Pancreas Transplant 2018 – Update of Current Indications and Outcomes

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Disclosures

In compliance with the accrediting board policies, the American Diabetes Association requires the following disclosure to the participants:

Name of Presenter: Jon Odorico, MD, FACS

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Board Member/Advisory Panel: Regenerative Medical Solutions, Inc.
Stock/Shareholder: Regenerative Medical Solutions, Inc.

Transplant Categories

USA SPK, PAK and PTA Transplants 1/1/1984 – 12/31/2016

- Simultaneous Pancreas Kidney (SPK)
  Chronic kidney disease
- Pancreas After Kidney (PAK, PASPK)
  Prior kidney transplant and satisfactory kidney function
- Pancreas Transplant Alone (PTA)
  Normal kidney function and impaired hypoglycemic awareness and multiple life-threatening hypoglycemic events or persistent problems despite trial of pump/CGM technology
Pancrak Transplant Volume at UW

Center Volume is Associated with Outcomes after Pancreas Transplantation

*annuallized


SPK Patient Survival

USA Primary DD Pancreas Transplants, 1/1/1966 –12/31/2016

SPK Pancreas Graft Function

USA Primary DD Pancreas Transplants, 1/1/1966 –12/31/2016
Candidates for Pancreas Transplantation – Expanding Indications

**Classical**
- Adults with T1D
- Chronic Kidney Disease / Hypoglycemia unawareness
- No or minimal Cardiac Disease
- BMI <30
- No active infections or cancer
- Few Re-transplants

**Current at UW**
- Adults with T1D or T2D and Type 3c
- Chronic Kidney Disease / Hypoglycemia unawareness
- Corrected Cardiac Disease
- BMI <35
- Treated Hep C+, HIV+, prior treated malignancies
- Re-transplants

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**T1D with Hypoglycemia Unawareness**

- **Hypoglycemic unawareness**: Frequent acute severe metabolic complications that are incapacitating or life threatening e.g. 911 calls, LOC, seizures, MVA, loss of job, glucagon use, excessive fear, etc.
- Consistent failure of other therapeutic approaches
- Early but progressive diabetic end-organ complications but without kidney disease or proteinuria
- Balance benefits of improving glycemia and downsides of immunosuppression
- Selected T1D non-uremic patients – low risk and high benefit

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**Prevalence of Hypoglycemia Unawareness**

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of patients</th>
<th>Impaired awareness of hypoglycemia (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td>302</td>
<td>23</td>
<td>Hepburn et al. (1990)</td>
</tr>
<tr>
<td>Germany</td>
<td>523</td>
<td>25</td>
<td>Mullhauser et al. (1991)</td>
</tr>
<tr>
<td>Denmark</td>
<td>411</td>
<td>27</td>
<td>Pramming et al. (1991)</td>
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<tr>
<td>USA</td>
<td>628</td>
<td>20</td>
<td>Orchard et al. (1991)</td>
</tr>
</tbody>
</table>

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12-month Frequency of Severe HYPOGLYCEMIA Requiring Assistance in Registry and Observational Studies

- 35.4% - U.S. T1D Exchange Registry (2013)
- 31.5% - Eurodiab Prospl Compl Study (2012)
- 36.7% - Danish-English survey (1995)
- 40.5% - Dutch study (2000)
- 46% - UK Hypoglycaemia Study Group in adults with T1D for >15 yrs (2007)

Real-world frequency of SH
- much higher than suggested by clinical trial data
- remains alarmingly high

Incidence of Severe Hypoglycemia

Fig. 2. Incidence of severe hypoglycemia in the U.K. Hypoglycaemia Study (UH). 

Glucagon and Epinephrine Response to Hypoglycemia is Blunted in Long-standing T1DM

The Clinical Reality of Hypoglycemia


Courtesy of Bernhard Hering
Measuring Hypoglycemia

- **Clarke Score** – 8 questions assessing exposure to moderate and severe hypoglycemia, and glycemic threshold for symptoms. Score of 4 or more implies impaired awareness.

- **Hypo Score** – based on 4 weeks of glucose readings +/- sx, self-reported episodes over previous year; Score range 0-3000. Median score 143; >1000=severe hypo, 400-1000=moderate hypo.

- **Lability Index (LI)** – based on 4 weeks of glucose records LI (mmol/L²/hwk⁻²) = \[\Sigma (\text{Gluc}_i - \text{Gluc}_0)²/\text{mean Gluc}_0\] - Range 0-1000, median 233; > 433 indicates problematic lability.

- Better discrimination than MAGE.

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**PTA Pancreas Graft Function**

USA Primary DD Pancreas Transplants, 1/1/1966 – 12/31/2014

**PTA Transplants at UW by Era: 1997-2001 vs. 2012-2016**
**Optimal Type 2 DM Patient For Pancreas Transplant**

- Insulin-dependent
- Primarily uremic T2DM – PAK or SPK
- Current UNOS Regulations:
  - if fasting C-peptide > 2 ng/ml → BMI ≤ 30 kg/m²
  - if fasting C-peptide < 2 ng/ml → No BMI restriction
- Relatively low insulin requirement <75-100 U/day (i.e., no evidence for severe insulin resistance)
- Avoid morbidly obese recipients with high insulin requirements and metabolic syndrome
- Mild to moderate co-morbidities (minimal to mild cardiovascular disease)

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**SPK Patient Survival by Diabetes Type**

**USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016**

![SPK Patient Survival by Diabetes Type](image)

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**SPK Pancreas and Kidney Graft Function by Diabetes Type**

**USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016**

![SPK Pancreas and Kidney Graft Function by Diabetes Type](image)
SPK Outcomes have improved in Patients with Type 2 DM

USA Primary DD: Pancreas Transplants 1/1/1995 – 12/31/2015

Other Categories

- DRIASM — extreme SQ/IM insulin resistance
- Post-gastric bypass insulin-deficient diabetes
- Total pancreatectomy, e.g. chronic pancreatitis, trauma, etc.
- Failed islet transplantation
- T1D assoc. w/ Multiple autoimmune dz syndrome (e.g. lupus, MS, psoriasis)
- Hep C+; HIV+
- Re-transplants

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The Case for Simultaneous Pancreas Kidney (SPK) Transplantation for Obese T2DM Patients

Talal M Al-Qaoud, Robert R Redfield III, Glen Leverson, Bridget Welch, Jon S Odorico
• Comparing BMI<30 T2DM recipients requiring insulin there was no difference in kidney graft and patient survival; non-statistically significant better pancreas graft survival in the BMI<30 group
• Comparing LDKTx vs. SPK transplant outcomes in obese (>30 BMI) uremic patients there was no significant difference in kidney graft or patient survival
• For selected low cardiac risk, IDDM T2DM uremic patients, an SPK can be a good option without BMI restriction
Advantages of PAK vs. SPK

**PAK**
- Better kidney?
- Excellent pancreas function
- Avoid dialysis – preemptive kidney transplant possible
- Short kidney and pancreas transplant waiting times
- Prove patient tolerates immunosuppression and surgery

**SPK**
- Excellent kidney function
- Better pancreas function?
- Single operation
- Lower rejection and immunological graft loss rates
**PAK is associated with similar patient survival benefits to SPK Transplants**

*UNOS/OPTN Analysis*

[Graph showing survival data for PAK, PASPK, and SPK transplants.]

*Source - UW Transplant Database*

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**What type of kidney has the longest function?**

[Graph showing survival rates for different types of kidney transplants over time.]


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**Kidney Graft Survival from the time of Kidney Transplant**

*PAK/PASPK vs. SPK*

[Graph showing comparison of survival rates.]

*Source - UW Transplant Database*

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**Pancreas Graft Survival**

*PAK/PASPK vs. SPK*

[Graph showing comparison of survival rates.]

*Source - UW Transplant Database*
A pancreas transplant conveys a survival advantage in kidney recipients

Survival Rates in Patients Surviving with Kidney Function at One Year: Influence of PAK

<table>
<thead>
<tr>
<th>12-Month Survivors</th>
<th>n</th>
<th>Unadjusted Kidney Graft Survival (%)</th>
<th>Patient Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPK, P</td>
<td>252</td>
<td>72.4</td>
<td>81.4</td>
</tr>
<tr>
<td>SPK, P (PAK)</td>
<td>119</td>
<td>81.2</td>
<td>87.6</td>
</tr>
<tr>
<td>LD KA</td>
<td>419</td>
<td>75.9</td>
<td>85.6</td>
</tr>
<tr>
<td>LD KA (PAK)</td>
<td>485</td>
<td>83.0</td>
<td>90.6</td>
</tr>
<tr>
<td>DI KA</td>
<td>344</td>
<td>69.1</td>
<td>80.2</td>
</tr>
<tr>
<td>DI KA (PAK)</td>
<td>176</td>
<td>76.0</td>
<td>87.2</td>
</tr>
<tr>
<td>SPK, P+</td>
<td>6486</td>
<td>83.1*</td>
<td>93.6*</td>
</tr>
</tbody>
</table>


After receiving a kidney transplant, is it better for the kidney to remain diabetic or to receive a pancreas transplant?

Very Short Waiting Time

High Transplant Rate – SPK and Solitary Pancreas Transplants

Source – SRTR June 2015 PIR release

Transplant Rate = # pts received a transplant / person-years observed at that program

Source – SRTR June 2015 PIR release
Zero Waiting List Mortality

What sets UW apart?
- Excellent Patient outcomes and satisfaction; short waiting times, very low waiting list mortality
- High center volume
- Specialize in PTA as well as SPK
- Pioneered UW organ preservation solution
- Use of DCD and pediatric donors
- Alemtuzumab use in pancreas transplantation
- No NGTs
- No ICU stay, short LOS
- Pancreatic allograft biopsies – understanding of rejection pathology
- Experienced team dedicated to comprehensive patient care

Comparable outcomes in SPK transplantation – T1DM v. T2DM

After adjusting for risk factors such as obesity, AA, age, PRA, etc. T2DM were not at higher risk.

Better quality kidney and shorter waiting time.