

Information on Pre-transplant Calcimimetic Treatment Improves Prediction Accuracy of Tertiary Hyperparathyroidism after Kidney Transplantation

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Introduction

- Tertiary hyperparathyroidism (THPT) is characterized by hyperparathormonemia and hypercalcemia after successful kidney transplantation (KTx).
- We aimed to ascertain whether pre-transplant calcimimetic use and dose information improved THPT prediction accuracy.

Results

- Of the **554 KTx**, **139 (25.1%)** received pre-transplant-calcimimetics, and **87 (15.7%)** developed THPT.
- Pre-transplant calcimimetic information significantly improved the accuracy of the predicted probability of THPT (**the CNRI and IDI were 0.91 [95% CI: 0.70–1.13, P < 0.001], and 0.09 [95% CI: 0.05–0.13, P < 0.001], respectively**).
- The bootstrapped ROC AUCs for Models 1 and 2 were **0.91** and **0.94**, respectively.

Materials and methods

- Retrospective cohort study of 554 KTx between 2010-2022.
- Definition of THPT serum Ca ≥ 10.5 mg/dL and intact-PTH > 80 pg/mL
- The pre-transplant calcimimetic dose was categorized into four groups according to cinacalcet dose (mg/kg).
- Two THPT prediction models (with or without calcimimetic information) by Logistic regression.
- The continuous net reclassification improvement (CNRI) and integrated discrimination improvement (IDI) was calculated.

Conclusion

- Pre-transplant calcimimetic information improved the accuracy of the prediction of THPT.
- The THPT prediction model that included pretransplant calcimimetic information contributes to the prevention and early treatment of THPT in the era of calcimimetics.
- Future studies should perform external validations using new cohorts or cohorts from other institutions.

Patient characteristics before KTx

	Non-THPT N = 467	THPT N = 87	P-value
Recipient age (years, IQR)	50 (38–62)	53 (46–62)	0.060
Recipient sex (male, %)	304 (65.1)	48 (55.2)	0.089
Dialysis vintage (months, IQR)	16 (5–38)	112 (48–167)	<0.001
Parathyroid gland size (mm, IQR)	6.3 (4.7–8.4)	9.4 (7.1–11.6)	<0.001
Calcimimetics before KTx (%)	84 (18.0)	55 (63.2)	<0.001
Calcimimetic dose (mg/kg, IQR)	0.4 (0.3–0.5)	0.6 (0.4–1.0)	<0.001
Corrected calcium (mg/dL, IQR)	9.2 (8.9–9.7)	9.8 (9.3–10.3)	<0.001
Intact PTH (pg/mL, IQR)	145 (78–240)	203 (154–317)	<0.001

Calcimimetic dose was converted into cinacalcet dose.

Logistic regression THPT prediction models

Variable	Model 1		Model 2	
	RC	OR(95% CI)	RC	OR(95% CI)
(Intercept)	-6.26		-7.57	
Dialysis duration (months, reference to < 6)				
6–20	-0.07	0.94(0.28–3.13)	-0.19	0.83(0.87–3.05)
21–53	0.11	1.11(0.36–3.41)	-0.52	0.59(0.17–2.13)
54–	2.40	11.0(4.12–29.6)	1.84	6.27(2.10–18.7)
Serum Ca (mg/dL, reference to < 8.9)				
8.9–9.2	-0.42	0.66(0.21–2.06)	0.23	1.26(0.33–4.80)
9.3–9.7	1.07	2.91(1.11–7.58)	1.43	4.18(1.38–12.6)
9.8–	1.82	6.20(2.33–16.5)	2.70	15.0(4.72–47.4)
Intact PTH (pg/mL, reference to < 85.0)				
85.0–157.0	1.55	4.71(1.51–14.7)	2.27	9.69(2.65–35.40)
158.0–247.0	2.70	14.9(4.80–46.5)	2.85	17.4(5.00–60.20)
248.0–	2.63	13.8(4.44–43.2)	3.17	23.8(6.73–83.90)
Parathyroid gland size (mm, reference to 0)				
0.1–5.7	0.83	2.29(0.86–6.08)	0.30	1.35(0.46–3.97)
5.8–8.8	1.45	4.27(1.74–10.5)	1.28	3.61(1.37–9.50)
8.9–	2.54	12.6(5.31–30.0)	2.33	10.2(3.65–28.8)
Calcimimetic dose (mg/kg, reference to 0)				
0.1–0.2	NA	NA	1.88	6.54(2.04–21.0)
0.3–0.4	NA	NA	2.23	9.32(3.02–28.8)
0.5–	NA	NA	2.95	19.1(6.55–55.7)

RC, regression coefficient.

The parathyroid gland size was defined as 0 when parathyroid gland was not detected by echography.

Calcimimetic dose was converted into cinacalcet dose and is only adopted as a predictive factor in Model 2.

Linear predictor(LP)=intercept+RC(dialysis duration)+...+RC (Calcimimetic dose)

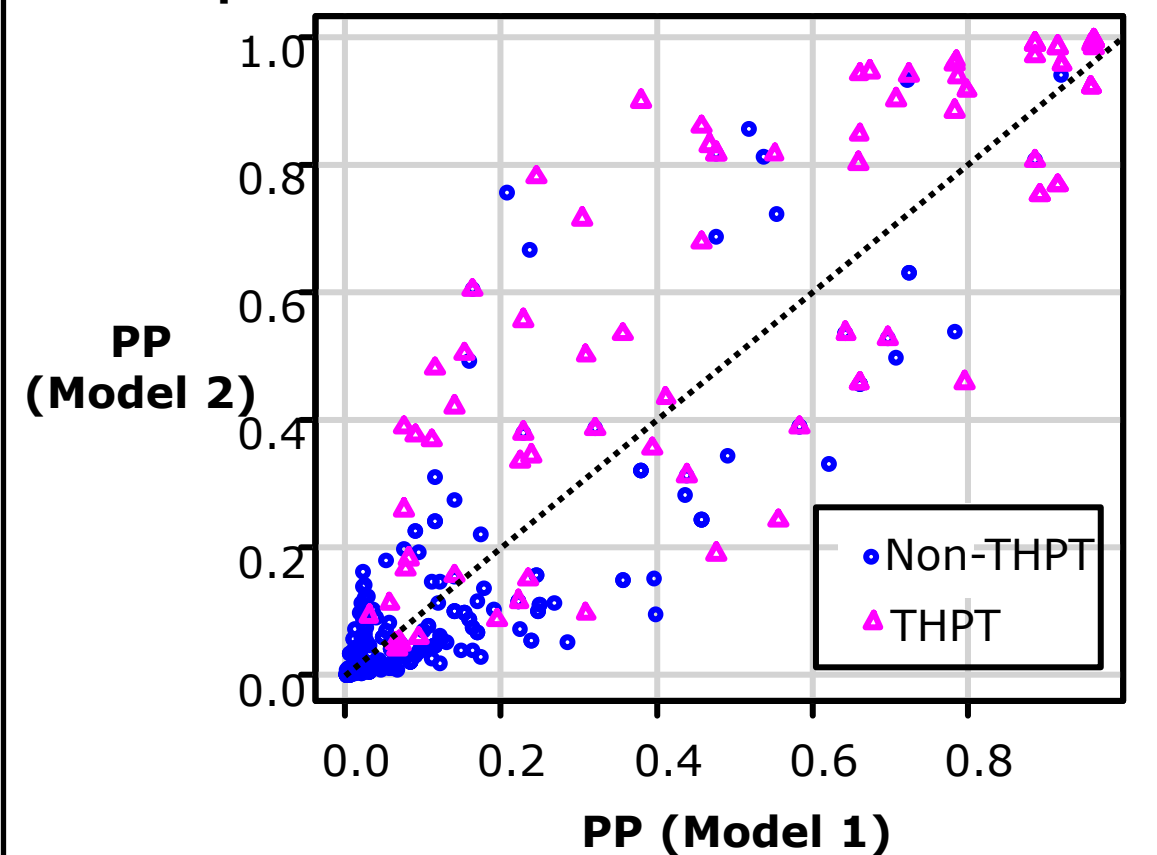
Predictive probability(PP)=exp(LP)/(1+exp(LP))

Internal validation by bootstrap for THPT prediction models

	Model 1	Model 2
ROC AUC obtained through bootstrap 1000 resampling	0.91	0.94
Slope (BOC)	0.11	0.16
Mean absolute error	0.03	0.03
0.9 Quantile of absolute error	0.06	0.08

BOC, bootstrap optimism corrected; ROC AUC, receiver operating characteristic area under the curve.

Scatter plots of the PPs of Model 1 and Model 2



CNRI: 0.91 [95% CI: 0.70–1.13, P < 0.001]
IDI: 0.09 [95% CI: 0.05–0.13, P < 0.001]
 The circles below the black dashed line or the triangles above it indicate that the THPT predictions have improved in Model 2 compared with Model 1.

ROC curves for the prediction of THPT from Model 1 and Model 2

