# Glucose management of the patients Underwent kidney transplantation or dialytic treatment.

ASAN MEDICAL CENTER
Diabetes Center
Diabetes Nurse Educator
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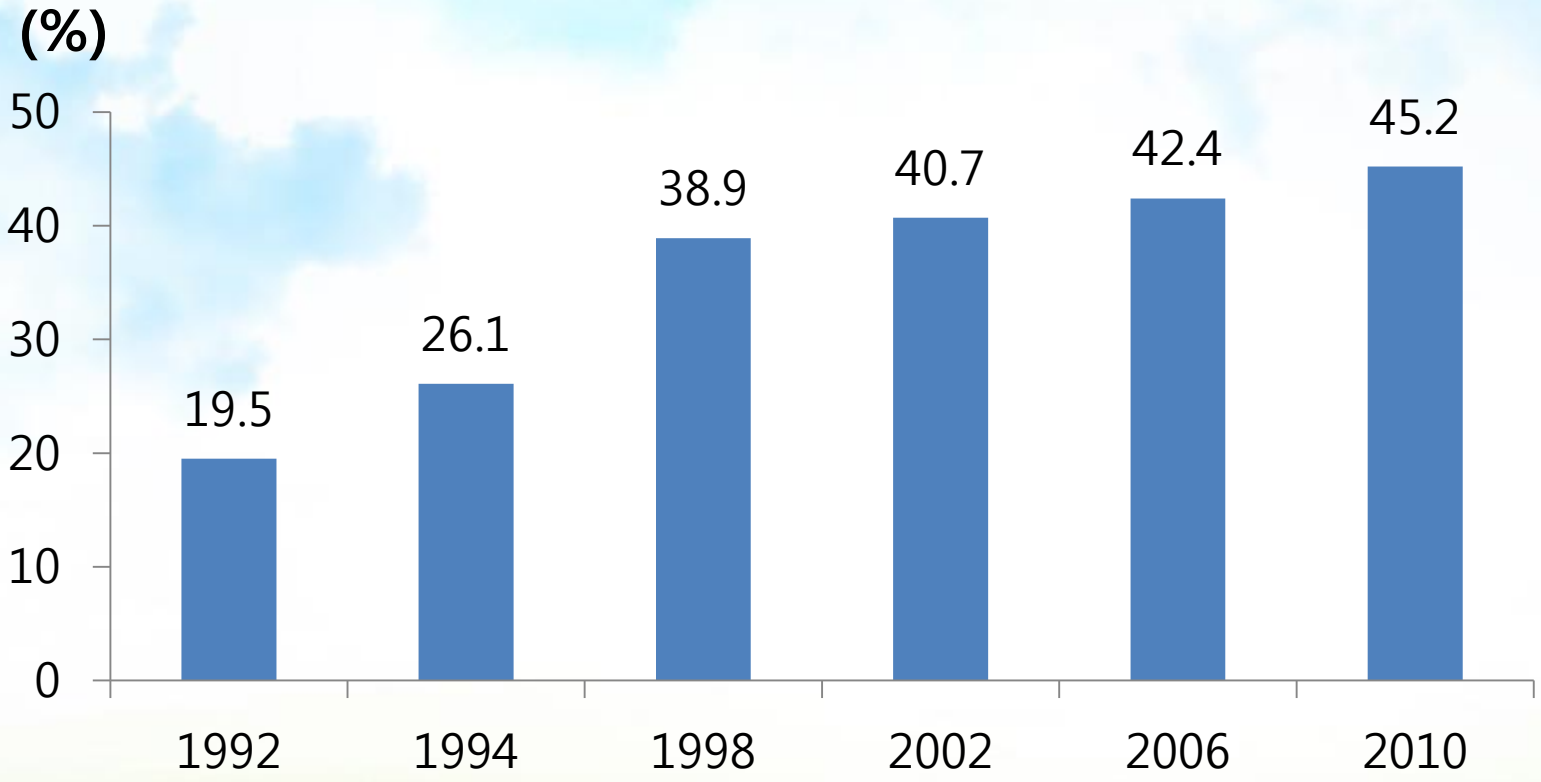
# Diabetic nephropathy in new renal replacement therapy in Korea




Jin DC. Korean J Intern Med 2011;26:123-31.

# National Diabetes Statistics Report, 2014 (USA, CDC)

## Kidney disease

• Diabetes was listed as the primary cause of kidney failure in 44% of all new cases in 2011.

• In 2011, 49,677 people of all ages began treatment for kidney failure due to diabetes.

• In 2011, a total of 228,924 people of all ages with kidney failure due to diabetes were living on chronic dialysis or with a kidney transplant.

Holly McFarland, Department Editor

# Transitioning from Peritoneal Dialysis to Renal Transplant: A Diabetes Management Case Study

Joanne Monaghan-Rourke

## Patient Profile

M.B. is a 54-year-old gentleman with a history of chronic kidney disease (CKD) presumed secondary to diabetic nephropathy. Diabetes type 2 was diagnosed approximately 25 years ago, insulin therapy was started eight years ago, and continuous cycling peritoneal dialysis (CCPD) was initiated five years ago. His medical provider had urged M.B. to start insulin for years preceding dialysis, but M.B. believed it was too inconvenient. He agreed to insulin when insulin pens were introduced to him.

M.B. is a highly educated, self-employed professional who is usually in control and resists taking direction from others. He works full-time and chose peritoneal dialysis

**The carbohydrate load provided by the chronic absorption of glucose may contribute to diminished appetite, decreased protein intake, and poor glycemic control in patients with diabetes (Crawford-Bonadio & Diaz-Buxo, 2004).**

He always felt full, so he skipped breakfast and lunch. He admitted that his nephrologist prescribed a daytime PD exchange, but M.B always skipped it. After working a 10-hour day, he came home and consumed a large dinner at 7:00 p.m. while starting his overnight dialysis. He self-adjusted his NPH insulin dosage according to whether he was using 4.25% or 2.5% dextrose dialysate. He also took less insulin if he ate a smaller dinner meal. M.B. checked his finger stick blood glucose level one to three times daily, and his reported values were 160 to 180 mg/dL in the morning, then 200 to 300 mg/dL one hour post-dinner.

# Education programmes for people with diabetic kidney disease (Review)

**Li T, Wu HM, Wang F, Huang CQ, Yang M, Dong BR, Liu GJ**

- **Adherence to complex regimens is often poor .**
- Require both intensive education and behavioral counseling.
- Looked for randomized trials (RCTs) comparing education programmes
  - Only two studies involving patients with DKD
  - **seemed to have some beneficial effects** on improvement of patients' knowledge of diabetes, self-efficacy, belief changes and self-management behavioral changes
  - small (207) numbers of patients enrolled
  - low methodological quality
- **Larger, high-quality RCTs are needed.**

Cochrane review, 2011, Issue 6

# A renal/diabetes care provider can have a significant impact

- by spending additional time listening to patients' concerns
- educating them on strategies to effectively manage hyperglycemia while avoiding hypoglycemia
- building trust in the healthcare team and treatment plan.

## Intended Patient Outcomes

- Have stable glycemic control while hospitalized post-renal transplant.
- Avoid hypoglycemia.
- Smooth outpatient transition for diabetes management.

# 신장이식 후 당뇨병의 자연 경과에 영향을 미치는 인자

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## Contributing Factors to Different Natural Courses of Posttansplantation Diabetes Mellitus in Renal Allograft Recipients

- **Aim**
  To demonstrate the detailed natural courses of PTDM according to the onset and persistency of hyperglycemia
  To investigate risk factors for development of different courses of PTDM in renal allograft recipients
- 77 renal allograft recipients
- 75 g oral glucose tolerance test at 0, 1, and 7 years after kidney transplantation
- Classified according to the onset and persistency of PTDM:
  - early PTMD (E-PTDM)
  - late PTDM (L-PTDM)
  - persistent PTDM (P-PTDM)
  - transient PTMD (T-PTDM)
  - non-PTDN (N-PTDM)

J Kor Endocrinol Soc 21:373~381, 2006

# Different clinical courses of post-transplantation diabetes mellitus

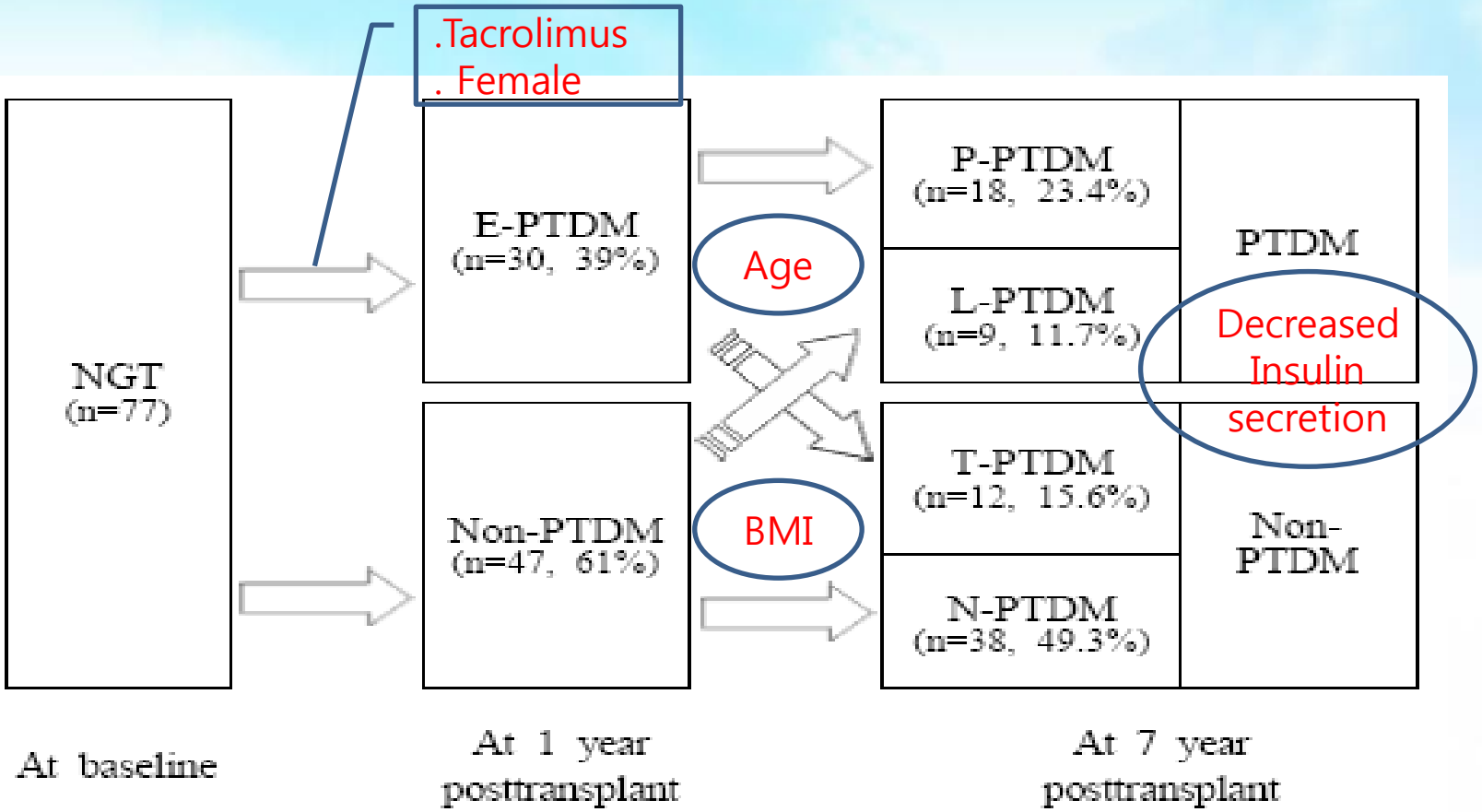



**Fig. 1.** Different clinical courses of posttransplantation diabetes mellitus (PTDM) in renal allograft recipients. E-PTDM, early PTDM NGT; L-PTDM, late PTDM NGT, normal glucose tolerance; N-PTDM, non-PTDM until 7 year posttmasplant; P-PTDM, persistent PTDM; T-PTDM, transient PTDM.

J Kor Endocrinol Soc 21:373~381, 2006

**Table 5.** Multivariate analysis of risk factors for P-PTDM vs. T-PTDM and L-PTDM vs. N-PTDM at 1 year posttransplant

| | P-PTDM vs. T-PTDM | | | L-PTDM vs. N-PTDM | | |
|---|---|---|---|---|---|---|
| Factors | Odds ratio | 95% CI | *P* | Odds ratio | 95% CI | *P* |
| Sex | 3.17 | 0.22~45.82 | NS | 0.63 | 0.09~4.62 | NS |
| Age | 1.16 | 1.00~1.35 | 0.045 | 0.95 | 0.86~1.05 | NS |
| Family history of diabetes* | 6.31 | 0.26~154.49 | NS | 0.44 | 0.04~4.68 | NS |
| Tacrolimus | 0.60 | 0.04~8.30 | NS | 2.30 | 0.31~16.86 | NS |
| BMI ($kg/m^2$) at year 1 | 1.53 | 0.86-2.75 | NS | 1.54 | 1.05~2.26 | 0.026 |

L-PTDM, late posttransplantation diabetes mellitus (PTDM); N-PTDM, non-PTDM until 7 year posttransplant; P-PTDM, persistent PTDM; T-PTDM, transient PTDM.

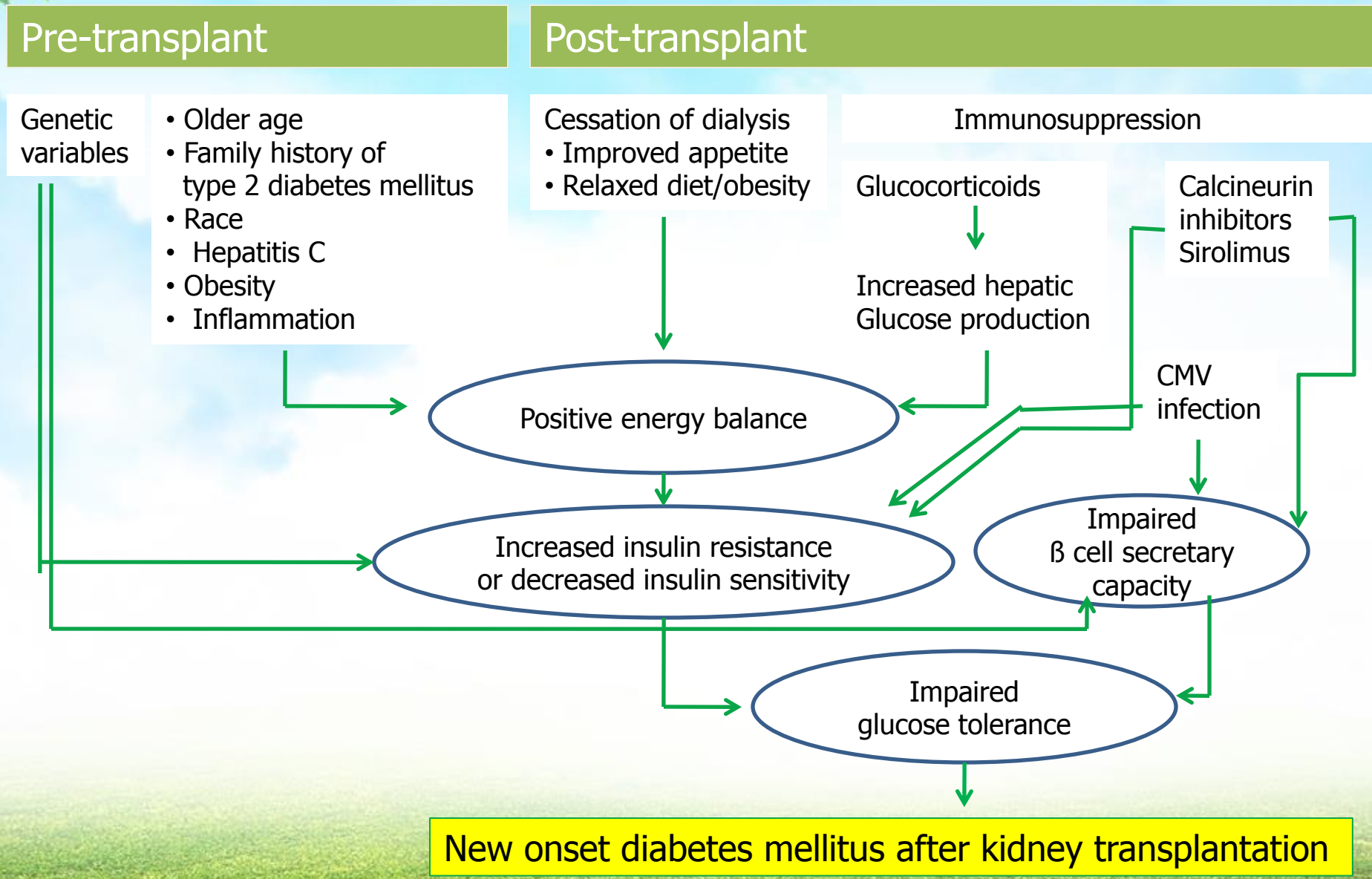
* Family history of diabetes in a first-degree relative.

**Conclusion:**

Since old age and female gender are not modifiable risk factors, it may be important **to modify immunosuppressive therapy regimens** for the prevention of E-PTDM and **control of body weight** for L-PTDM.

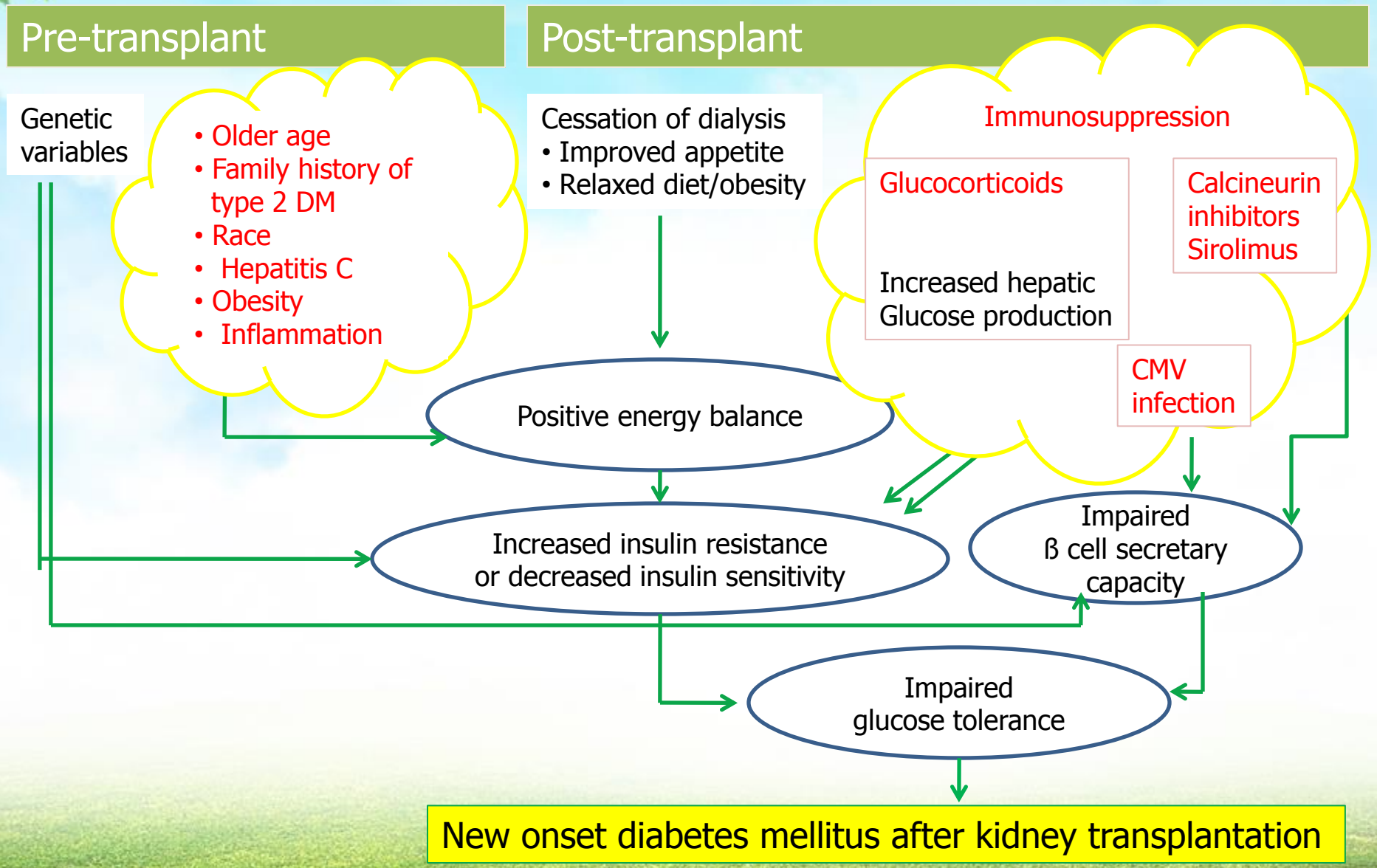
J Kor Endocrinol Soc 21:373~381, 2006

# Mechanism in the pathogenesis of NODAT




Diabetes care 36; 1406-1412; 2013

# Post-Transplant Diabetes Risk Factors




Diabetes care 36; 1406-1412; 2013

# Diagnostic criteria, according to the WHO, for new-onset diabetes after transplantation

| | Diabetes | Impaired fasting glucose | Impaired glucose tolerance |
|---|---|---|---|
| Random plasma glucose | 11.1 mmol/l (200 mg/dl)+Symptoms | - | - |
| Fasting plasma glucose | ≥ 7.0 mmol/l (≥ 126 mg/dl) | 6.1–6.9 mmol/l (110–125 mg/dl) | - |
| 2-h plasma glucose after 75 g glucose | ≥ 11.1 mmol/l (200 mg/dl) | - | 7.8–11.0 mmol/l (140–199 mg/dl) |
| HbA1c* | > 6.5% (48 mmol/mol) | - | Pre-diabetes:42–47 mmol/mol (6.0–6.4%) |

(* not yet considered diagnostic in the immediate post-transplant period)

Diabet. Med. 31, 1284–1292 (2014)

# Management of new-onset diabetes after transplantation

## Immunosuppression regimens

(1) stop or reduce dose of tacrolimus, ciclosporin or corticosteroids;

(2) if using tacrolimus-based therapy, consider a switch to ciclosporin, mycophenolate mofetil or azathioprine;

(3) if using ciclosporin-based therapy, consider a switch to mycophenolate mofetil or azathioprine

Diabet. Med. 31, 1284–1292 (2014)

# Management of new-onset diabetes after transplantation

## Anti-hyperglycemic therapy

- ✓ intensive lifestyle interventions  possibly effective, but may not be sustainable
- ✓ recommend a stepwise approach similar to Type 2 diabetes
- ✓ Acute, severe hyperglycemia in the post-transplant phase
  → most safely be managed with insulin therapy

Diabet. Med. 31, 1284–1292 (2014)

# Management of new-onset diabetes after transplantation

**Screening for diabetes-related complications**
ongoing screening for complications, including retinal screening, and screening for foot complications.

**Multidisciplinary management**
- ✓ increased risk of complications, with renal and cardiovascular morbidity increasing significantly
- ✓ Undertaken a joint multidisciplinary setting, involving nephrologists, diabetologists and specialist nursing/dietetic teams
  → in order to provide seamless care.

Diabet. Med. 31, 1284–1292 (2014)

# Areas of uncertainty in the prevention, diagnosis and management

| | Areas of uncertainty |
|---|---|
| Prevention | • Intensive lifestyle intervention to prevent NODAT<br>• Use of risk scores to focus intervention to prevent NODAT<br>• Use of risk scores to guide immunosuppression regimen to prevent NODAT<br>• Use of drugs pre-transplant to prevent NODAT |
| Diagnosis | •Use of regular post-meal glucose/capillary glucose to diagnose NODAT<br>• Use of HbA1c to diagnose NODAT |
| Management | •Use of change in immunosuppression regimen in early NODAT<br>• Use of oral hypoglycaemic agents in early NODAT<br>• Optimum insulin regimens in NODAT |

Diabet. Med. 31, 1284–1292 (2014)

REVIEW

# Diagnosis, management and treatment of glucometabolic disorders emerging after kidney transplantation

## A position statement from the Nordic Transplantation Societies

Mads Hornum,[1] Jørn P. Lindahl,[2] Bengt von Zur-Mühlen,[3] Trond Jenssen[2,4] and Bo Feldt-Rasmussen[1]

- Present guidelines for early risk factor assessment
- A screening/treatment strategy for disturbed glucose metabolism ( both before and after transplantation)
- The aim was to avoid the increased cardiovascular disease and mortality rates associated with NODAT.

Transplant International; Nov 26(11); 1049-60:2013

# Diabetes diagnosed during pre-transplant work-up

| | |
|---|---|
| Medical history | Diabetes in first-degree relatives<br>Gestational diabetes<br>Steroid diabetes<br>Prescription of gout medicine<br>Primary renal disease |
| Measurement of glucose metabolism | FPG<br>OGTT<br>HbA1c<br>C-peptide |
| Screening for metabolic syndrome and CVD risk factors and preplanned treatments | Age<br>BMI<br>Waist circumference<br>Lipid profile<br>(TG, LDL, HDL, ApoB/ApoA1)<br>Blood pressure<br>Smoking<br>Preplanned steroid treatment post-transplant |

Transplant International; Nov 26(11); 1049-60:2013

# Treatment and management of glucometabolic disorders emerging after kidney transplantation

- During hospitalization, the treatment targets should be:
  - ✓Fasting morning plasma glucose 4–7 mmol/l (72–126 mg/dl)
  - ✓Preprandial plasma glucose 4–10 mmol/l (72–180 mg/dl)
  - ✓Plasma glucose at night-time 4–10 mmol/l (72–180 mg/dl)
- The treatment targets should not be too low and not too aggressive
- Consider to use a progressive strategy in the supplementation of insulin where the use of steroid is increased
  ( usual insulin demand is increased by approximately 40% when treating with a prednisolone dose of 50 mg)
- If the insulin dose per 24 h required is modest (below 20 IE per day)
  → could be shifted to oral anti-hyperglycaemic agents

Transplant International; Nov 26(11); 1049-60:2013

# Diabetes and Kidney Transplantation: Past, Present, and Future

Giselle Guerra · Amna Ilahe · Gaetano Ciancio

## Management of Kidney Allograft in Diabetic or NODAT Recipients

- Selection on the type of kidney transplant: living kidney transplant
- Tight glycemic control : less than 7%
- Hyperlipidemia
  decrease LDL cholesterol to less than 100 mg/dL
  if pre-existing cardiovascular disease exists : less than 70 mg/Dl
- Hypertension
  10 mmHg rise : risk for death 18% ↑ , graft failure 17% ↑

Curr Diab Rep (2012) 12:597–603

# Updates on the Management of Diabetes in Dialysis Patients

Connie M. Rhee,* Angela M. Leung,† Csaba P. Kovesdy,‡§ Katherine E. Lynch,¶
Gregory A. Brent,† and Kamyar Kalantar-Zadeh*

**1. Challenging**

- given changes in glucose homeostasis
- the unclear accuracy of glycemic control metrics
- the altered pharmacokinetics of glucose-lowering drugs by kidney dysfunction, the uremic milieu, and dialysis therapy

**2. "Burnt-Out Diabetes"**

**3. Conventional methods of glycemic control assessment are confounded**

**4. Uncertainty surrounding the optimal glycemic target in this population**

**5. Require dose adjustment or avoidance in dialysis patients.**

Semin Dial ;Mar 27(2); 135-45:2014

# Monitoring of Glycemic Control in Dialysis Patients

TABLE 1. Comparison of methods of glycemic control assessment

| Glycemic metric | Period of assessment | Confounders | Strengths | Limitations |
|---|---|---|---|---|
| Hemoglobin A1c | 2–3 months | *Falsely increase:*<br>Elevated blood urea nitrogen level<br>Metabolic acidosis<br>*Falsely decrease:*<br>Anemia<br>Blood transfusions<br>Hemoglobinopathies and other disorders of shortened erythrocyte life span<br>Erythropoietin-stimulating agents<br>Protein-energy wasting | Routinely available in clinical laboratories<br>Metric in the general population upon which therapeutic targets are set based on outcome studies | |
| Fructosamine | 2 weeks | Altered serum protein states (i.e., peritoneal dialysate protein losses)<br>Malnutrition<br>Hepatic disease<br>Thyroid dysfunction<br>Pregnancy<br>Hyperuricemia<br>Smoking<br>Steroid use | Robust in states of altered hemoglobin level and erythropoiesis | Target range in CKD unknown<br>Not routinely available in clinical laboratories<br>Limited data on outcomes (i.e., microvascular complications) |
| Glycated Albumin | 2 weeks | Altered serum protein states (i.e., peritoneal dialysate protein losses)<br>Malnutrition<br>Hepatic disease<br>Thyroid dysfunction<br>Pregnancy<br>Hyperuricemia<br>Smoking<br>Steroid use | Robust in states of altered hemoglobin level and erythropoiesis | Target range in CKD unknown<br>Not routinely available in clinical laboratories<br>Limited data on outcomes (i.e., microvascular complications) |

Adapted from Kovesdy CP, Sharma K, Kalantar-Zadeh K. AJKD 52: 766–777, 2008.

Semin Dial ;Mar 27(2); 135-45:2014

Ronco C, Rosner MH, Crepaldi C (eds): Peritoneal Dialysis – State-of-the-Art 2012.
Contrib Nephrol. Basel, Karger, 2012, vol 178, pp 271–277

# Improving the Care of Diabetic Patients on Peritoneal Dialysis

Pranav Dalal · Madhukar Misra

## Key Factors that Determine Outcomes in the Diabetic PD Patient

**Nonmodifiable risk factors(largely)**

- Demographics
- Genetics

**Modifiable risk factors**

- the residual renal function (RRF) : glucose control
- Infections ; glucose control
- volume status – salt, fluid intake ; patient education
- the functional and structural integrity of the peritoneal membrane ; a glucose- sparing regimen like icodextrin or amino acid- based PD solutions

Contrib Nephrol;178; 271-7,2012

# Blood Sugar Control in the Diabetic Patient on Peritoneal Dialysis

- No studies have specifically addressed glycemic control criteria

- Outcomes in diabetic patients are not different than diabetic patients on PD

- Marked hyperglycemia is associated with increased mortality in diabetic patients on PD.

- Uremia alters the insulin metabolism, responsiveness and excretion→ making it difficult to control blood sugar in the PD patients.

Contrib Nephrol;178; 271-7,2012

# Blood Sugar Control in the Diabetic Patient on Peritoneal Dialysis

- About 60– 80% of instilled glucose in PD solution is absorbed in a 4- hour dwell, corresponding to daily intake of 100– 300 g glucose.
- This is equivalent to 20–30% of daily caloric intake.
- Use of one bag of icodextrin or amino acid- containing solution reduces the glucose load by 15– 30%.
- Metabolites of icodextrin are known to cause an overestimation of blood glucose(GDHPQQ system)
- IP insulin administration : require 26% less insulin but the risk of peritonitis was higher,
  - peritoneal fibroblast proliferation
  - hepatic subcapsular steatosis

Contrib Nephrol;178; 271-7,2012

# In summary

- A renal/diabetes care provider can have a significant impact
- A screening/treatment strategy for disturbed glucose metabolism ( both before and after transplantation)
- Management of new-onset diabetes after transplantation ; Multidisciplinary management provide seamless care.
- The treatment of diabetes in dialysis patients is Challenging.

경청해주셔서 감사합니다.