POST TRANSPLANT DIABETES MELLITUS [PTDM]

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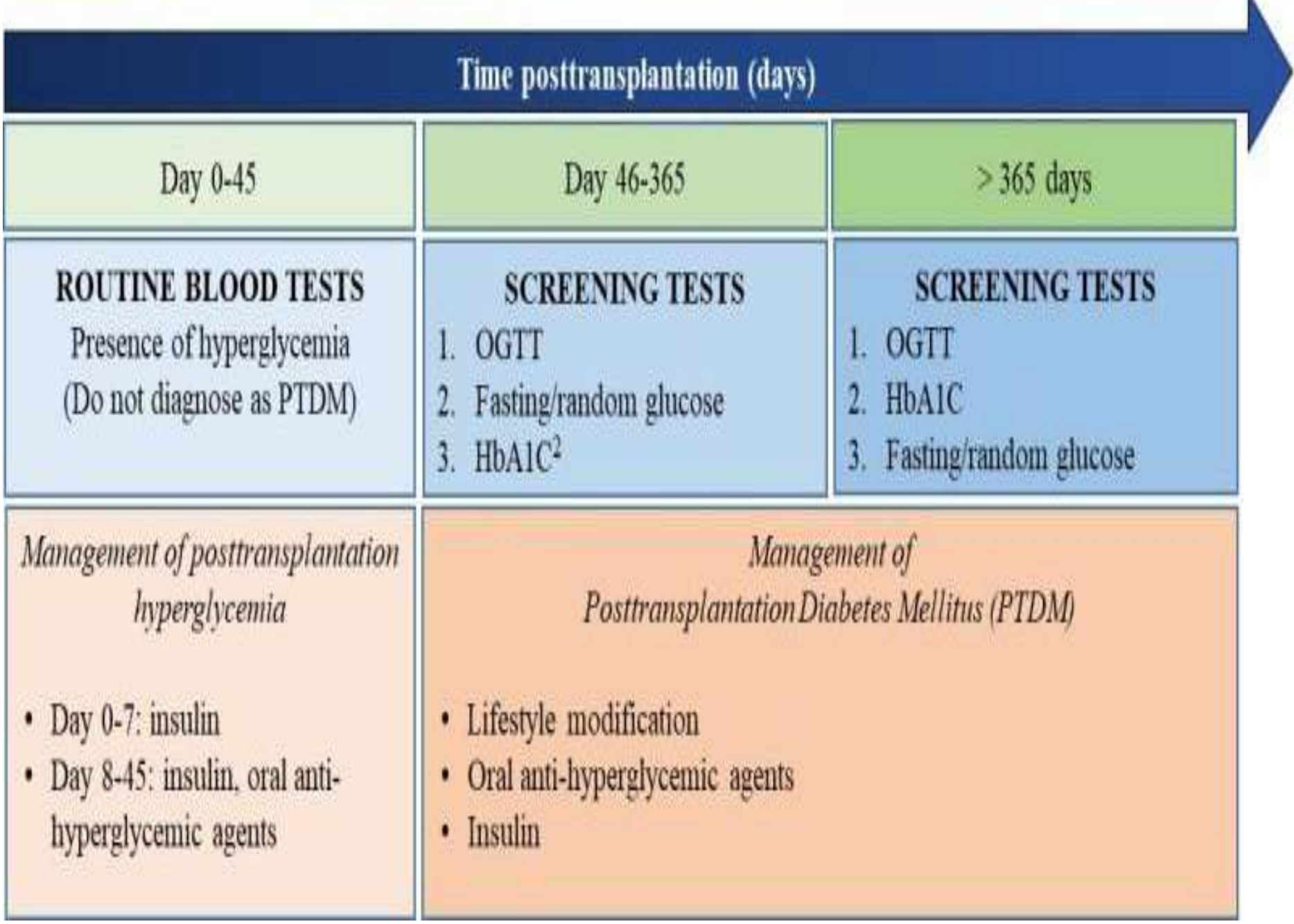
INTRODUCTION

- 15-20% of non diabetic kidney transplant recipients develop PTDM by 6 months.
- **PTDM -** Includes all post transplant diabetes first recognised after transplant regardless of prediabetic pre transplant, but excludes transient post-transplant hyperglycemia in 1st 6 week post transplant.
- HbA1c should **not** be used for **3 month** post Tx (False low HbA1c levels due to anaemia (erythropoietin treatment or blood cell transfusions).
- Fasting glucose has a low sensitivity for diagnosing PTDM.
- **OGTT** is considered **gold standard** for diagnosis of PTDM and for screening preTx (2024 international consensus).



Pham PT , Sindhu HS et al. PTDM after SOT 2019

Risk Factors

Non-modifiable	Potentially modifiable	Modifiable[4]	End-organ specific diagnosis
African American, Hispanic Age > 45 years Male recipient Family history of diabetes mellitus Human Leukocyte Antigen (HLA) mismatches HLA A30, B27, B42 Acute rejection history Deceased donor Male donor Genetic polymorphism (e.g. TCF7L2 rs7903146, PPAR-α rs4253728)	Hepatitis C virus[1] Cytomegalovirus[2] Pretransplant IGT/IFG Proteinuria Hypomagnesemia[3]	Obesity (body mass index ≥ 30) LDL cholesterol Steroids, tacrolimus, cyclosporine, sirolimus Vitamin D deficiency	End stage kidney disease due to polycystic kidney disease End stage liver disease due to HCV infection or non-alcoholic steatohepatitis (NASH) End stage lung disease due to cystic fibrosis

Pham PT , Sindhu HS et al. PTDM after SOT 2019

TRIALS/META ANALYSIS

- 2004 meta-analysis showed PTDM in 9.8% with tac vs CsA (DIRECT study).
- In ELITE study at one year higher rates of PTDM in low dose tacrolimus (8.4%) compared to std. dose of CSA(6%),low dose CSA (4.2 %) and low dose sirolimus.
- Recent meta-analysis of 56 randomized controlled trials demonstrated less PTDM and better overall graft survival with CNI minimisation stratergies using new agents such as belatacept or tofacitinib.

IMMUNOSUPPRESSANTS -PTDM

Cyclosporine vs tacrolimus

- Tacrolimus 2-3 times more diabetogenic.
- Marked beta cell toxicity , calcineurin inhibition, insulin hyposecretion.
- Trough level > 15 ng/ml first month high risk for PTDM.
- PTDM incidence with CNIs: **10–25%** in 36 months post-transplant.

Prednisone

- >10mg/day dose -- 1.8 fold increased risk (increases with further increase in dose).
- 5 percent per 0.01 mg/kg per day increase in prednisolone dose - PTDM risk increases.

ADJUSTING IMMUNOSUPRESSION

Steroids

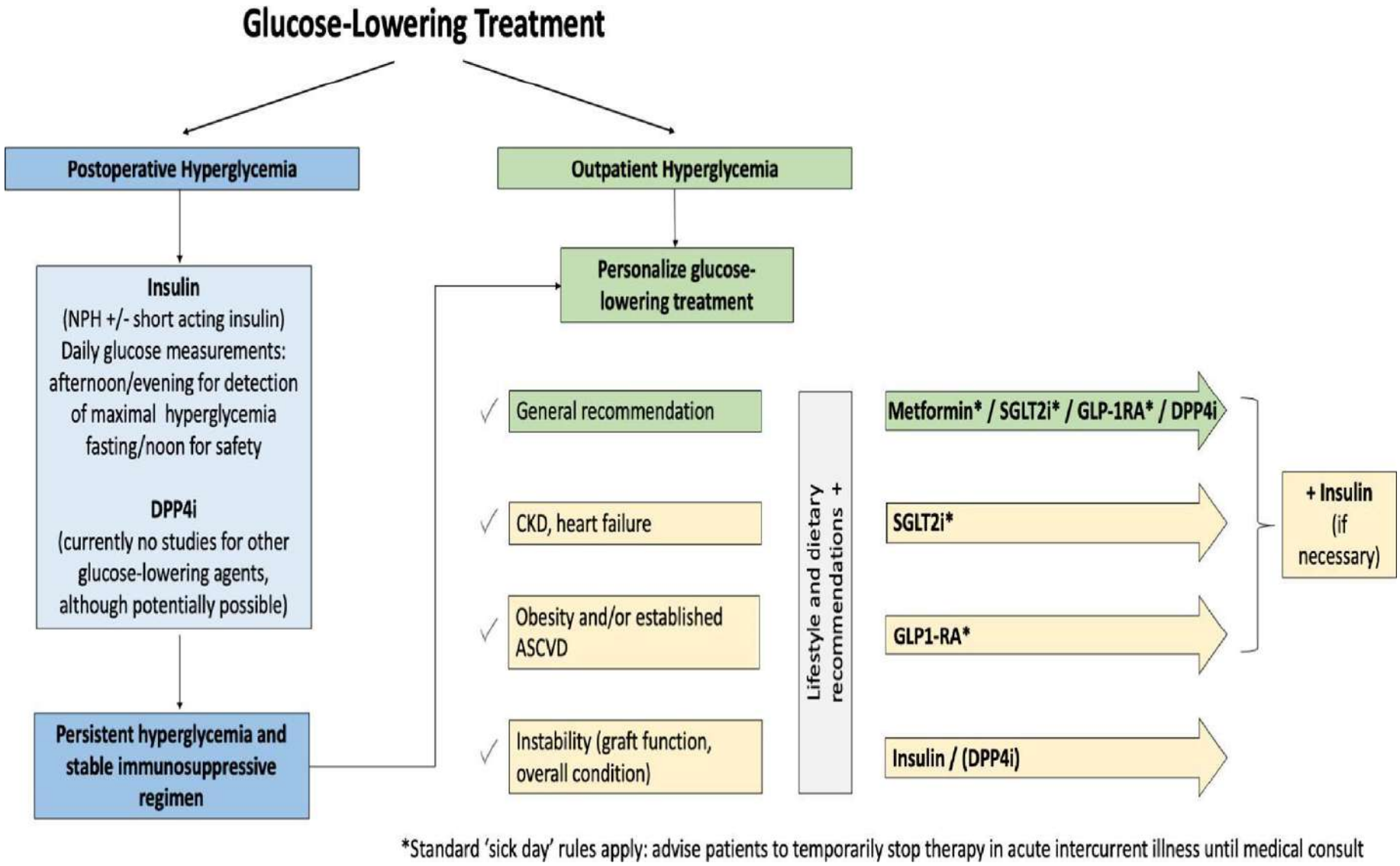
- Steroid minimisation as early as possible.
- Prednisolone dose reduction to 5 mg at one year (PTDM from 55 to 34%).
- Few study have found that there is no significant difference between 5mg prednisolone compared to complete steroid withdrawal at 5 years posttransplant (CSWD 22.5% vs. CCS 21.5%).
- No controlled data on the effect of late withdrawal of low dose steroids in patients with established PTDM.

- **CNI**

- Dose reduction without increasing risk for rejection.
- Change from tacro to Cyclosporin for PTDM is not recommended
- Effect of tacrolimus on glucose may be reversible even if agent is not discontinued
- Conversion to sirolimus may worsen insulin resistance, not recommended

Newer onset diabetes after transplantation , 2003 International consensus guidelines

Glucose-lowering treatment in KTRs: suggested algorithm



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