

# Remission, recurrence and control rates in patients with ACTH-dependent Cushing's syndrome-a monocentric, retrospective analysis

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## Introduction

Transsphenoidal surgery is the gold standard in Cushing's disease and leads to remission in 60-95% of patients. Recurrence is a major risk depending on tumor size, tumor invasiveness and surgical experience. We wondered which impact remission and recurrence might have on control rates of hypercortisolism. We conducted a systematic analysis of our cohort of patients with Cushing's syndrome (CS) after undergoing surgical therapy to evaluate both the time of remission, and the time until recurrence.

## Methods

We analysed the course of the disease in 74 patients with ACTH-dependent Cushing's syndrome (63: Cushing's disease (CD); 11 ectopic Cushing's syndrome (ECS)). All patients underwent surgery as first line therapy and in cases where relapse occurred, each received further surgery, radiotherapy, adrenostatic therapy or bilateral adrenalectomy. The outcomes of interest were biochemical remission/control of hypercortisolism, clinical remission and recurrence, with evaluations conducted 10 d, 1, 2, 3, 6 and 12 months after first surgery and then annually after, and a follow-up time of 8 to 474 months.

Clinical remission was defined by the absence of Cushing stigmata, or in the case of missing stigmata when first diagnosed, the cessation of symptoms. Biochemical remission/control was defined as normal urinary free cortisol levels, normal salivary cortisol levels at midnight and/or cortisol <1,8 µg/dl after 1 mg overnight dexamethasone suppression test. Patients receiving glucocorticoid replacement were classified as controlled. Data was extracted from the medical records of patients and analysis conducted using the Kaplan-Meier method.

## Results

The outcome after surgery is shown in Fig. 1. In patients with CD the biochemical control rates at 1, 2 and 3 years were 77, 81, and 77%. The corresponding clinical response rates were 45% at 1 year and 70% at 2 and 3 years. In contrast, patients with ECS showed considerably higher biochemical remission rates with 100% at 1, 2 and 3 years. 16 years after surgery the rates of patients in biochemical and clinical remission converged. The cumulative recurrence free remission rate in CD was 71% at 1 and 2, and 54% at 5 years (Fig. 2).

In patients having second transsphenoidal surgery the remission rate was poor with 50% at 1 and 2 years, and 40% at 5 years (Fig. 3).

	CD	ectopic
n	63	11
Remission after first treatment n	46 (73%)	10 (90.9%)
Persistent disease after first treatment n	17 (27%)	1 (9.1%)
Further treatment in persistent disease n	17 (27%)	1 (9.1%)
Second TSS n	8 (12.7%)	
Remission after second TSS n	3 (0.38%)	
BADX n	11	1
Medication n	3	
Adjuvant pituitary radiotherapy n	5	
Development of recurrence n (after initial remission)	9 (14.3%)	1 (9.1%)
Median time to recurrence (years)	6 (1-16)	5
Biochemical remission at final follow up n	59 (93.7%)	11 (100%)

Fig.1: Outcome

## Conclusion

Patients with CS of ectopic origin present better long-term remission rates than patients with CD. In CD the outcome of patients in remission after initial surgery is associated with higher remission rates in the long-term, while the absence of remission after first TSS or the occurrence of early relapse are related to a noticeably poorer outcome.

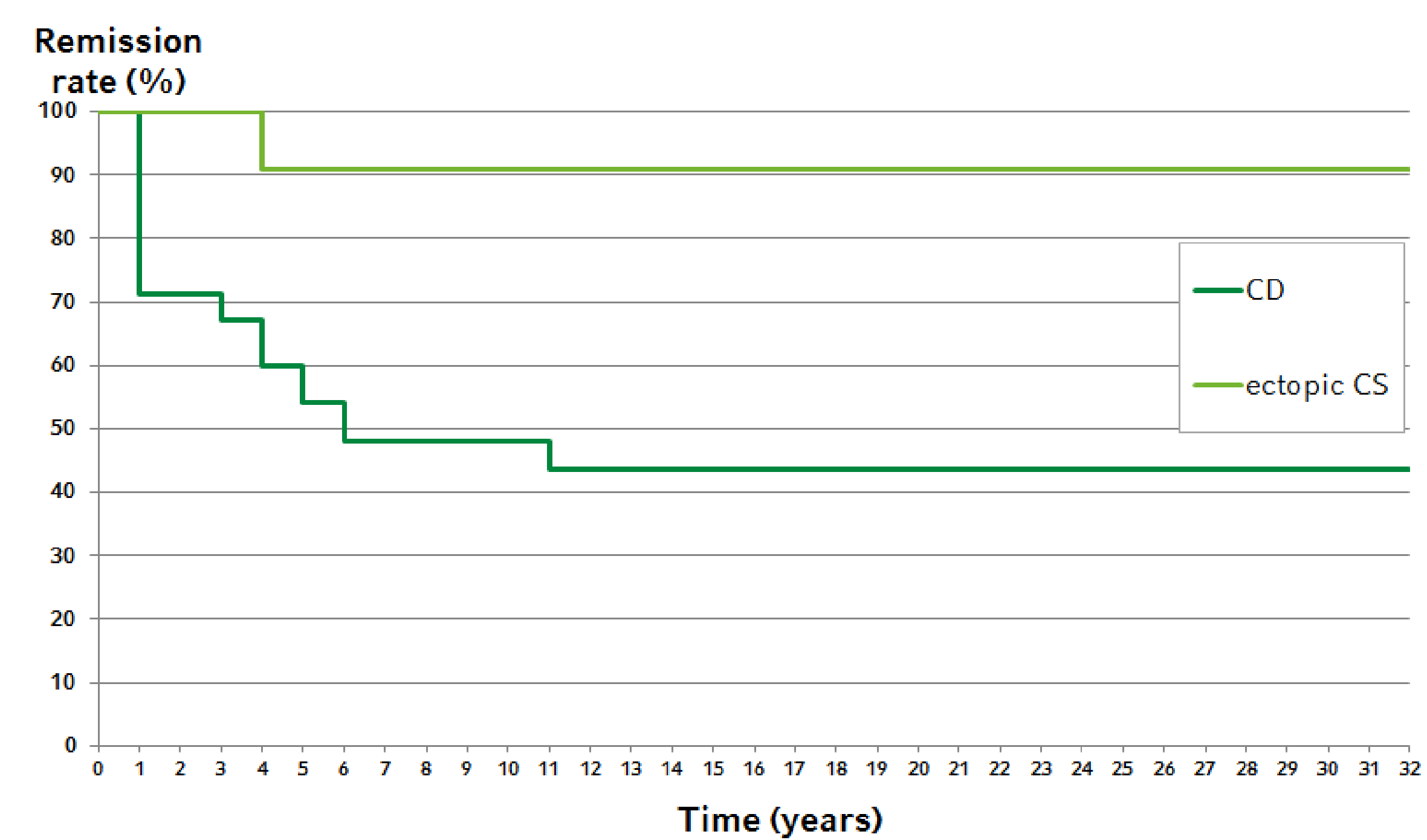


Fig.2: Cumulative rate of remission after first surgery

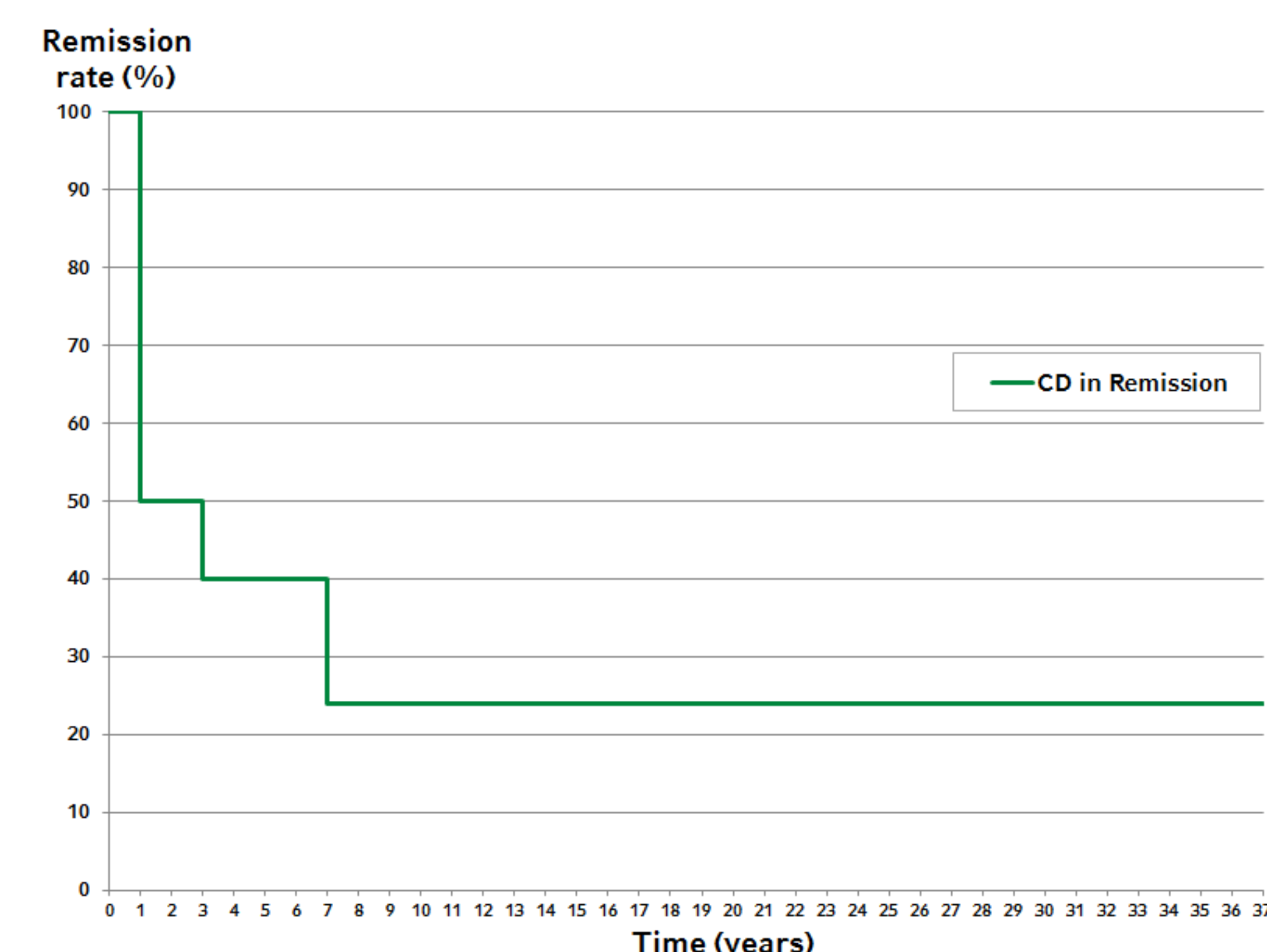


Fig.3: Cumulative rate of remission after second TSS