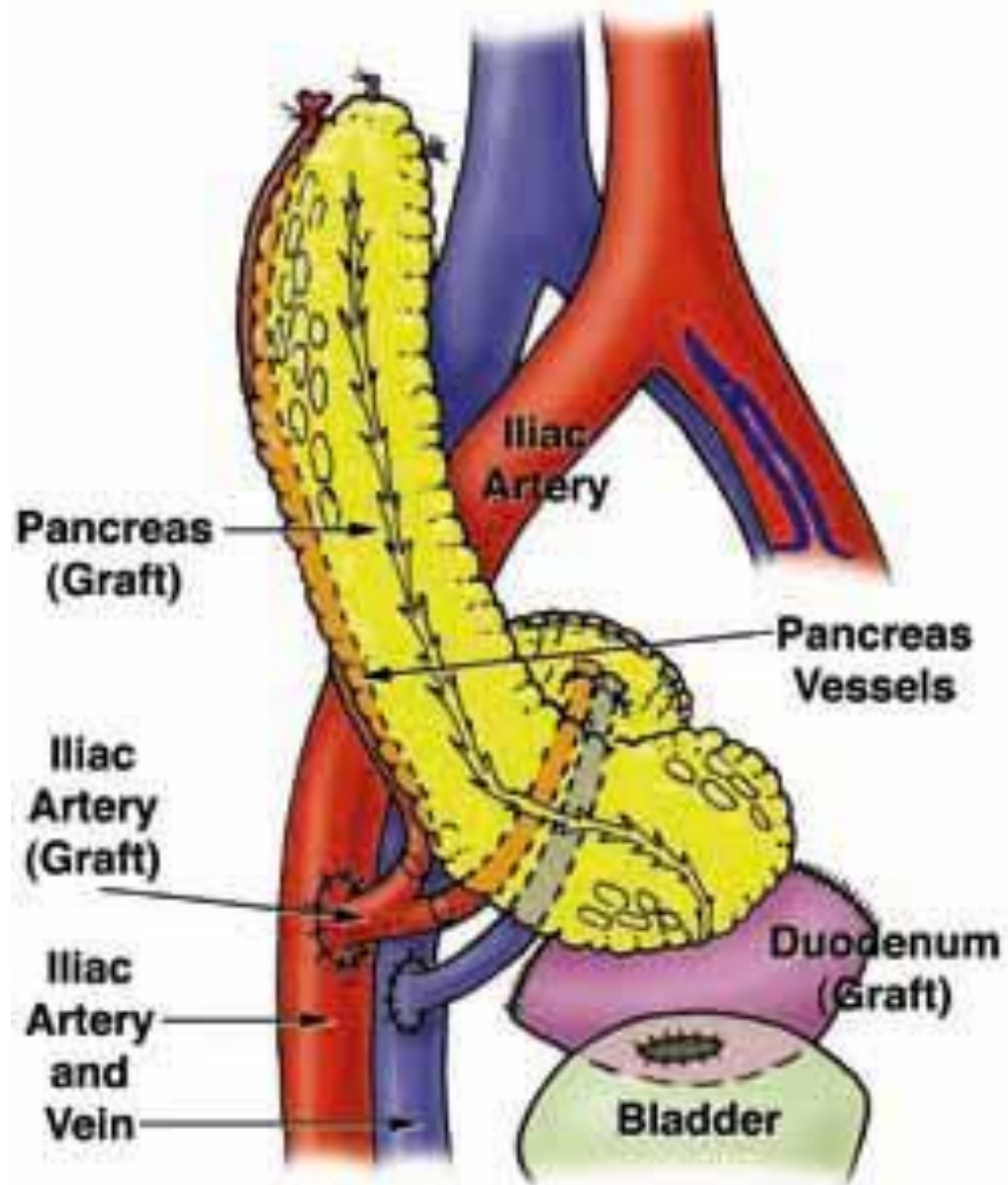






Duct Management (Exocrine)

Bladder vs Enteric



Pro and Cons

- Bladder drainage
 - the ability to monitor pancreatic allograft function via urinary amylase
 - cystoscopically directed biopsy
 - urological complications
 - including metabolic acidosis and volume depletion secondary to sodium bicarbonate wasting,
 - reflux pancreatitis,
 - urinary tract infections (UTI)
 - Haematuria
 - Conversion the enteric route in 20–25%

Sollinger HW, Messing EM, Eckhoff DE *et al.* Urological complications in 210 consecutive simultaneous pancreas-kidney transplants with bladder drainage. *Ann Surg* 1993; 218: 561

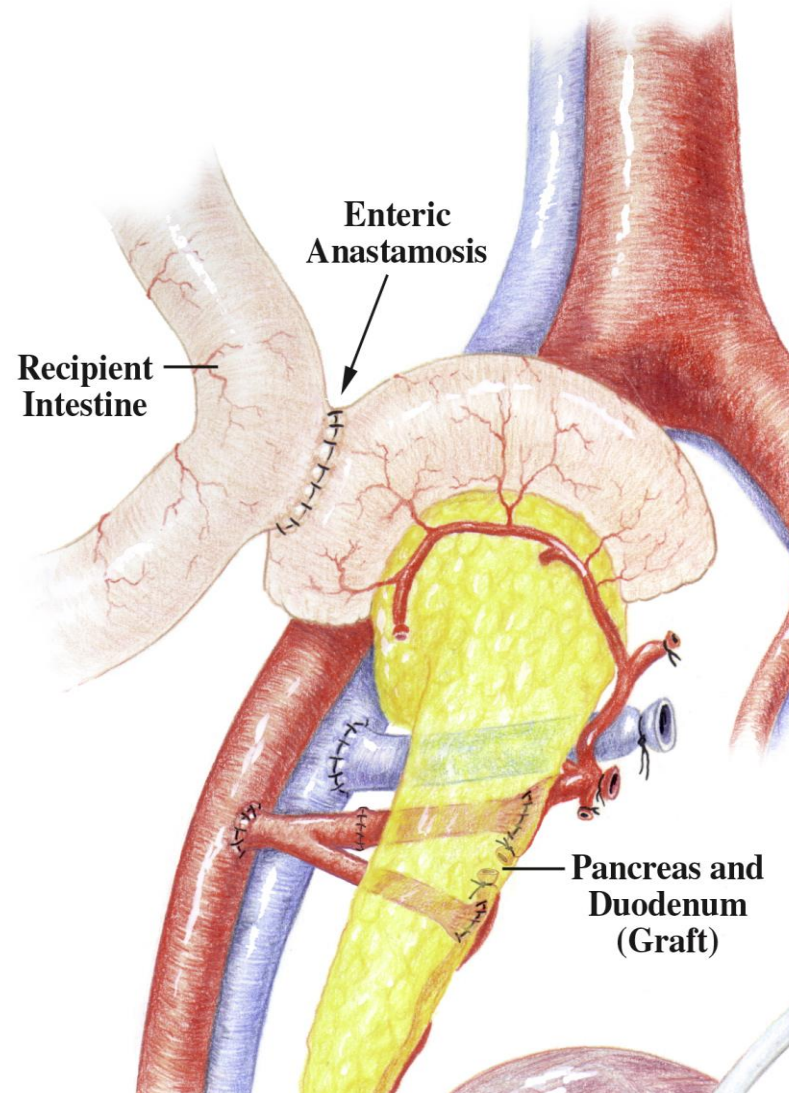
Sutherland DE, Gruessner A. Pancreas transplantation in the United States as reported to the United Network for Organ Sharing (UNOS) and analyzed by the International Pancreas Transplant Registry. *Clin Transpl* 1995; 47: 49

Enteric Drainage

1. Avoids the urological complications of BD
2. Hard to monitoring pancreas allograft function.

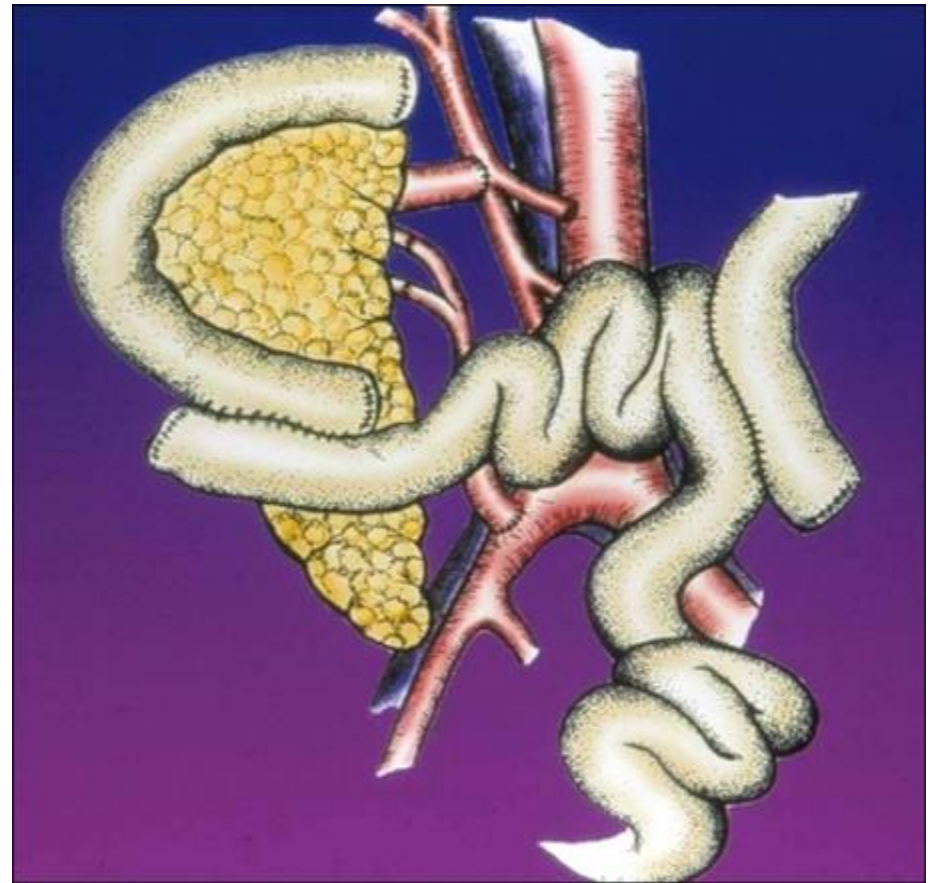
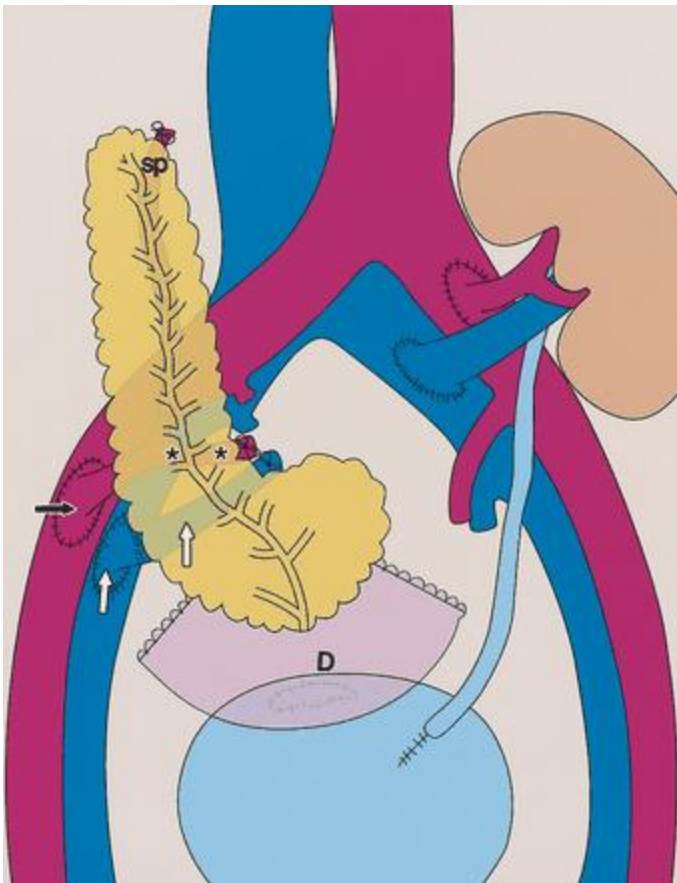
Gaber AO, Shokouh-Amiri MH, Hathaway DK *et al.* Results of pancreas transplantation with portal venous and enteric drainage. *Ann Surg* 1995; 221: 613

Newell KA, Bruce DS, Cronin DC *et al.* Comparison of pancreas transplantation with portal venous and enteric exocrine drainage to the standard technique utilizing bladder drainage of exocrine secretions. *Transplantation* 1996; 62: 1353



Venous Drainage

Systemic vs Portal



Pro and Cons

- Systemic Drainage

Peripheral hyperinsulinemia, insulin resistance

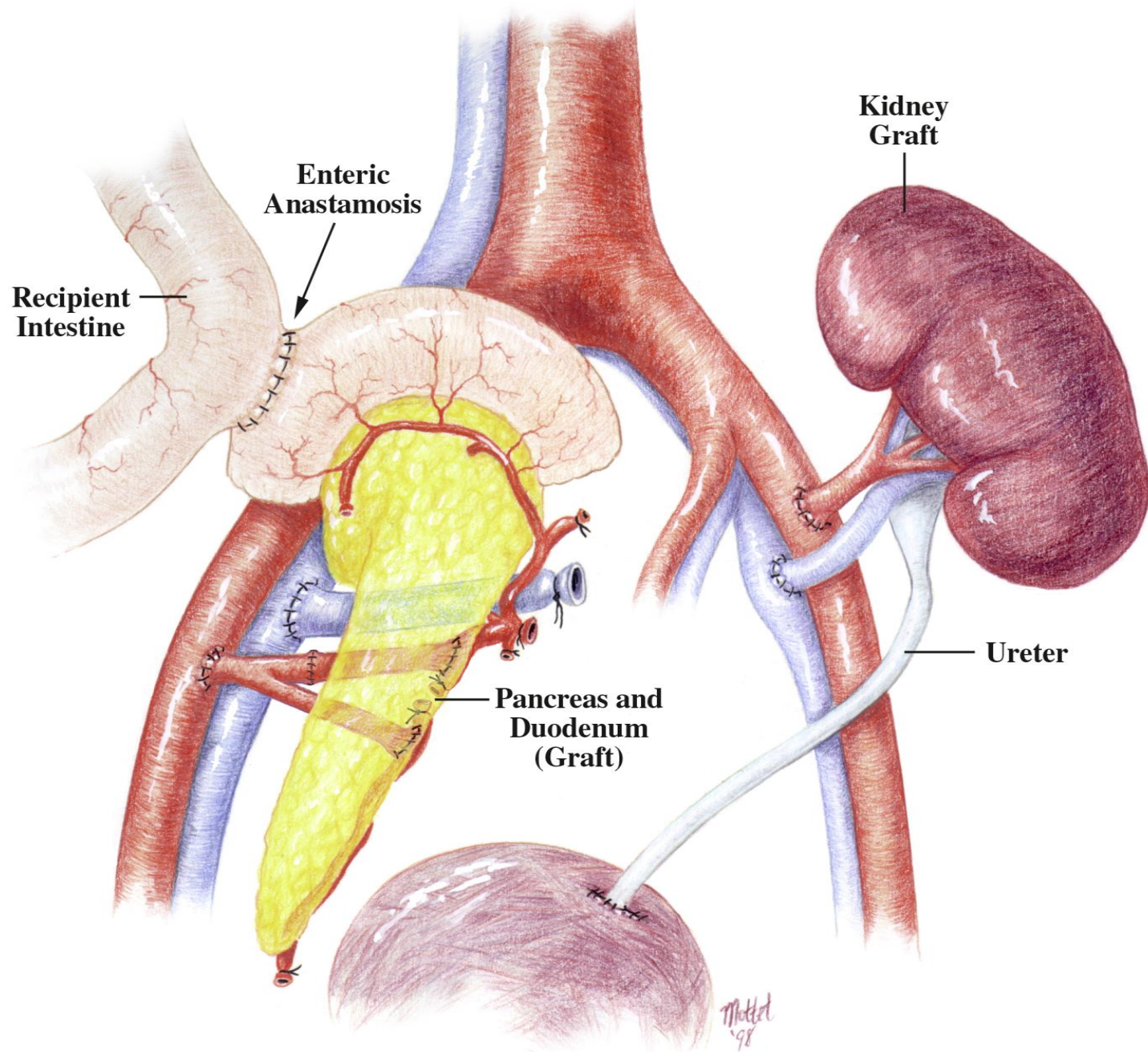
Progressive arteriosclerosis

- Portal Drainage

Technically challenging

Lower insulin level, better glucose control?

Gaber AO, Shokouh-Amiri MH, Hathaway DK et al. Results of pancreas transplantation with portal venous and enteric drainage. Ann Surg 1995; 221: 613



Survival After Pancreas Transplantation in Patients With Diabetes and Preserved Kidney Function

Jeffrey M. Venstrom, BS

Maureen A. McBride, PhD

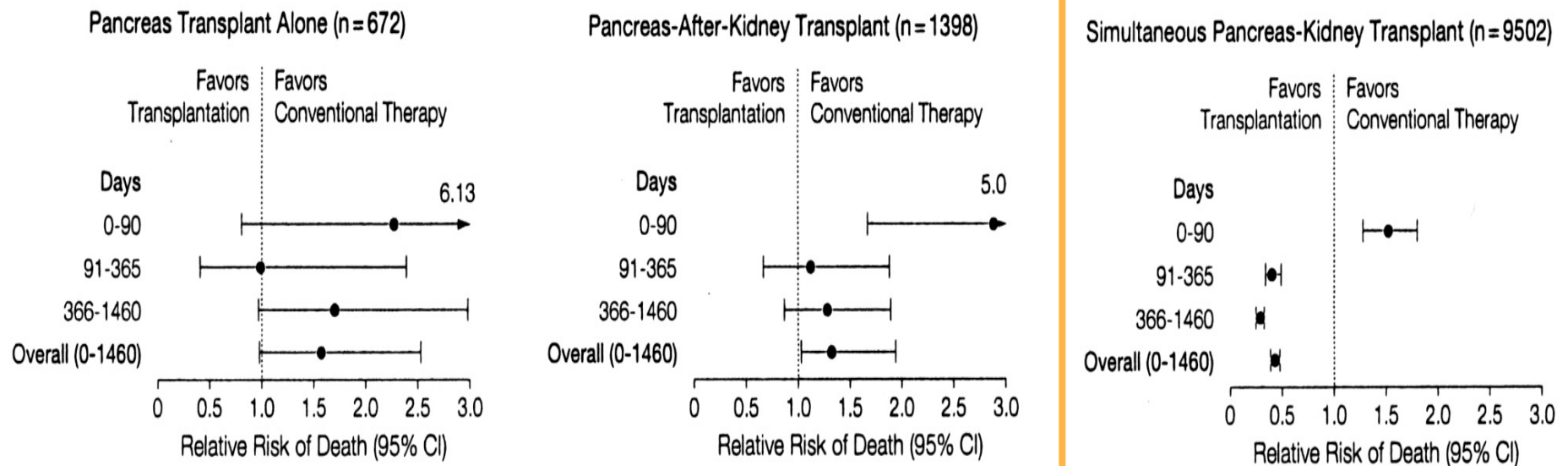
Kristina I. Rother, MD

Boaz Hirshberg, MD

Trevor J. Orchard, MD, MMedSci

David M. Harlan, MD

Figure 1. Relative Risk of Mortality, by Transplant Type



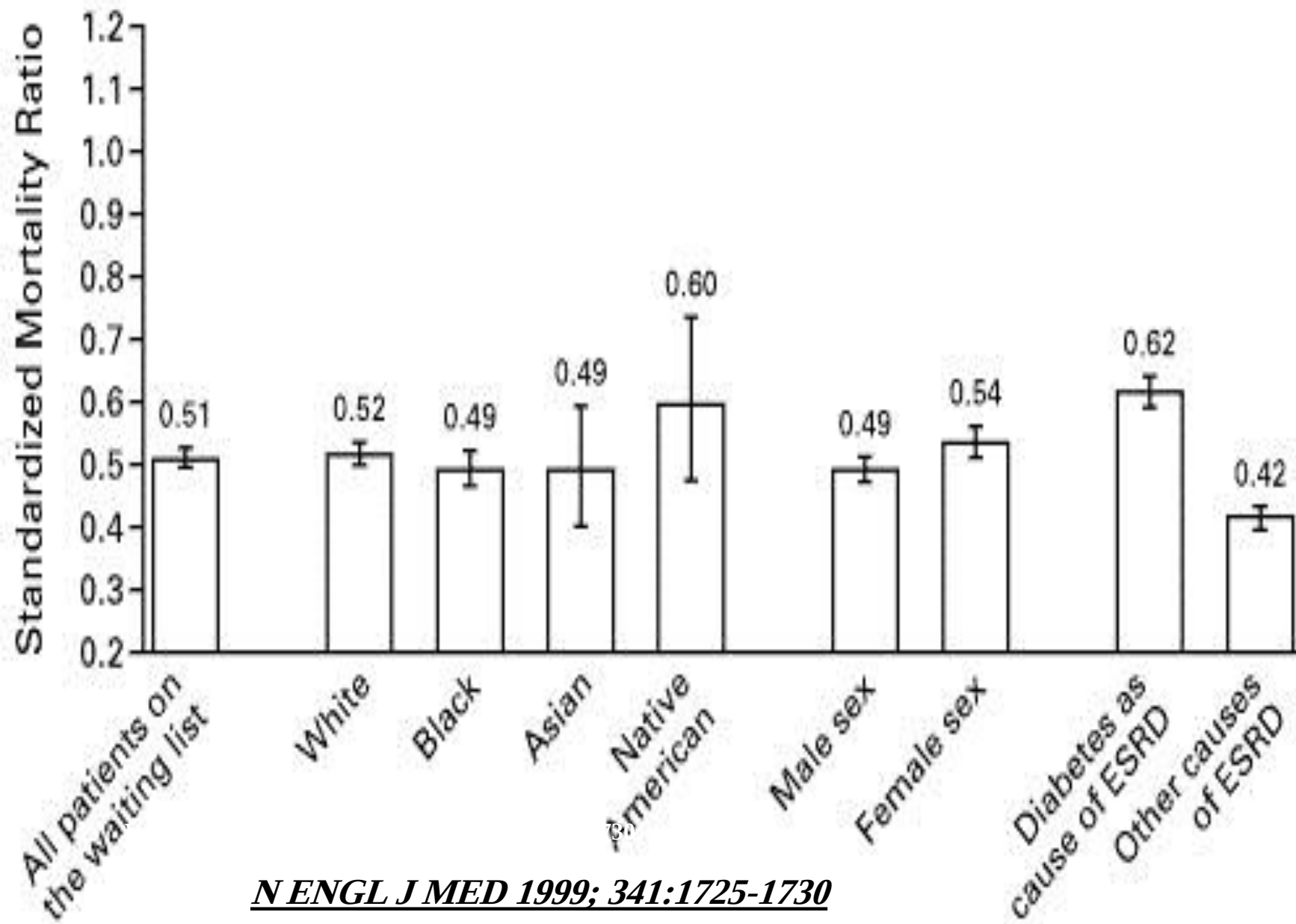
TX options for T1DM with Chronic Kidney Disease

- Dialysis

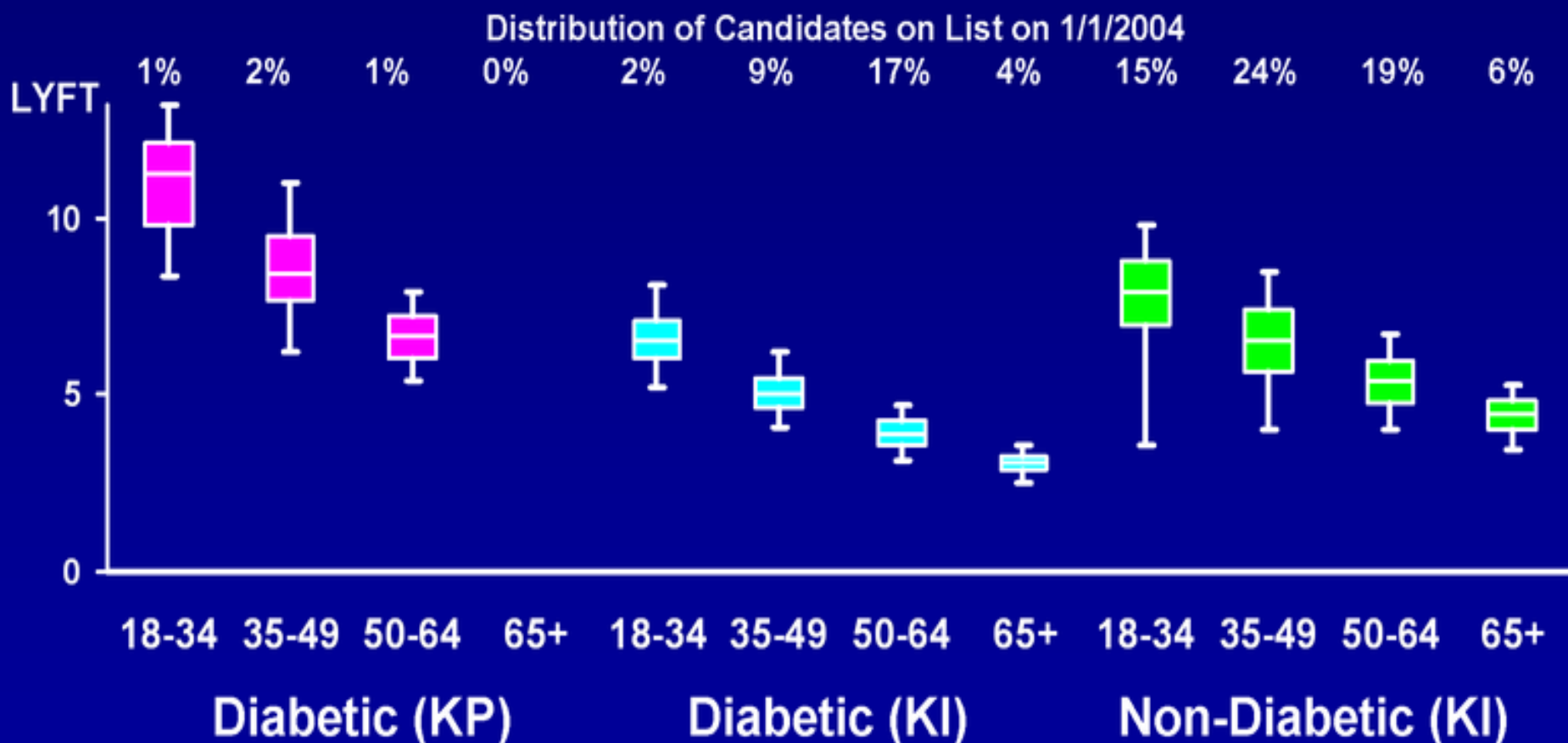
- KT (DD/LT)

- SPK

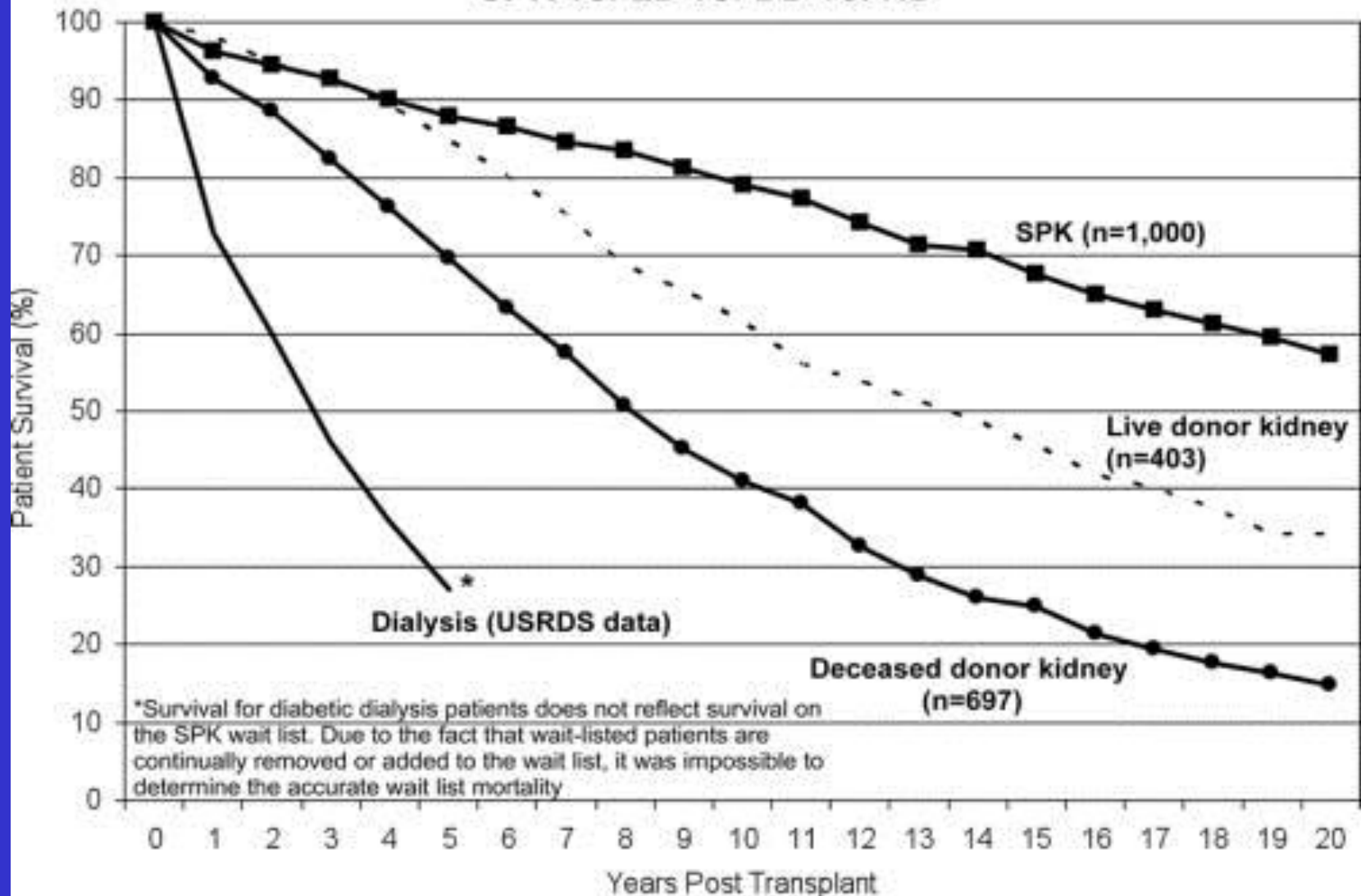
- PAK



Distribution of KI & KP LYFT By Candidate Age and Diabetes Status Donor: Average SCD (Donor Age=32 yrs)



Patient Survival, Type 1 Diabetics SPK vs. LD vs. DD vs. HD



SPK vs DDKT

- SPK has higher postoperative mortality (2%) in first 90 days
- SPK has better outcome after 12 months

1- better glycemic control

2- better donor

3- better renal allograft survival

Diabetes Care 2009; 32:600–602.

Am JTransplant 2005; 5:374–382.

Clin Transplant 2009; 23:732–739.

Transplantation 2009; 87:1402–1410.

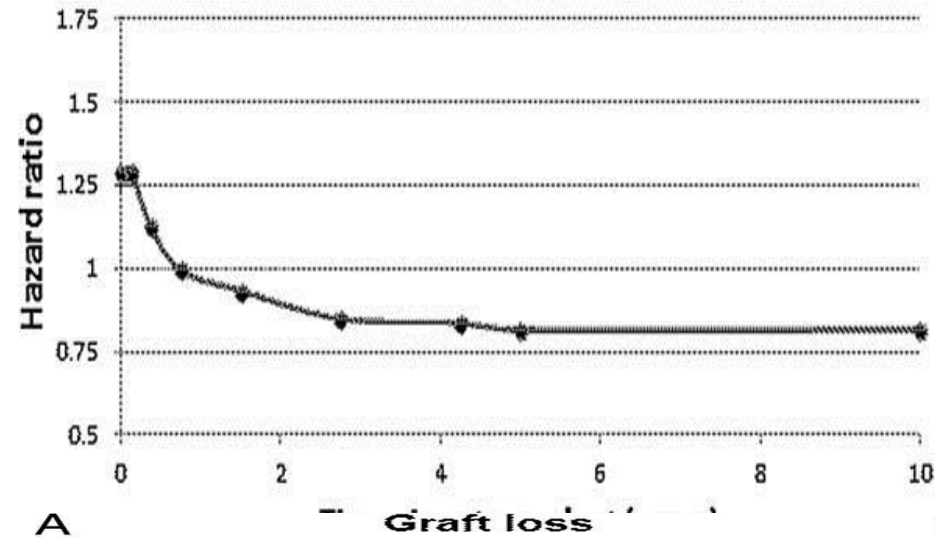
Transplantation 2007; 83:1156–1161.

SPK vs DDKT

(Donor and recipient match analysis)

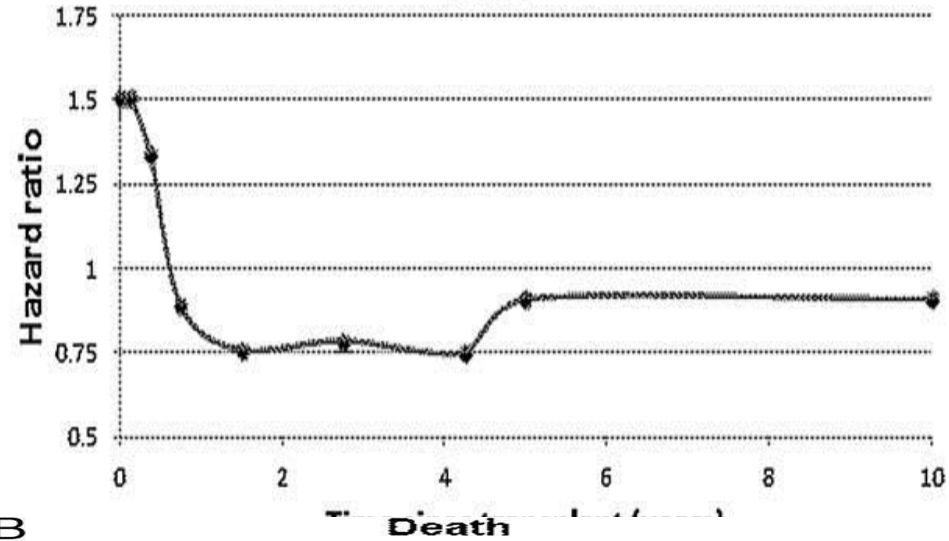
A

Graft Loss



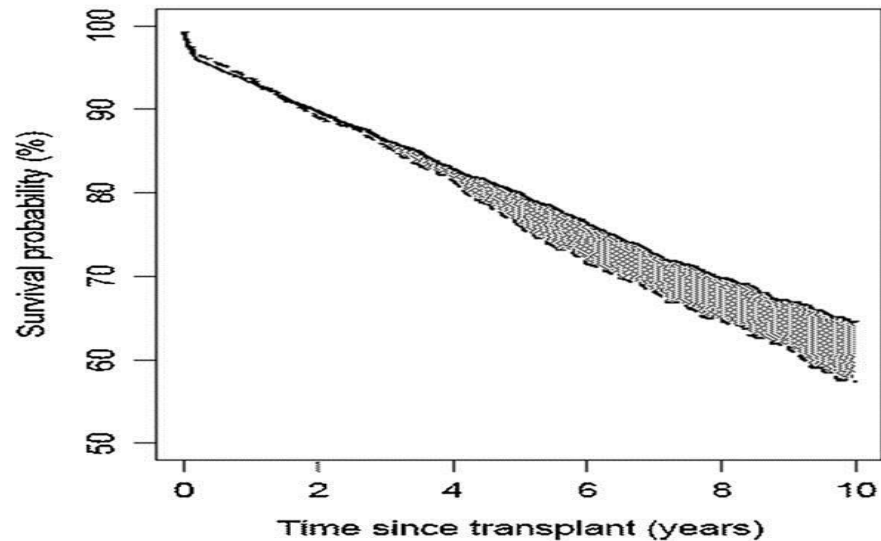
B

Death



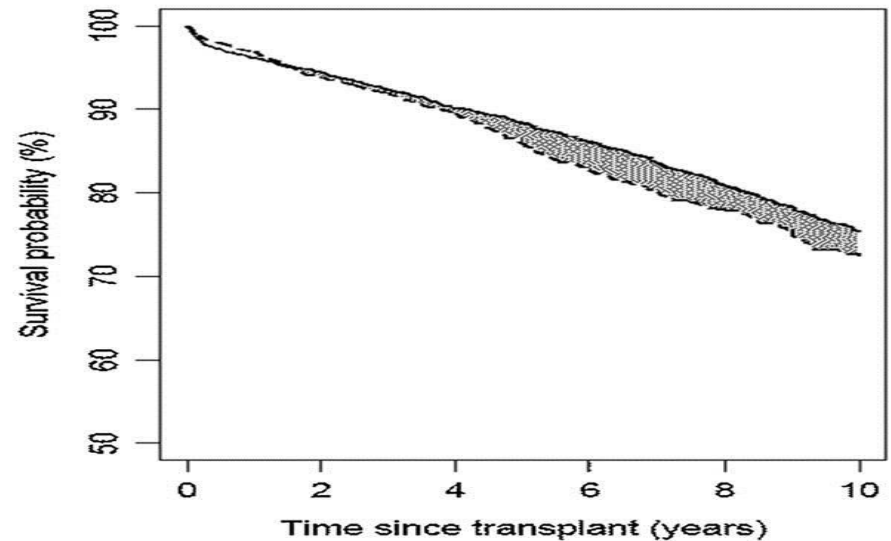
A

Graft loss



B

Death



SPK vs LDKT

OPTN/UNOS *Clin J Am Soc Nephrol 2009; 4:845–852.*

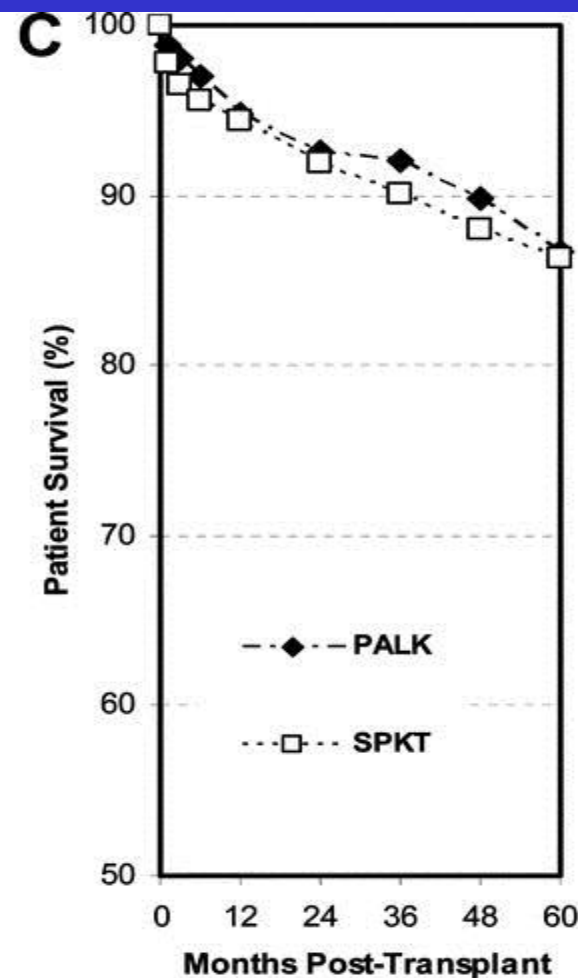
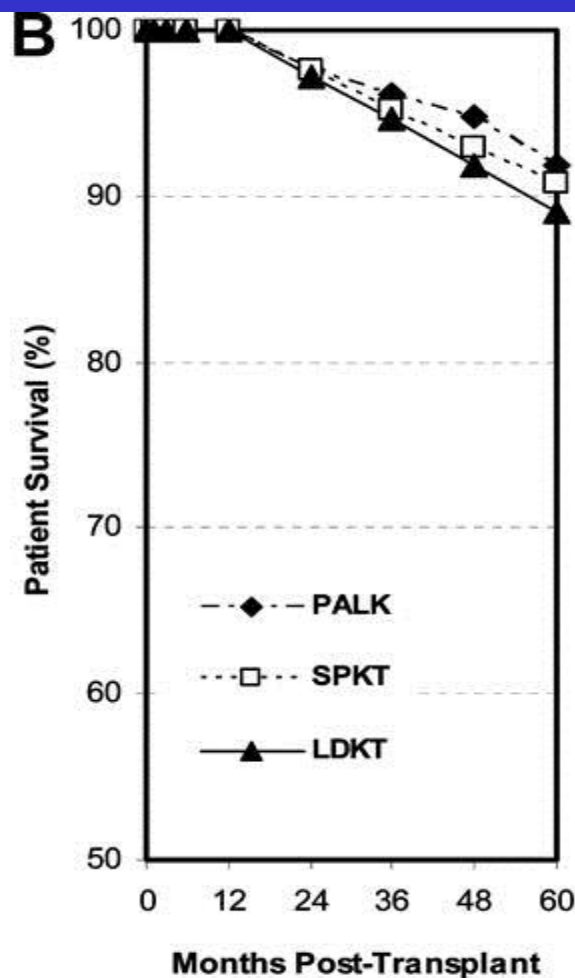
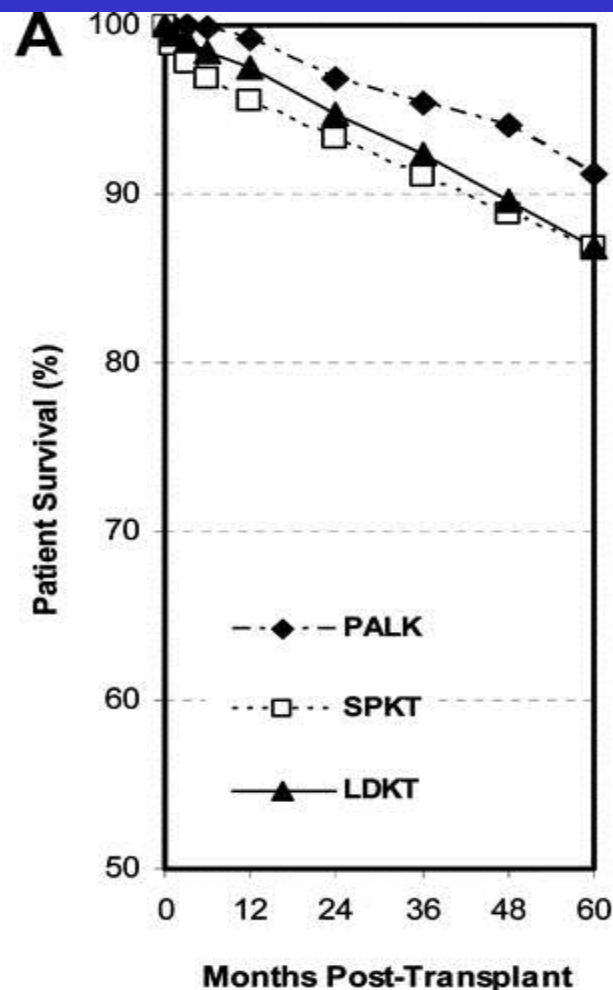
Collaborative Transplant Study

J Am Soc Nephrol 2009;19:1557–1563.

Clin J Am Soc Nephrol 2010; 5:549–552.

- Patient survival (5 year) was higher in the SPK cohort (85 vs. 80%)
- The survival benefit was due to less cardiovascular death in particular due to long-term glycemic control in SPK recipients
- A successful SPK transplant with as little as 12 months of pancreas function is associated with superior outcomes compared with LDKA

Pancreas after living donor kidney vs SPK



No at risk

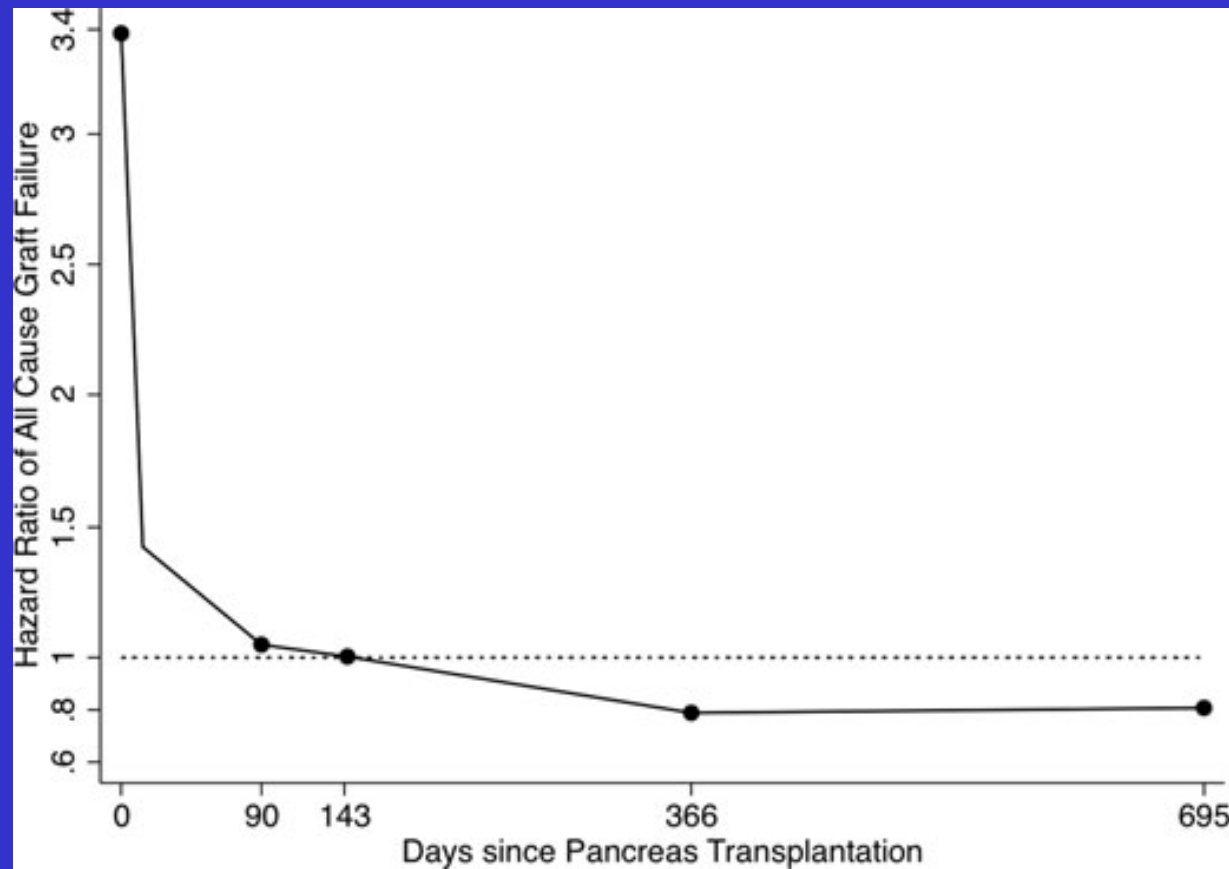
PALK	807	757	671	553	413	290
SPKT	5580	4522	3565	2770	2098	1488
LDKT	3461	2934	2388	1854	1374	971

	807	671	553	413	290	173
	5580	3565	2770	2098	1488	913
	3461	2388	1854	1374	971	573

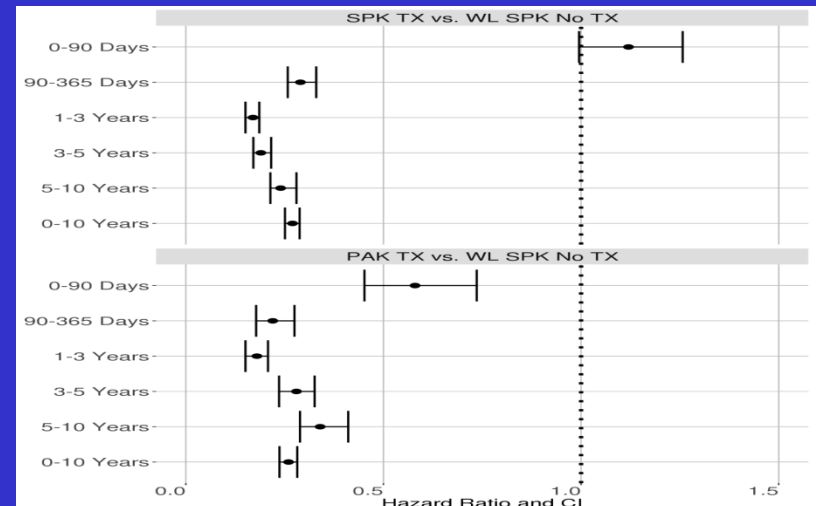
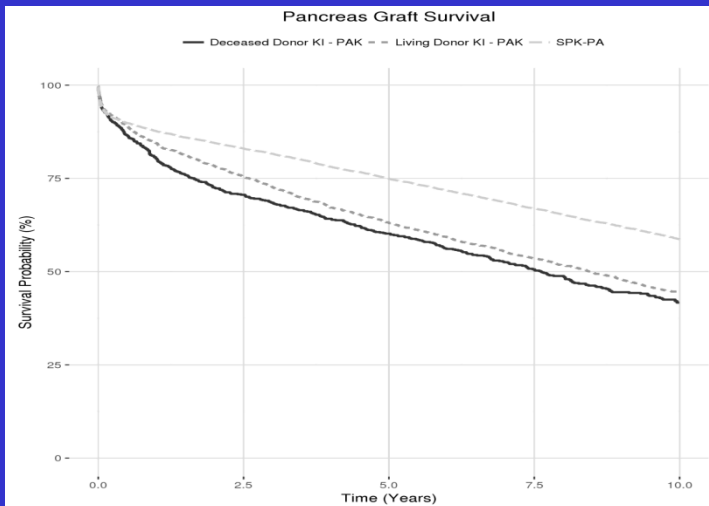
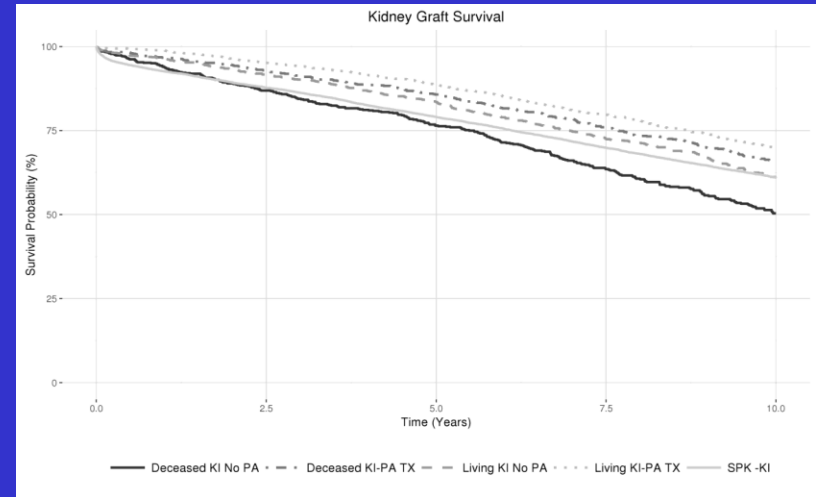
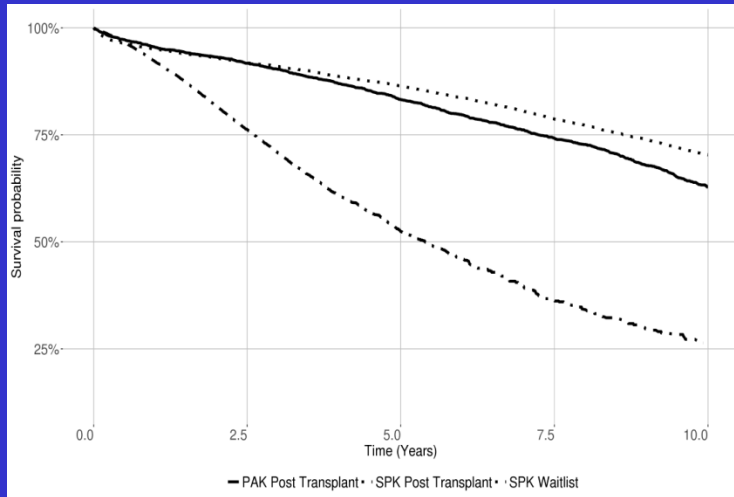
	807	541	396	266	166	105
	5580	4099	3248	2517	1897	1349

Transplantation 2010; 89:1496-1503

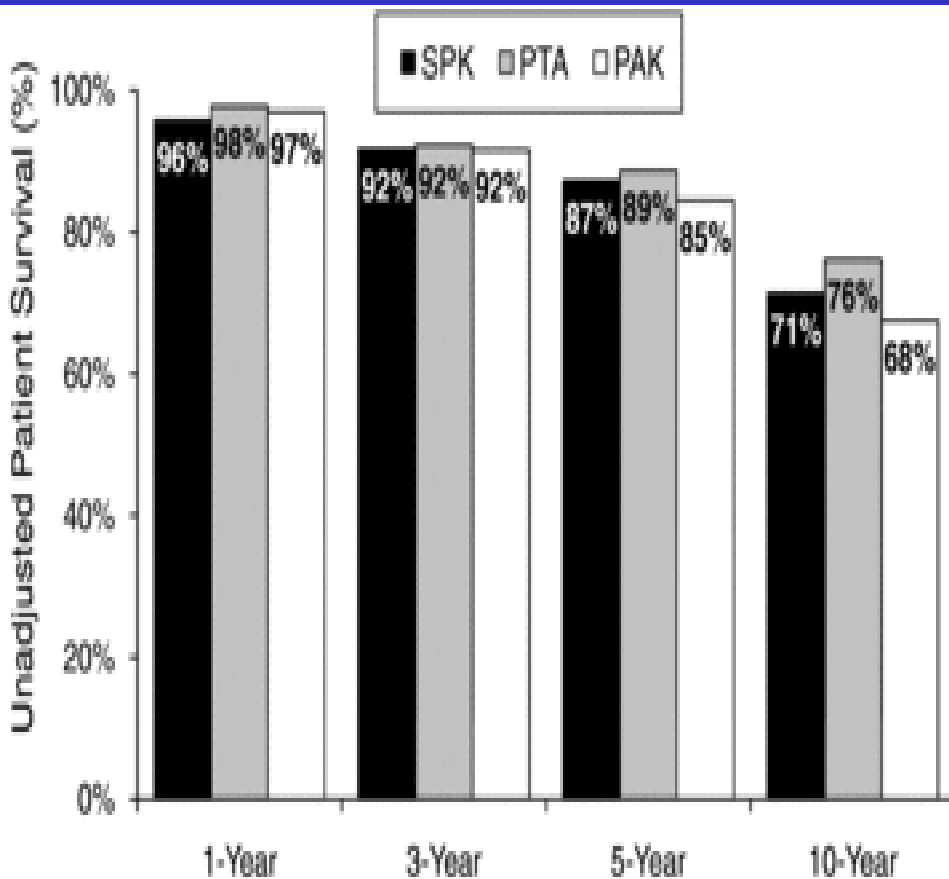
The Impact of Pancreas Transplantation on Kidney Allograft Survival



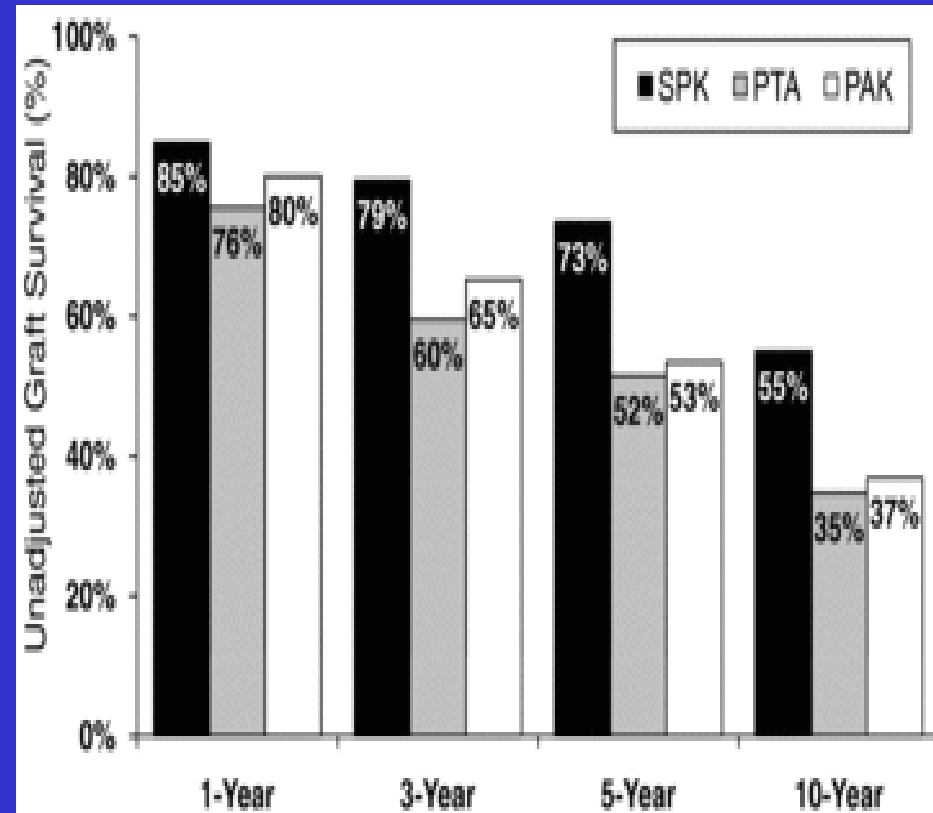
The survival advantage of pancreas after kidney transplant



Results



Source: 2009 OPTN/SRTR Annual Report, Table 1.13.



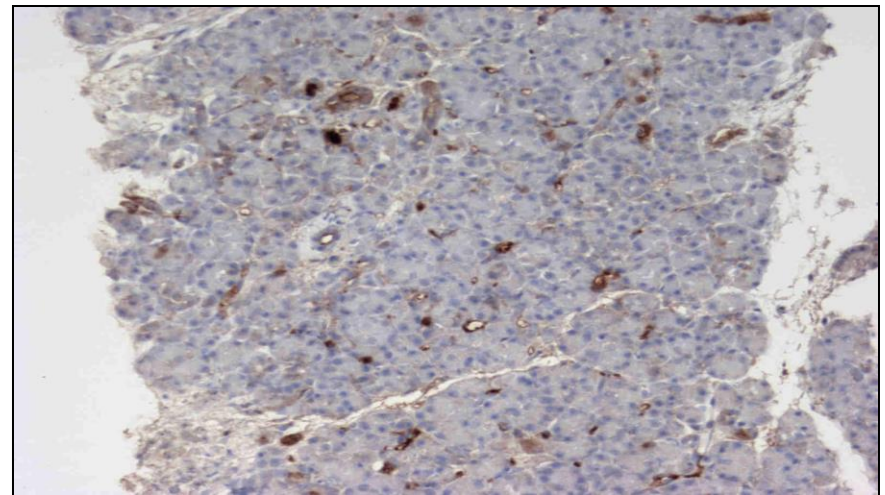
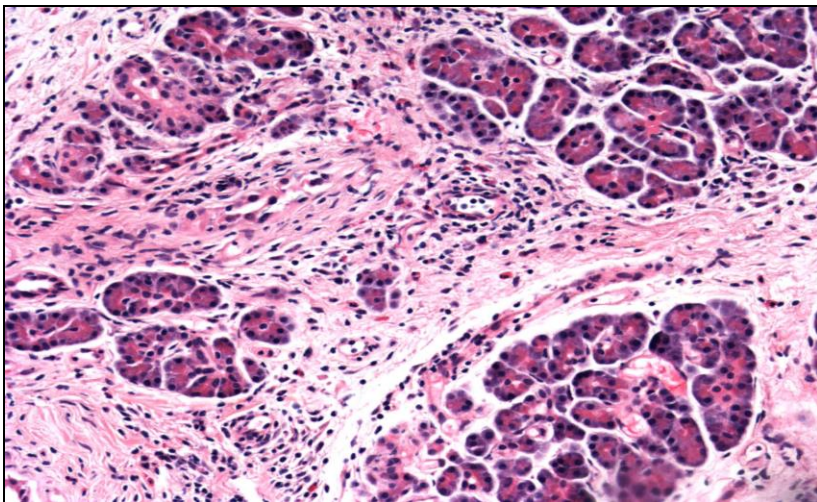
*Death is included as an event.

Source: 2009 OPTN/SRTR Annual Report, Table 1.13.

Am J Transplant. 2017;1:387.

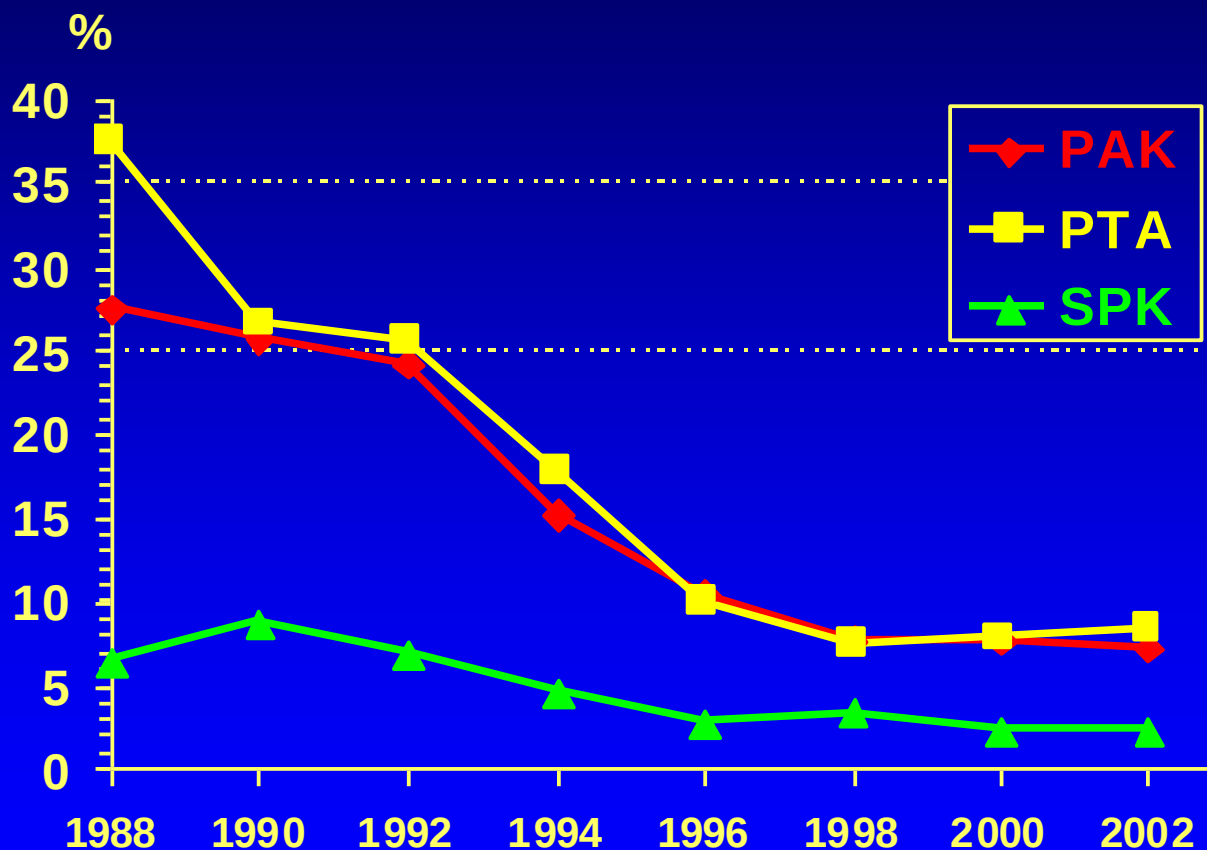
Diagnosis and Management of pancreas allograft rejection

- Isolated pancreas rejection in SPK occurs 5-10%
- Serum lipase is more sensitive than amylase;
Amylase : PV+ 73% PV-54% Accuracy 70%
- Rejection response directed towards epithelial cells (acinar and ductal cells), not islets



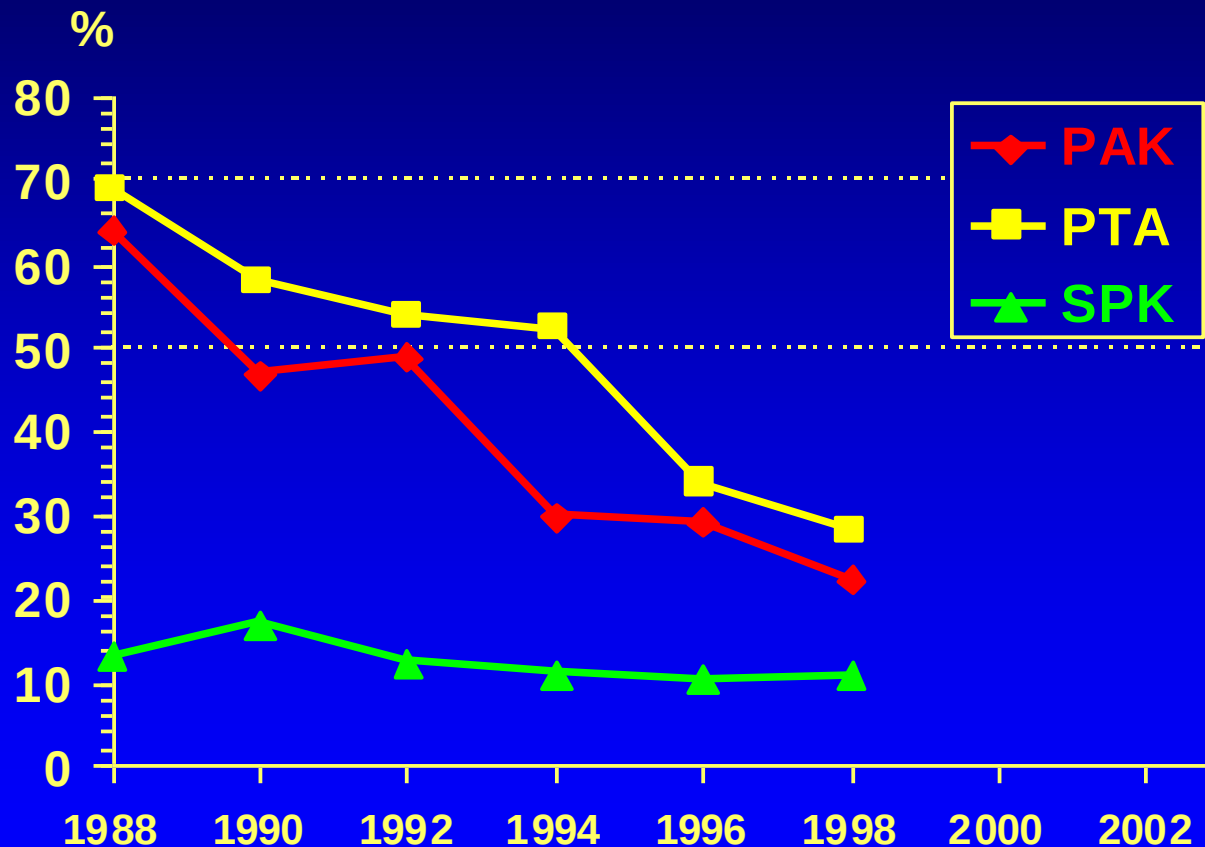
1-Year Immunological Graft Loss

USA DD Primary Pancreas Transplants, 10/1/1988 – 12/31/2003



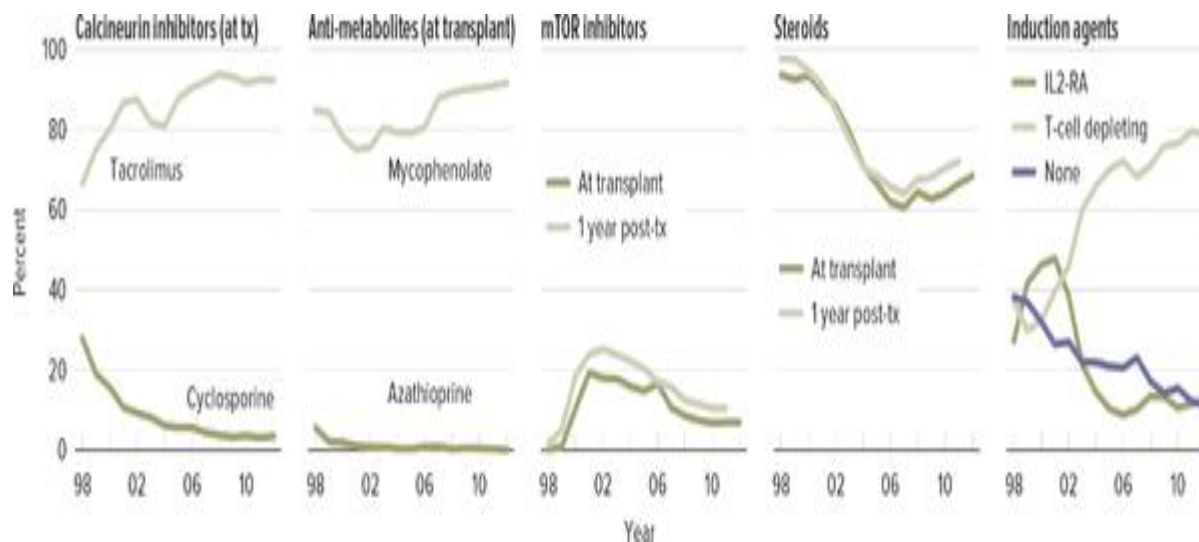
5-Year Immunological Graft Loss

USA DD Primary Pancreas Transplants, 10/1/1988 – 12/31/2003



Immunosuppression after Pancreas Transplantation

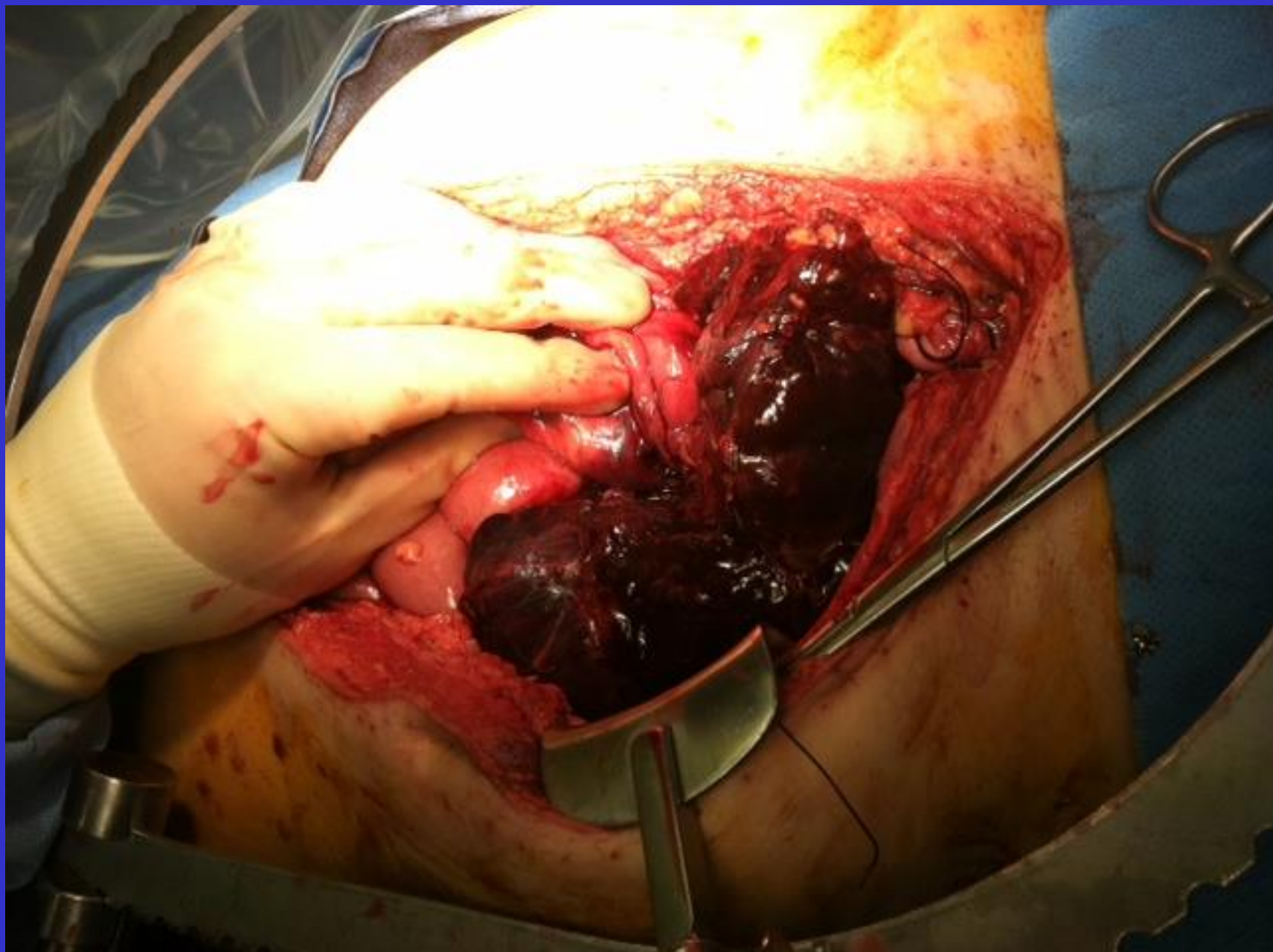
OPTN/SRTR 2012 Annual Data Report: Pancreas



Early and Late Causes of Graft Failure

Cause	%
Thrombosis	55.0%
Infections	19.8%
Pancreatitis	17.5%
Leak	5.5%
Bleeding	1.1%
Other	1.1%

	Total
Still functioning	795 (51.3%)
Partial function	18 (1.2%)
Immunologic failure	309 (20.0%)
Technical failure	255 (16.5%)
Death with function (DWF)	140 (9.0%)
Primary nonfunction	11(0.7%)
Other/Unknown	21 (1.3%)
Total n	1549



**Effect of Pancreas
Transplantation on Secondary
Complications of Diabetes**

Quality of Life after Pancreas TX

- More positive health perceptions
- Greater ability to function socially
- Normal routine activities
- More likely to view themselves as healthier
- Satisfaction with diet flexibility and health

Transplantation. 2000 Dec 27;70(12):1736-46.

Clin Transplant. 2009 Sep-Oct;23(5):600-5.

Eur J Surg. 1996 Dec;162(12):933-40.

Clin Transplant. 2006 Jan-Feb;20(1):19-25.

Clin Transplant. 1994 Jun;8(3 Pt 1):239-45.

Diabetologia. 1991 Aug;34 Suppl 1:S145-9.

Clin Transplant. 1992 Jun;6(3 part 1):165-71.

Coronary artery disease

- Atherosclerosis can regress
- Diastolic dysfunction returns to normal after 4 years.
- Rates of myocardial infarction and acute pulmonary edema are lower in recipients of SPK than in patients with diabetes given KTA
- Improvement in left ventricular geometry
- Stabilisation and improvement of cardiac autonomic function

Diabetes Care 2002; **25**: 906–11.

Kidney Int 2001; **60**: 1964–71.

Transpl Int 2005; **18**: 1054–60.

Peripheral Neuropathy

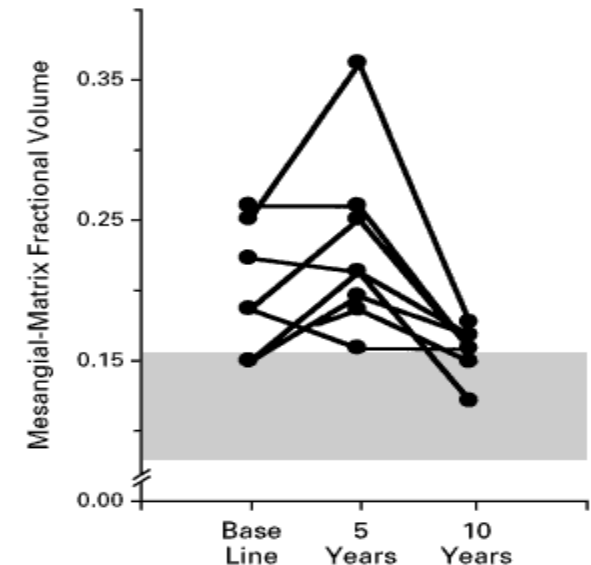
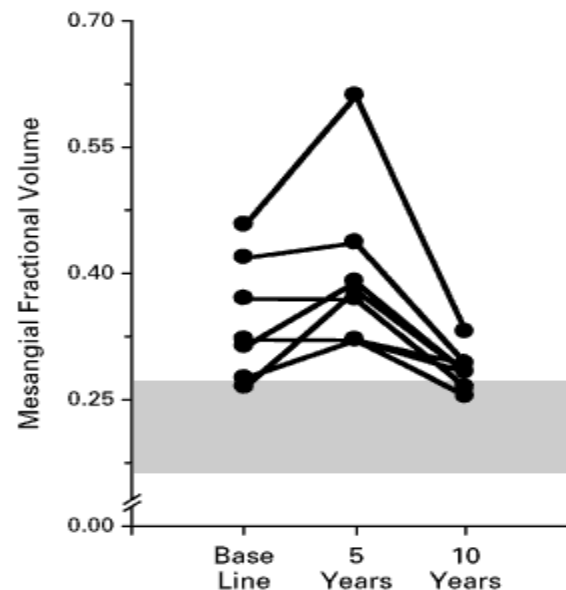
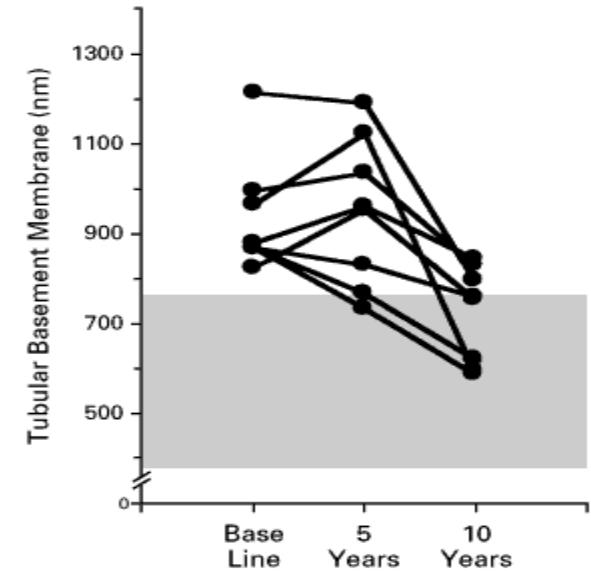
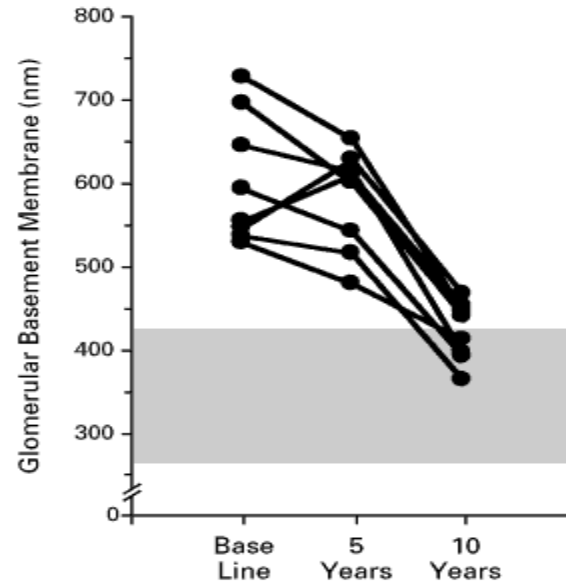
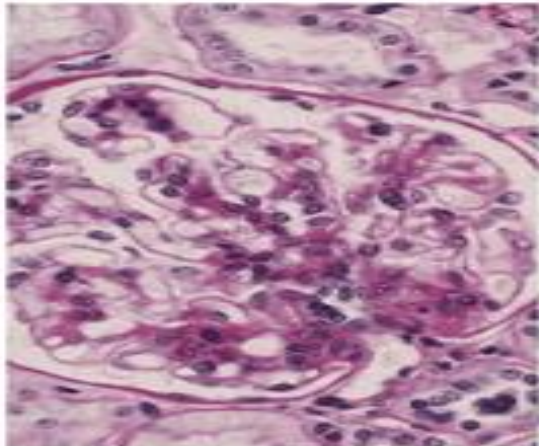
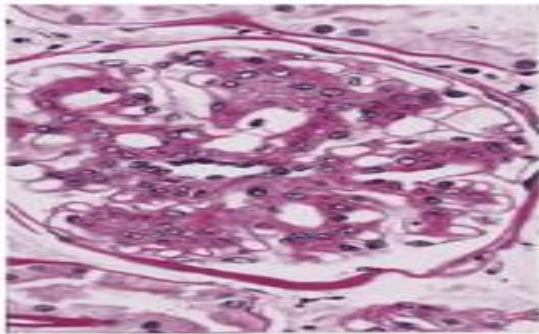
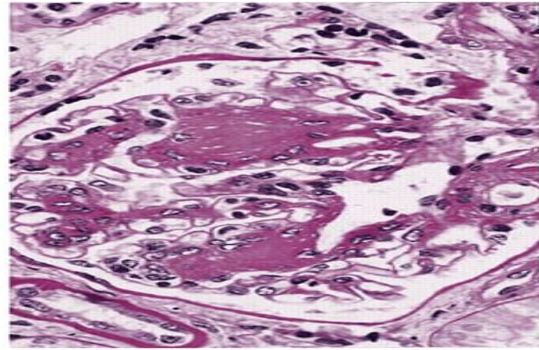
- Improvement in peripheral neuropathy, paraesthesia, autonomic neuropathy, and sensory amplitudes have been reported.
- Patients with abnormal cardiorespiratory reflexes have reduced rates of death

N Engl J Med 1990; **322**: 1031–37.

Diabetologia 1997; **40**: 1110–12.

Transplantation 1997; **63**: 830–38

Reversal of lesions of diabetic nephropathy after pancreas transplantation. *N Engl J Med* 1998; 339: 69–75.



Cerebrovascular and peripheral vascular diseases

Carotid intimal thickness has been seen to improve

Peripheral vascular disease ?

Transplantation 2000; **69**: 574–81.

Transpl Int 2003; **16**: 128–32.

Diabetes Care 2004; **27**: 1706–11.

Retinopathy

- Retinopathy can deteriorate in 10–35%
- The benefits become apparent after a few years.
- Cataracts, might deteriorate (? Steroids, CNI)
- Regression of diabetic retinopathy in 43% of patients given SPK versus 23% given KTA.

Clin Transplant 1999;13: 356–62.

Arch Ophthalmol 1984; 102: 527–32.

Ophthalmology 1994; 101: 1071–76.

N Engl J Med 1988; 318: 208–14.

Pancreas Transplant for type 2 DM

- Islets have abnormal function
- Limited cases

Long-term patient and graft survival

(n = 17)

Alive at 1 yr post-transplant

16

Euglycemia at 1 yr post-transplant

16

Alive at long-term follow-up (mean 3.3 yr)

12

Long-term deaths

4

Sepsis

2

Suicide

1

Unknown cause

1

Euglycemia at long-term follow-up

11 (65%)

Outcomes of SPK in Type 2 Diabetic Recipients

- 8.6% were performed in recipients with a type 2 DM.
- type 2 DM was not associated with increased risk for death or kidney or pancreas failure when compared with type 1 DM

Pancreas transplantation in type 2 diabetes mellitus

Age <55–60 years

BMI <30–32 kg/m²

Fasting C-peptide level <10 ng/ml

Total daily insulin dose <1 u/kg/day

Insulin-requiring for minimum of 5 years

Presence of ‘complicated’ diabetes including glucose hyperlability

Absence of smoking, major amputation, severe cardiac, or vascular disease

History of dietary and medication compliance

Thank you