

Online-Only Appendix

1. Immunosuppression Schedule

The main immunosuppressive regimens consisted of calcineurin inhibitors (CsA or tacrolimus) and glucocorticoids. Calcineurin inhibitors were started 2 days before the transplantation. Initially the doses of CsA (10 mg/kg) and tacrolimus (0.3 mg/kg) were administered twice daily. The target trough levels of CsA and tacrolimus were as follows: 1) months 0–3: 150–300 ng/ml for CsA and 10–20 ng/ml for tacrolimus; 2) months 3–6: 150–200 ng/ml for CsA and 10–15 ng/ml for tacrolimus; and 3) 6 months: 75–150 ng/ml for CsA and 8–10 ng/ml for tacrolimus. Administration of oral prednisolone at 1 mg/kg/day began 2 days before the transplantation. Methylprednisolone was administered intravenously for the first 4 postoperative days in a tapered fashion: day 0, 1 g; day 1, 500 mg; day 2, 250 mg; and day 3, 60 mg. Administration of oral prednisolone began after the 4th posttransplantation day at 30 mg/day and was gradually tapered to 10 mg/day within 1 month. For acute rejection, a total of 2 g methylprednisolone was administered for 5 days. For the triple regimen, the target plasma trough levels of CsA and tacrolimus were lower than those for the double regimen: 75–100 ng/ml for CsA and 5–10 ng/ml for tacrolimus.

2. Patients enrollment

We initially recruited 805 unrelated transplant recipients for this study. Among them, 103 patients were excluded because they had a recorded fasting plasma glucose (FPG) level ≥ 5.5 mmol/L. Thirty patients had diabetes before transplantation, 35 patients had repeated renal allograft operation, and 13 patients were younger than 18 years. We were left with 624 patients.

3. Patients phenotyping

According to our previous study (15), cases of persistent PTDM (patients who developed diabetes within one year posttransplantation and remained diabetic) and late PTDM (L-PTDM; patients who developed diabetes after one year posttransplantation) were assigned to the PTDM group. Transient PTDM cases (T-PTDM; patients who developed diabetes within one year posttransplantation but eventually recovered to normoglycemia without medication) were classified as non-PTDM. Among 174 PTDM patients, 106 patients had L-PTDM. We classified L-PTDM patients with the PTDM group. There were 98 patients with T-PTDM and we classified these patients with the non-PTDM group.

4. Genetic effect on prevalence of L-PTDM and T-PTDM

There was no significant difference in the prevalence of L-PTDM among the PTDM group according to genotype ($p=0.723$). Also there was no significant difference in the prevalence of T-PTDM among the non-PTDM group according to genotype ($p=0.304$).

	RR	RW	WW	p
L-PTDM	41 (58.6%)	50 (61.0%)	15 (68.2%)	0.723
Total PTDM	70	82	22	

	RR	RW	WW	P
T-PTDM	32 (41.4%)	52 (39.0%)	14 (31.8%)	0.304
Non-PTDM	137	224	89	

4. Steroid Dose

We analyzed the dose of glucocorticoids at the time of development of PTDM. Prednisolone (Solondo®) and Deflazacort (Calcort®) were the main glucocorticoid regimens used in prevention of rejection. The usual dose of prednisolone was 10 mg/day and that of deflazacort was 12 mg/day, because prednisolone is known to be 1.2-1.5 times more potent than deflazacort, we converted the deflazacort dose to a corresponding prednisolone dose by multiplying by 0.8. We got the following results;

- 1) There was no significant difference in the cumulative dose of steroid according to genotype (RR 18,688 ± 1,936 mg, RW 17,849 ± 1,599 mg, WW 18,006 ± 3,300mg, p=0.943).
- 2) There was no significant difference in steroid dose (transformed dose) between the PTDM and non-PTDM groups (PTDM group; 9.55 ± 1.50 mg/day prednisolone vs. non-PTDM group; 9.57 ± 1.39 mg/day prednisolone, p=0.892).

4. Patient visiting schedule

(1) Follow-up frequency

- ① First month after discharge: 3 times/week
- ② 2nd month after discharge: 2 times/week
- ③ 3rd month after discharge: 1 time/week - every 10 days
- ④ 4th month after discharge: every 10-14 days
- ⑤ 5th month after discharge: every 3 weeks
- ⑥ 6th ~12 month after discharge: every month
- ⑦ After 1 year: every 1 - 2 months

(2) Follow up data collection

- ① Every visit: blood pressure, body weight, pulse rate, complete blood count, BUN/Creatinine, drug-level (cyclosporine or tacrolimus), serum electrolyte, urine

analysis, plasma glucose, lipid profiles (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride)

- ② Every 2-3 months: liver function test, HbA1c (if indicated)
- ③ Every 1 year: 24-hour urine collection for proteinuria and creatinine clearance, viral hepatitis study (HBV and HCV), bone densitometry, parathyroid hormone level (PTH), plasma insulin
- ④ Frequently performed: chest PA X-ray, cancer surveillance (AFP, CEA, etc)

References

1. Hur KY, Kim MS, Kim YS, Kang ES, Nam JH, Kim SH, Nam CM, Ahn CW, Cha BS, Kim SI, Lee HC: Risk factors associated with the onset and progression of posttransplantation diabetes in renal allograft recipients. *Diabetes Care* 30:609-615, 2007
- 2 Kang ES, Kim MS, Kim YS, Hur KY, Han SJ, Nam CM, Ahn CW, Cha BS, Kim SI, Lee HC. A Variant of the Transcription Factor 7-like 2 (TCF7L2) Gene and the Risk of Post-transplant Diabetes Mellitus (PTDM) in Renal Allograft Recipients. *Diabetes Care*. 2007 Oct 12; [Epub ahead of print]