



# Restoration of HPA axis is rapid in subclinical Cushing's syndrome after adrenalectomy

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## INTRODUCTION

- Subclinical Cushing's syndrome (SC) is a status of cortisol excess defined by dynamic hormonal tests in patients with adrenal incidentaloma who have no overt syndrome of Cushing's syndrome.
- SC is assumed that cortisol production is insufficient to cause a clinically recognizable syndrome and to suppress the release of CRH and ACTH.
- Differences in hormonal levels or recovery time of the hypothalamic-pituitary-adrenocortical (HPA) axis after adrenalectomy between patients with overt Cushing's syndrome (OC) and SC remain unknown.

## METHOD

- Thirty-six patients (10 with OC and 26 with SC) with adrenal Cushing's syndrome who underwent adrenalectomy from 2004 to 2014 were reviewed retrospectively.
- Patients were treated with glucocorticoid after adrenalectomy and were reevaluated at discharge and every 1 months thereafter using a morning cortisol or rapid ACTH stimulation test.

## RESULTS

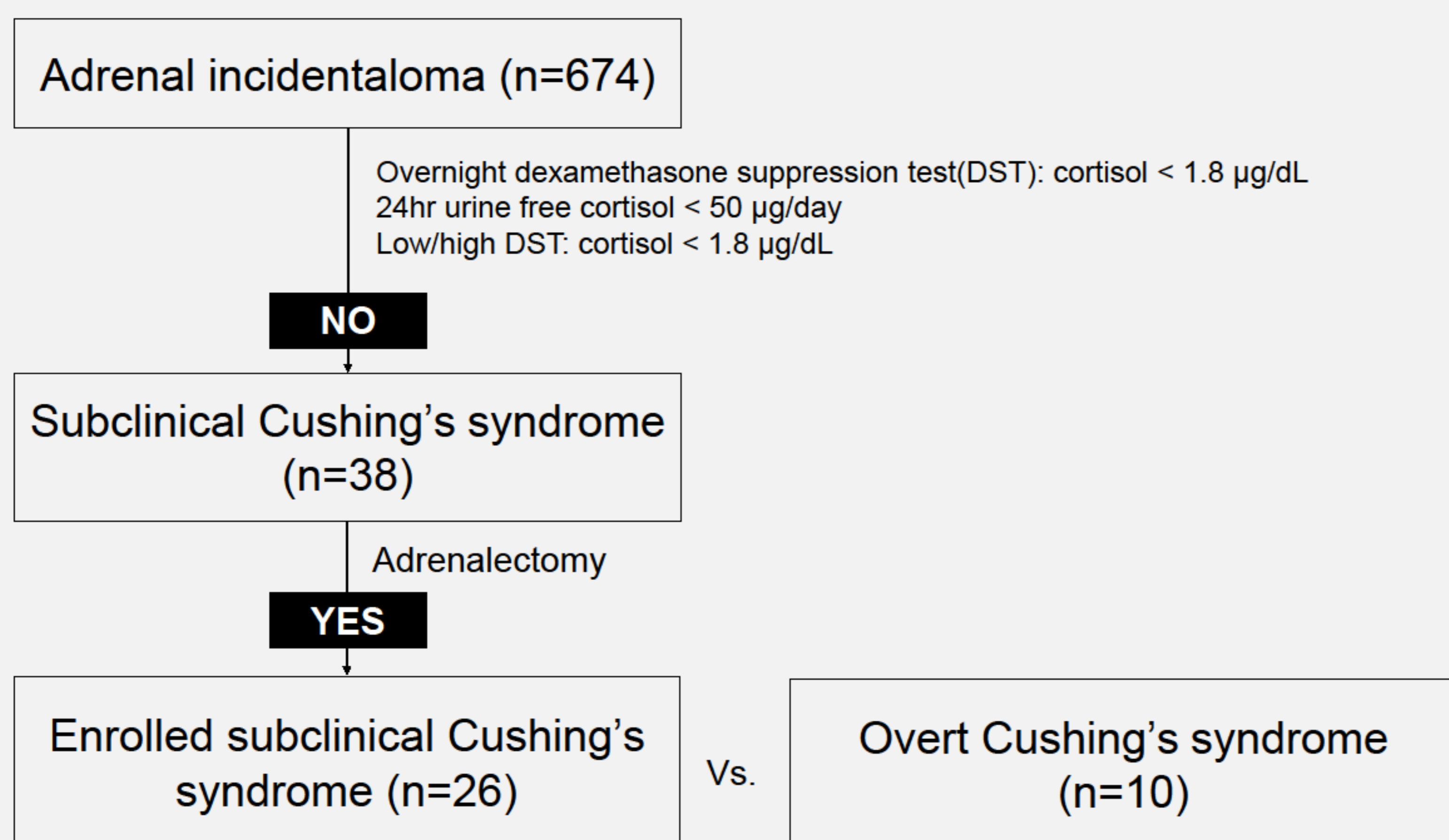


Figure 1. Study design.

Table 2. Relationship between recovery time and preoperative cortisol levels

	Recovery time (months)	Basal UFC (µg/day)	P-cortisol after ODST (µg/dL)
Median (range)	5 (0-30)	74.0 (26-1450.0)	7.4 (2.1-24.1)
$\rho^\ddagger$		0.485*	0.645**
$R^{2\ddagger}$		0.197*	0.465**

	UFC after LDST (µg/day)	P-cortisol after LDST (µg/dL)	UFC after HDST (µg/day)	P-cortisol after HDST (µg/dL)
Median (range)	48.3 (5.0-830.0)	11.1 (2.7-29.7)	57.0 (9.0-963.0)	10.3 (2.2-39.1)
$\rho^\ddagger$	0.729**	0.688**	0.697**	0.606**
$R^{2\ddagger}$	0.598**	0.472**	0.495**	0.303*

UFC, 24-h urine free cortisol; P-cortisol, plasma cortisol; ODST, 1 mg overnight dexamethasone suppression test; LDST, 4 mg low-dose dexamethasone suppression test; HDST, 16 mg high-dose dexamethasone suppression test

\*  $p < 0.05$

\*\*  $p < 0.001$

$\rho$  (Spearman's rho) represents the correlation coefficient between recovery time and the clinical parameters of cortisol excretion

$\ddagger R^2$  was calculated by linear regression analysis

Table 1. Baseline characteristics of patients with subclinical and overt Cushing's syndrome

	Overt (N=10)	Subclinical (N=26)	p value
Age (years)	47.3±12.3	56.0±9.3	0.028
Gender (Female, %)	9 (90.0)	19 (73.1)	0.274
BMI, kg/m <sup>2</sup>	23.7±3.2	24.6±3.9	0.391
Hypertension (%)	7 (70.0)	11 (42.3)	0.137
Diabetes mellitus (%)	5 (50.0)	7 (26.9)	0.188
Obesity (%)*	6 (60.0)	17 (65.4)	0.763
Tumor size (cm)	2.7±0.7	2.4±0.9	0.348
Tumor location (Right, %)	2 (20.0)	7 (26.9)	0.667
ACTH, pg/mL	11.7±6.0	24.3±16.1	0.023
Basal UFC, µg/day	520.1±432.0	71.9±33.1	0.010
Cortisol after ODST, µg/dL	18.1±6.0	7.8±5.9	0.001
UFC after LDST, µg/day	472.8±208.4	56.8±77.7	<0.001
Cortisol after LDST, µg/dL	22.2±6.2	8.7±6.1	<0.001
UFC after HDST, µg/day	487.8±284.2	74.1±113.5	0.001
Cortisol after HDST, µg/dL	21.1±5.8	10.2±9.0	0.001
DHEA-S, µg/dL	20.3±14.1	43.5±71.7	0.490
Recovery time (median, range, months)	17.0 (5-30)	4.0 (0-14)	<0.001

BMI, body mass index; UFC, 24-h urine free cortisol; ODST, overnight dexamethasone suppression test; LDST, low-dose dexamethasone suppression test; HDST, high-dose dexamethasone suppression test

\* Description of the criteria for obesity

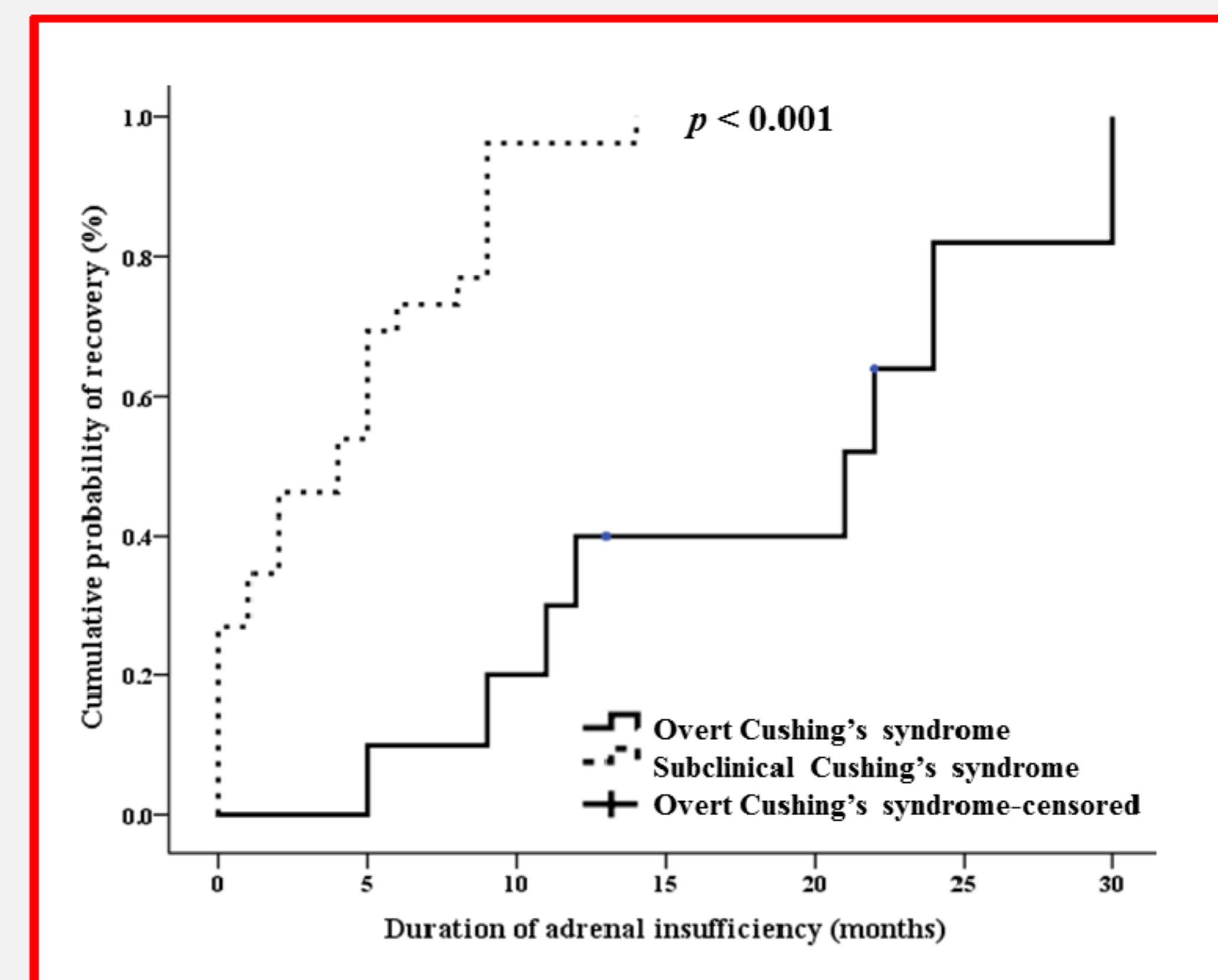


Figure 2. Cumulative probability of adrenal function recovery in patients with overt and subclinical Cushing's syndrome

## CONCLUSION

- The degree of cortisol excess differs between the two disease categories, and the time to adrenal function recovery was associated with the degree of cortisol excess.
- The HPA axis recovery time after adrenalectomy in patients with SC is rapid (within several months) and is dependent on the degree of cortisol excess.
- Routine postoperative glucocorticoid replacement is not necessary in some patients with SC.

