Tour Report

Report on participation of the ICMR International Fellow (ICMR-IF) in Training/Research abroad.		
1	Name and designation of ICMR-IF	Dr. MANJUNATH MARUTI. POL
2	Address	Dr.Manjunath Maruti Pol Additional Professor Surgery Department of Surgical Disciplines Room No# 416, fourth floor, Surgery block, All India Institute of Medical Sciences (AIIMS), Ansari Nagar, New Delhi-110029
3	Frontline area of research in whichtraining/research was carried out	Clinical Fellowship in Kidney and Pancreas and Intestine Transplantation Surgery at Royal Adelaide Hospital, Government of South Australia.
4	Name & address of Professor and host institute	Dr. Shantanu Bhattacharjya Director of Transplant Surgery and Surgery in Renal Failure, Central Adelaide Local Health Network (CALHN). Level 3, 3A477, Royal Adelaide Hospital Port Road Adelaide 5000
5	Duration of fellowship with exact date	9 months, w.e.f 17-04-2023 to 16-01-2024
6	Highlights of work conducted	
	i). Technique/expertise acquired	Annexure 1
	ii). Research results, including any papers, prepared/ submitted for publication	Annexure 2
	iii). Proposed utilization of the experience in India	I underwent training (pre, peri and postoperative management) in multivisceral transplant (kidney, pancreas, intestine and liver) transplantation surgery. The surgical technique, research in kidney pancreas, intestine and liver transplant will be utilized for treatment of patients with type 1 diabetes mellitus with renal failure, intestinal and liver failure patients. Also, provide training (fellowship training) to interested government hospital surgeons (posted for training on deputation at AIIMS Delhi) and transfer knowledge and skills to treat patients requiring above said transplant surgery.

डॉ० मंजुनाथ मारुति पोल
Dr. MANJUNATH MARUTI POL
अपर आचार्य / Additional Professor
शल्य चिकित्सा विभाग / Dept. of Surgical Disciplines
अखिल भारतीय आयुर्विज्ञान संस्थान / A.I.I.M.S.
अंसारी नगर, नई दिल्ली / Ansari Nagar, New Delhi-110029

Signature of ICMR-IF

ICMR Sanction No.: No. INDO/FRC/452/(Y -04)/2022-23-IH &HRD. Dated: 19.10.2022

Testimonial

I, Dr. Manjunath Maruti Pol (an international medical graduate sponsored by ICMR, Government of India) was a part of our organisation from April 18, 2023, to January 12, 2024. He worked as an international clinical fellow in the Department of Renal and Transplant Surgery (RAH ID: 3101904, APHRA reg number: MED0002718465), Central and Northern Adelaide Renal and Transplantation Services (CNARTS), Royal Adelaide Hospital, SA Health, Government of South Australia, Adelaide, SA.

During his tenure in the department, he showed proficiency academically and clinically. He has assisted in 143 surgeries and was a primary assistant in all multivisceral retrieval and transplant surgeries. He has been well-trained in both warm and cold dissection of the kidney, pancreas, liver, and intestine, and their transplant surgery. He was primary assisted in laparoscopic live donor nephrectomies (both right and left). He has been trained in deceased brain-dead (DBD) and deceased cardiac donor (DCD) multivisceral retrieval and recipient's management by enhanced recovery after surgery (ERAS) protocols. He assisted several kidney transplants performed through small skin crease incision using ice bag technique (IBT). He has been trained in patient selection, perioperative management, assessment of organ quality, surgical techniques, post-op management, and immunosuppressant drug dosage titration, and follow-up care.

Dr. Pol has assisted significant number of surgeries involving complex vascular anatomy and surgeries in recipients with exhausted sites for implantation; that is, patients undergoing fourth kidney transplant for failed grafts, transplants following lung transplants, en-bloc kidney transplants (both conventional and new castles technique), simultaneous graft nephrectomy and implantation of new kidney graft on the same iliac vessels, dual kidney-graft implantation in bilateral iliac fossa (retrieved from marginal diabetic donor), simultaneous left-sided native nephrectomy and transplantation of pancreas on to left renal vessels and duodenogastrostomy, and ipsilateral & contralateral simultaneous pancreas-and-kidney (SPK) transplant. He has been trained in the management of complex SPK transplants requiring pancreas salvage surgery like duodenum resection followed by pancreatico-jenunostomy, graft pancreaticoduodenectomy & pancreatico-jenunostomy (dunking), and graft pancreatectomy for life-threatening complications such as fungal infection, GI bleed, graft rejection, and graft failure.

He has been well-trained in advanced vascular anastomosis techniques for cases with complex vascular anatomy like endarterectomy (with or without shunt) for densely calcified atherosclerotic arteries, the use of PTFE grafts for vessel anastomosis, use of proximal vessels like the common iliac artery & vein, inferior vena cava, and left renal vein.

Annexure-1

Dr. Pol has assisted in surgeries involving complex urological complications such as multiple site ureteral strictures and entire length ureteral necrosis managed by reimplantation of the ureter, uretero-ureteric anastomosis, creation of a boari flap, uretroenteric conduit, surgical creation of a nephrostomy, etc. He has been trained in the salvage of graft in severe hilar vessel bleeds by in-situ perfusion technique, intra-and immediate post-operative methods of assessment of organ quality & perfusion using the methylene blue (demonstrating capillary flow to kidney, pancreas, and intestine grafts), laparoscopic fenestration for lymphocele, single-port laparoscopic Tenckhoff's insertion for peritoneal dialysis, endoscopic PEG insertion, and retroperitoneoscopic native nephrectomy for symptomatic polycystic kidney disease followed by simultaneous or staged kidney transplantation. He is also trained in the postoperative management of pancreas graft rejection following SPK, titration of immunosuppressants (oral, parenteral, and via feeding jejunostomy tubes) in multivisceral transplants, management of fluid overload with and without CVVH in the ICU, treatment of post-transplant sepsis, graft biopsies, and graft nephrectomy.

Dr. Pol's pleasing bedside manners and good communication skills allowed him to get along well with patients and garner their trust. He always has a kind word for patients, relatives, junior and senior colleagues, and staff members. He is extremely sincere, committed, and dedicated to the practice of multivisceral transplant and general surgery, and he has lived up to the increasing responsibilities assigned to him. During the initial course of his training, he performed vascular anastomosis (one side), bowel anastomosis, DCD's, and DBD's under supervision. As part of the assessment in the end, he independently performed three vascular access procedures, two DBDs, eight DCDs, two kidney transplants with IBT, twenty-six ureteroneocystomy (as part of transplants), one ureteroureterostomy, and management by ERAS protocol. Dr. Pol provided training to three registrars and supervised them while they performed ureteroneocystostomy, diversion ileostomy, TAP catheter insertion, abdominal wall closure, and research paper writing. Dr. Pol has been taught the nuances of SPK and bowel transplants.

Dr. Pol's sound knowledge and academic participation, clinical research, paper presentations at international conferences, scientific paper writing and publication are qualities that will take him a long way in his profession. He has a bright future due to his intelligence, perseverance, and ability to work effectively as an individual and team member in a hierarchical system. Dr. Pol will be an asset to any team or organisation he is part of. I wish him all the best for his future endeavours.

डॉ० मंजुनाथ मारुति पोल
Dr. MANJUNATH MARUTI POL
अपर आचार्य /Additional Professor
शल्य चिकित्सा विभाग / Dept. of Surgical Disciplines
अखिल भारतीय आयुर्विज्ञान संस्थान / A.I.I.M.S.
अंसारी नगर, नई दिल्ली / Ansari Nagar, New Delhi-110029

Research report

1. Title: To study the factors that determines success of pancreatic transplantation. Prospective observational study.

2. Aims and objectives:
   2.1 Primary outcome:
   - To study risk factors associated with increase in the success rate of diabetic pancreas transplants recipients
   - Risk factors meaning: Age, sex, weight, condition and co-morbidity of the donor. Types of surgery, surgical technique, perfusion fluid (live and diseased donor), and postoperative titration of immunosuppressant's (Induction and maintenance therapy).

   2.2 Secondary outcome
   - Organ preservation technique after graft retrieval both in live and diseased donor versus end point (onset of graft function)
   - Surgical techniques applied (especially in complex surgical anatomy) versus end point (graft survival and patient survival)
   - Study immunosuppressive protocols in diabetic pancreatic transplant recipients versus end point (graft survival and patient survival)
   - Causes of morbidity (graft thrombosis, infections, pancreatitis, anastomotic or duodenal leaks, bleeding and relaparotomy) leading to graft loss and mortality in recipient's undergone pancreas transplant.

3. Justification
   - Insulin-dependent diabetes mellitus is associated with a high Incidence of treatment problems and secondary complications (blindness, amputations, and kidney failure) exceeds the usual side effects of immunosuppression.
   - Pancreas transplantation is not considered experimental procedure anymore. Benefits of a transplant are obvious when the problems of diabetes clearly exceed the potential side effects of chronic immunosuppression.
   - Worldwide around 37000 cases of Pancreas transplants have been reported to the International Pancreas Transplant Registry from December 16, 1966, through December 31, 2010. In India Pancreas transplantation surgery is rarely performed as there is often reluctance to recommend this procedure to patients because of its complexity and risks.
   - India is now considered the capital city of world of diabetics. Therefore, it is necessary for surgeons in India to get trained in pancreatic transplant and reduce the primary and secondary complications arising due to diabetes mellitus.

Annexure -2.

- The objectives of pancreas transplantation are to make them insulin-independent and normoglycemic, improve day-to-day quality of life, and ameliorate secondary complications.

4. Methodology:

4.1 Study design: Prospective observational study

4.2 Inclusion criteria

- Type 1 diabetes mellitus with hypogyycemia of unawareness
- Type 1 diabetese mellitus with end stage renal disease

4.3 Exclusion criteria for donors

- Diabetic sibling or family members
- History of gestational diabetes mellitus
- Serum amylase > 110
- Age > 45 years
- Weight < 30kg or BMI >30

Results:

Total transplant cases assisted 143 cases.

Discussion:

For the simultaneous pancreas-kidney transplant, the organs come from the same deceased donor.

Kidney transplant alone for diabetic nephropathy has a poor prognosis. The decision in such patients is to whether to do a kidney transplant alone with subsequent pancreas transplant instead of a combined operation is dependent on several factors eg, availability of potential living donor, the urgency to come off dialysis, waiting time for an SPK. Currently, SPK and PAK are offered to people with insulin-dependent diabetes (type 1 or a few selected type2) with chronic renal failure, and diabetes with hypoglycemia of unawareness.

Pancreas graft survival after PAK (pancreas after kidney) is clearly less than the pancreas survival in SPK (simultaneous pancreas and kidney transplant).

Based on these principles, the prototype recipient for PTx is a patient with

Type 1 diabetes:

- Without detectable c-peptide, poor metabolic control and/or progressive secondary complications of diabetes.

Type 2 diabetes:

- With high insulin needs, low to mild insulin resistance, and non- or mildly obese, may achieve insulin-independence after pancreas transplant (PTx) and enjoy results similar to those of patients with type 1 diabetes.

Patient assessment for pancreas transplantation:

1. Medical history, physical examination, previous red blood cell transfusions, etc.;
2. Immunological studies: Blood group type, HLA, cytotoxic antibodies, luminex, etc.;
3. Radiological exams: Abdominal ultrasound and chest and abdominal X-ray; CECT or CT angio for landing site (site of implantation)
4. Endoscopic procedures: Colonoscopy in patients ≥ 50 years old included on the waiting list;
5. Extensive blood test including evaluation of diabetes, viral serology and prostate specific antigen in male patients older than 40 years; and
6. In patients with a history of autoimmune diseases (lupus, vasculitis, etc.), deep vein thrombosis, pulmonary embolism, acute stroke, heart attack or family history of venous thromboembolism, a complete study of thrombophilia should be performed.

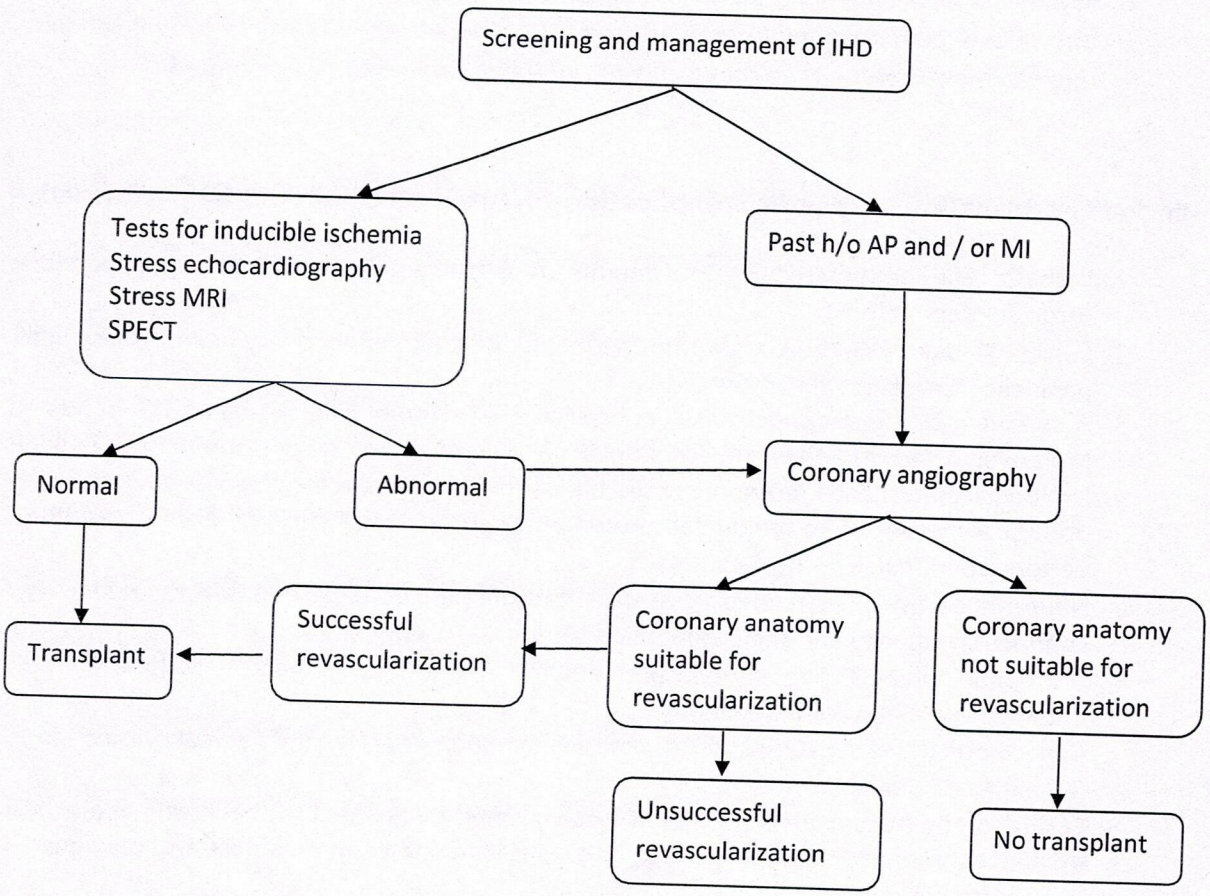
Physical examination, a specific complication-oriented study should be performed:

1. Diabetic retinopathy screening (documents on photocoagulation treatment and possible surgical interventions);
2. Cardiovascular evaluation: algorithm to identify the status of coronary heart disease in all pancreas transplant candidates (fig 1)
3. Assessment of the peripheral vascular disease. Evaluation of iliac axis by a CT-A or MRI-A. Moreover, a carotid and aortic-iliac duplex ultrasound should be performed in all patients;
4. Urological status: each recipient should be assessed by the Urology Service to assess the urological status due to the diabetic autonomic neuropathy. A prostate exam should be performed in males > 40 years.
5. Neurological evaluation: clinical assessment of the peripheral neuropathy, the nerve conduction velocity and the autonomic status;
6. Hormonal studies: C-peptide measurement and immunological markers of the DM (anti-insulin and anti-GAD antibodies);
7. Gynecological examination in fertile females (a mammography and vaginal cytology in females > 35 years);
8. Evaluation by the pancreas transplant surgery team: assessment of the intestinal function, existence of associated diseases such as gallstones, state of vascular axis and previous abdominal surgery
9. Complete infectious diseases screening; and
10. Psychological evaluation

Contraindications of Recipient pancreas transplantation (SPK, PAK, PAT):

1. Active infection
2. Severe coagulation abnormalities
3. Positive cross match
4. Drug addiction (including alcoholism)
5. Complex coronary artery lesions, ejection fraction < 50% and recent myocardial infarction
6. Previous history of treatment noncompliance
7. Severe psychiatric disorder
8. Neoplasia
9. Morbid obesity, and
10. Read indication and contraindications in the kidney-pancreas transplant (selection criteria).

Figure 1. Algorithm for cardiac assessment



Indication:

1. pancreas alone transplant is for Type 1 and 2 DM with hypoglycemia of unawareness
2. Type-1 diabetes with end-stage renal failure on dialysis or requiring dialysis within six months (GFR < 20ml/min). – for SPK
3. Pancreas after kidney is for pancreas transplant for patients who have already undergone live kidney transplant in the past.
4. Severe complications of diabetes mellitus with frequent and severe hypoglycemia or ketoacidosis.

Recipient (Risk factors)

Patient selection for SPK transplantation recipients:

1. Age ≤ 55 years. Patients of older age should be considered individually
2. Absence of severe peripheral arterial disease or coronary heart disease
3. Absence of several motor sensory neuropathy or peripheral autonomic impairment
4. Fulfilment of the kidney transplantation criteria
5. Absence of severe mental disorders, and
6. Ability to understand the possible post-surgery complications and the treatment follow-up.

Recipient Absolute contraindications:

1. Age over 65,
2. Major cardiovascular risk defined as significant coronary artery disease which is not correctable
3. Myocardial infarction within six months
4. Left ventricular ejection fraction < 30%
5. Pulmonary artery systolic pressure over 50mm Hg,
6. Incurable malignancy except localized skin cancer,
7. Prostate cancer,
8. Active sepsis (hypotension or inotrope support, Elevated Pro-calcitonin)
9. Peptic ulcer disease, immune suppression,
10. A major psychiatric history which can result in non-adherence to the treatment, and any inability to withstand surgery.

Recipient Relative contraindications:

1. Patients ≤ 18 years or > 55 years
2. Recent retinal hemorrhage
3. Cerebrovascular accident with long-term impairment,
4. Active infection hepatitis B or C virus,
5. Body mass index ≥ 30 kg/m,
6. Insulin requirements >1.5 units/kg per day,
7. Extensive aorta/iliac and/or peripheral vascular disease: No site for implantation
8. Continued abuse of alcohol, tobacco or drugs.
9. Advanced age (> 50 years)
10. Active smoking (it is recommended to stop smoking prior to the inclusion on the waiting list)
11. HIV+, HCV+, HBV+: (HCV + cases - treatment is recommended prior to the inclusion on the waiting list).

Patients with ESRD could be included in the waiting list when creatinine clearance < 30 mL/min (stage IV).

Donor selection criteria: An ideal pancreas donor (age ≤ 40 years, low BMI, death due to trauma, short stay in the ICU, and hemodynamic stability without, or with low dose, vasoactive amines)

- High dose of inotropes means dopamine > 10 u or two inotropes.
- Inclusion of high-risk groups: this can result in high rates of graft rejection and low graft survival after transplantation.

The donor organ may be rejected due to:

1. Donors age > 45 years, and < 18 years
   - Age < 18 years: grafts present a lower β-cell mass, require a greater technical challenge and are associated with a greater number of complications, especially vascular thrombosis. However, pancreas from pediatric donors over three years of age and with a weight of ≥ 25 kg have been harvested and transplanted
   - Age > 45 – 50 years years: reduced graft survival and increased complications such as vascular thrombosis, intra-abdominal infections and duodenal or anastomotic leaks, which affects the graft and recipient survival.
   - Pancreas donor > 45 years: Decision to harvest should be individualized by studying the medical history (especially previous cardiovascular diseases),

weight, previous physical activity and lifestyle, cause of death, time in the intensive care unit, etc.

2. Cause of death (e.g., stroke);
3. Currently, hyperglycemia or hyperamylasemia are not considered absolute contraindications for transplantation

   ➢ Previous hyperglycaemia:

   - The presence of hyperglycemia in brain-dead patients is not uncommon.
   - In the absence of a history of diabetes, this hyperglycemia is not a contraindication to donation
   - It may be related to the trauma itself (as a consequence of the destruction of areas of the central nervous system related to metabolic functions), result from acute injury and the secondary release of catecholamines and steroids or it may be related to the administration of exogenous glucose and steroids

   ➢ Previous hyperamylasemia:

   - An isolated elevation of amylase in the blood without associated lesions is not a contraindication for donation, as the use of this type of pancreas does not affect graft function after transplantation
   - High levels of amylase in the blood are observed in up to 40% of donors and may sometimes contraindicate donation
   - Hyperamylasemia is frequently associated with death due to traumatic brain injury, direct trauma to the salivary glands, secondary to pancreatitis, metastasis and chronic renal disease, contraindicating donation in all cases.

4. Cold ischemia time (greater than 8 h (DBD) or 12 h (DCD), depending on the type of donation);

   - It has been considered that a pancreatic graft can be transplanted up to 30 h after pancreas extraction.
   - Recent studies showed a higher rate of graft failure when the cold ischemia time (CIT) increased. Authors have reported an increase in the incidence of complications such as anastomotic leaks, thrombosis, pancreatitis and infections, and they recommended to not exceed the limit of 20 h.
   - The development of early pancreatitis after transplantation has been associated with several factors, including advanced age, high body mass index (BMI), prolonged ischemic times.
   - Currently, it would be advisable in the
     - In DBD a cold ischemia time of < 12 h,
     - In DCD a cold ischemia < 8 h.

5. The use of vasopressors in the ICU or cardiac arrest; and

- Marginal donors: hemodynamically unstable at the time of extraction are considered marginal
- Marginal donors corresponds to those donors who require high doses of dopamine (> 10 µg/kg/min) or the use of two vasopressors at the time of extraction.
- Pancreas is a low-flow organ, so hemodynamic instability before or during extraction may contribute to the presence of inadequate perfusion and the development of graft thrombosis and postoperative pancreatitis.
- In a donor's pre-procurement DCD patients, the functional impact and evolutionary curve over time of liver and pancreatic enzymes should be carefully evaluated to rule out severe damage in both organs.
- In particular, in DBD patients, the time of pre-procurement cardiac arrest should not exceed 15 min, although the functional impact should always be assessed individually

6. The macroscopic aspect of the pancreas allograft:

- The macroscopic appearance of the pancreas at the time of extraction is the most relevant data to decide the graft's viability.
- Gross examination of pancreas or post-retrieval back table assessment: The presence of signs of acute pancreatitis, glandular edema, hematoma, fatty infiltration, and hardened consistency is considered on the macroscopic evaluation of the pancreas as such factors increase the risk of post-transplant complications.

- Contraindicate the pancreatic extraction:

  a) The presence of acute or chronic pancreatitis signs, e.g., the existence of pseudocysts or an important fatty infiltration,
  b) traumatic injury to the pancreas
  c) calcification or fatty infiltration of pancreas
  d) atherosclerotic vessels
  e) extensive pancreatic oedema

- Pancreatic oedema may be the result of over hydration of the donor during the ICU stay. The use of grafts with oedema depend on the direct examination by the surgeon and the improvement of the organ after the administration of albumin and diuretics.
- The most important factor for deciding the validity of the pancreas remains the inspection by a senior transplant surgeon: following is not indicated:

  a) A pancreas with calcifications,
  b) Fibrosis or fatty infiltration should not be considered valid.

c) the existence of vessels with intense atheromatosis,
d) A pale coloration suggests ischemia,
e) while an intense yellow colour may be a consequence of fatty infiltration related to obesity or alcoholism

- The organ should have a soft consistency with no indurated areas on palpation and little or no fatty infiltration.

7. Bowel ischemia / ischemic colitis: is an absolute contraindication
8. Diabetes mellitus or a family history of diabetes
9. Pancreas with fibrosis (atrophied pancreas) or fat deposition (fatty pancreas) upon retrieval is discarded because they are associated with severe reperfusion pancreatitis resulting in morbidity and mortality.
10. Donors BMI > 30 kg/m2 are declined for donation.

- High body mass index (BMI) (> 30 kg/m2);
  - Donor obesity is considered to be one of the factors that contraindicate the use of the pancreas graft. Contraindication for pancreas transplant is donor with a BMI > 30 kg/m2
  - Donor obesity is an important risk factor for surgical complications
    - Grafts present intra- and peri-glandular fatty infiltration.
    - Its preservation is not always optimal.
    - These pancreases are more susceptible to ischemia-reperfusion injury
    - Have an increased incidence of pancreatitis, thrombosis and intra-abdominal infections.
    - Possible subclinical diabetes of the obese donor may play in the subsequent function of the graft has been highlighted
  - BMI greater than 30 kg/m2 and the presence of peri-pancreatic fluid collections

- A lower donor weight < 30kg's also represents a risk factor
  - presence of small vessels increases the technical requirements, graft thrombosis was the main cause of graft loss on these occasions

11. Retrieval injury: higher discard rates
12. Pancreatic disease, prior surgery of the duodenum, pancreas, or splenectomy, malignant tumor, positive serology for infectious diseases (HIV or acquired immune-deficiency syndrome, hepatitis B and C),
13. Chronic liver disease, history of chronic alcohol abuse are other factors that might determine the exclusion of donors
14. Cause of death (e.g., stroke);
    - The ideal donor for pancreas transplantation is a young man without associated diseases who has died by trauma

- Therefore, the cause of death would not be a risk factor in itself but rather the vascular disease. In one study: Donor death due to stroke appeared as an independent risk factor for allograft thrombosis after an SPK transplantation. Thrombosis could be related to age and not to the cause of death.
- The existence of coronary artery disease and intracranial atherosclerosis are associated with systemic vascular involvement.

Pancreas transplant indications after a kidney transplant (pancreas after kidney)

1. Type 1 diabetes mellitus (DM): Previous living or deceased donor kidney transplantation;
2. Pancreatic graft failure after an SPK transplantation;
3. Tolerance for an increase in immunosuppressive therapy; and
4. Stable performance of the renal graft in all the cases (creatinine clearance > 40 mL/min)

Pancreas transplant alone

Type 1 DM patients without ESRD. A creatinine clearance > 60 mL/min and a proteinuria < 2 g/d.

Inclusion criteria:

1. Uncontrolled DM (severe hypoglycemia, hyperglycaemia or ketoacidosis) that compromise the quality of life; and
2. Failure of the continuous subcutaneous insulin infusion and continuous glucose monitoring.

Indications in type 2 DM and other types of diabetes (MODY): Pancreas transplantation within these patients is limited to a stringent group. Low resistance and lack of insulin production

Type 2 diabetes:

- With high insulin needs, low to mild insulin resistance, and non- or mildly obese, may achieve insulin-independence after PTx and enjoy results similar to those of patients with type 1 diabetes.

Definition of insulin resistant (IR):

- Insulin resistant when requiring > 1 unit/kg/day of exogenous insulin to maintain glycemic control. Patients requiring > 200 units of exogenous insulin per day are considered severely insulin resistant.

Indication:

1. Age < 55 yr
2. BMI < 30 kg/m2
3. Insulin dependence (generally - ≥ 5 years with insulin therapy & Insulin requirements < 75 IU/d)
4. Total insulin requirements < 1 U/kg of IBW/d (≥ 0.2 and < 1 U/kg/d)
5. Presence of renal failure (dialysis dependent or pre-dialysis advanced kidney disease e.g., diabetic nephropathy with GFR ≤ 20 mL/min per 1.73 m2
6. Fasting c-peptide < 10 ng/mL (ideally C-peptide values < 5 ng/mL)
7. Low cardiac and vascular disease risk
8. History of medical and dietary compliance
9. Others:
   - Minimal or corrected cardiac disease,
   - Minimal to mild iliac disease, and
   - Absence of tobacco and substance abuse.