

# Dynamics of ACTH after Stimulation with Metyrapone

## DYNAMO

Noe S.<sup>1</sup>, von Werder A.<sup>1</sup>, Baehr M.<sup>1</sup>, Jakoubov R.<sup>1</sup>, Schneider H.<sup>2</sup>, Thaler M.<sup>2</sup>, Lupp P.<sup>2</sup>, Neu B.<sup>1</sup>

<sup>1</sup> Klinikum rechts der Isar, TU München, II. Medizinische Klinik und Poliklinik

<sup>2</sup> Klinikum rechts der Isar, TU München, Institut für Klinische Chemie und Pathobiochemie

## Background

Metyrapone test was developed on the assumption that ACTH does not rise and might paradoxically even fall in the early phase after application. This is contradictory to other stimulation tests of ACTH reserve. We therefore re-investigated the dynamics of ACTH following oral Metyrapone application.

## Methods

Patients from a tertiary endocrine center at a University Hospital in Munich, Germany, were tested using Metyrapone (Metopirone®, HRA Pharma, France), administered at a dose of 40 mg/kg bodyweight at 8 a.m. Levels of ACTH were determined at 0, 60, 120, 180, and 240 minutes. Patients were categorized according to their need of glucocorticoid substitution at the end of follow-up. The study was approved by the local Ethics Committee with a limitation to 25 patients.

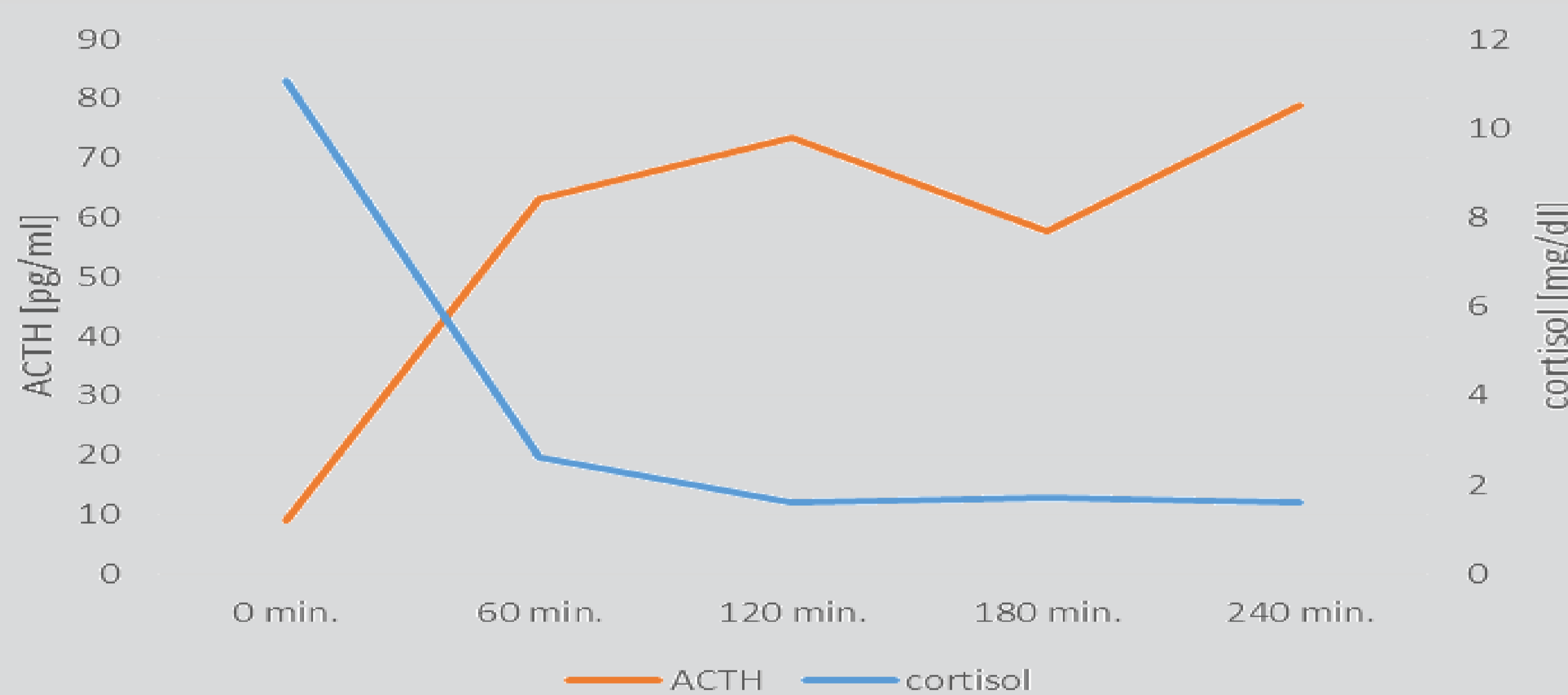


Figure 1: The course of ACTH and cortisol after Metyrapone application in the whole population.

## Results

Of 25 patients, 15 (60%) were female. Median age was 54 years (range 21 – 79). ACTH (median (IQR)) was 9.1 (5.9-15.5) pg/ml before stimulation and 63.0 (12.2-185.3), 73.5 (27.0-122.7), 57.6 (27.9-146.9), and 78.9 (27.5-162.1) pg/ml at 60, 120, 180, and 240 minutes, respectively. There was a (median) 4 fold and a 6 fold rise in ACTH compared to the basal level at 60 and 120 minutes, respectively.

Analyzing groups as categorized by the need of glucocorticoid substitution during the course of clinical follow up ( $\pm 13.6$  months; range 0 – 39 months), there were significant differences in ACTH concentrations between non-insufficient and sufficient subjects at 60 minutes (141.7 vs. 16.6 pg/ml;  $p < 0.001$ ) and at 120 minutes (108.6 vs. 22.3 pg/ml;  $p < 0.001$ ). Using ROC analysis on substitution status with ACTH at 60 min, and ACTH at 120 minutes, AUCs of 0.83 ( $p = 0.007$ ) and 0.93 ( $p = 0.001$ ) were achieved, respectively. Best factor in logistic regression to predict need for substitution was ACTH concentration at 120 minutes ( $p = 0.013$ , Coef. 0.05 [0.01-0.10]).

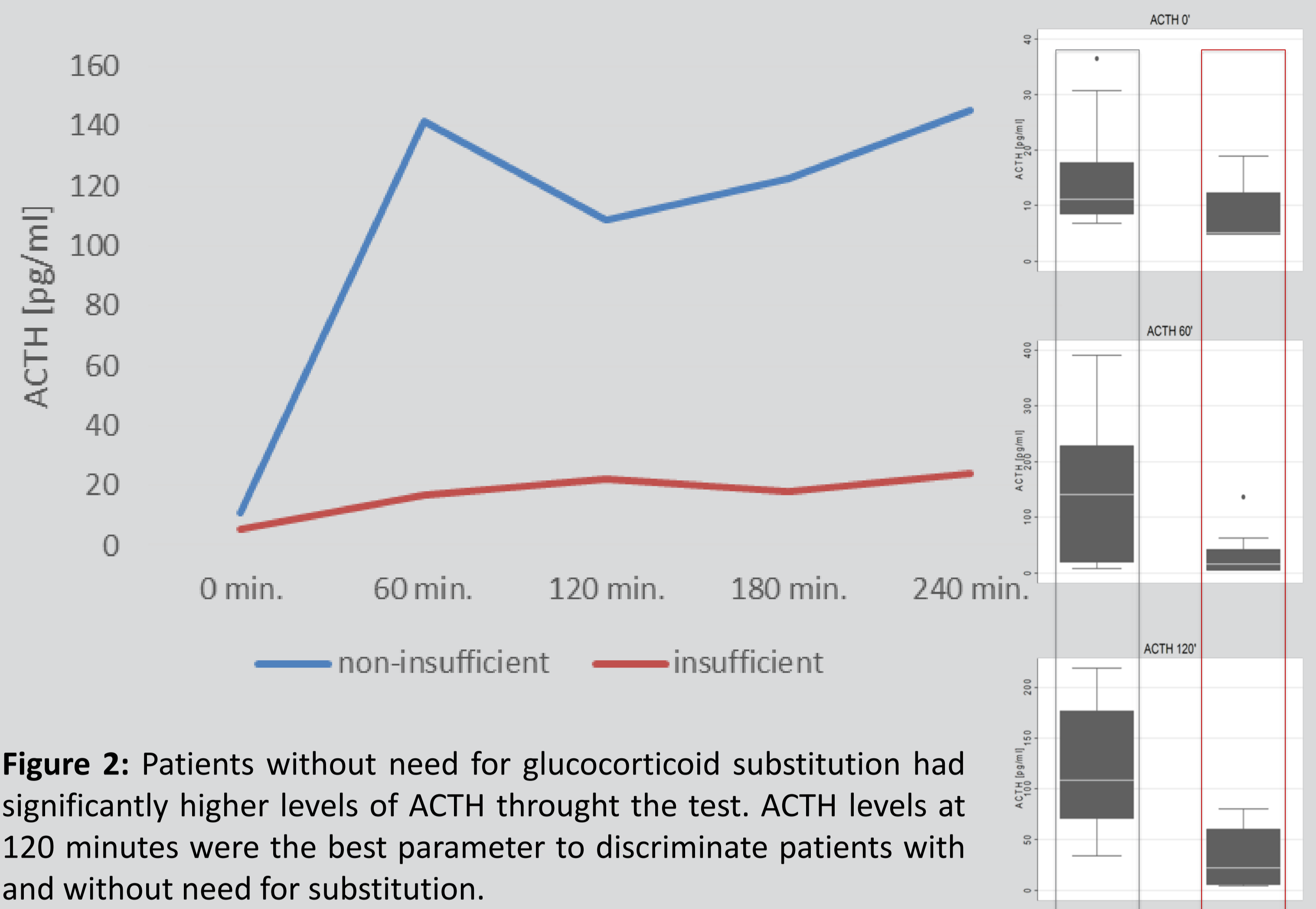


Figure 2: Patients without need for glucocorticoid substitution had significantly higher levels of ACTH throughout the test. ACTH levels at 120 minutes were the best parameter to discriminate patients with and without need for substitution.

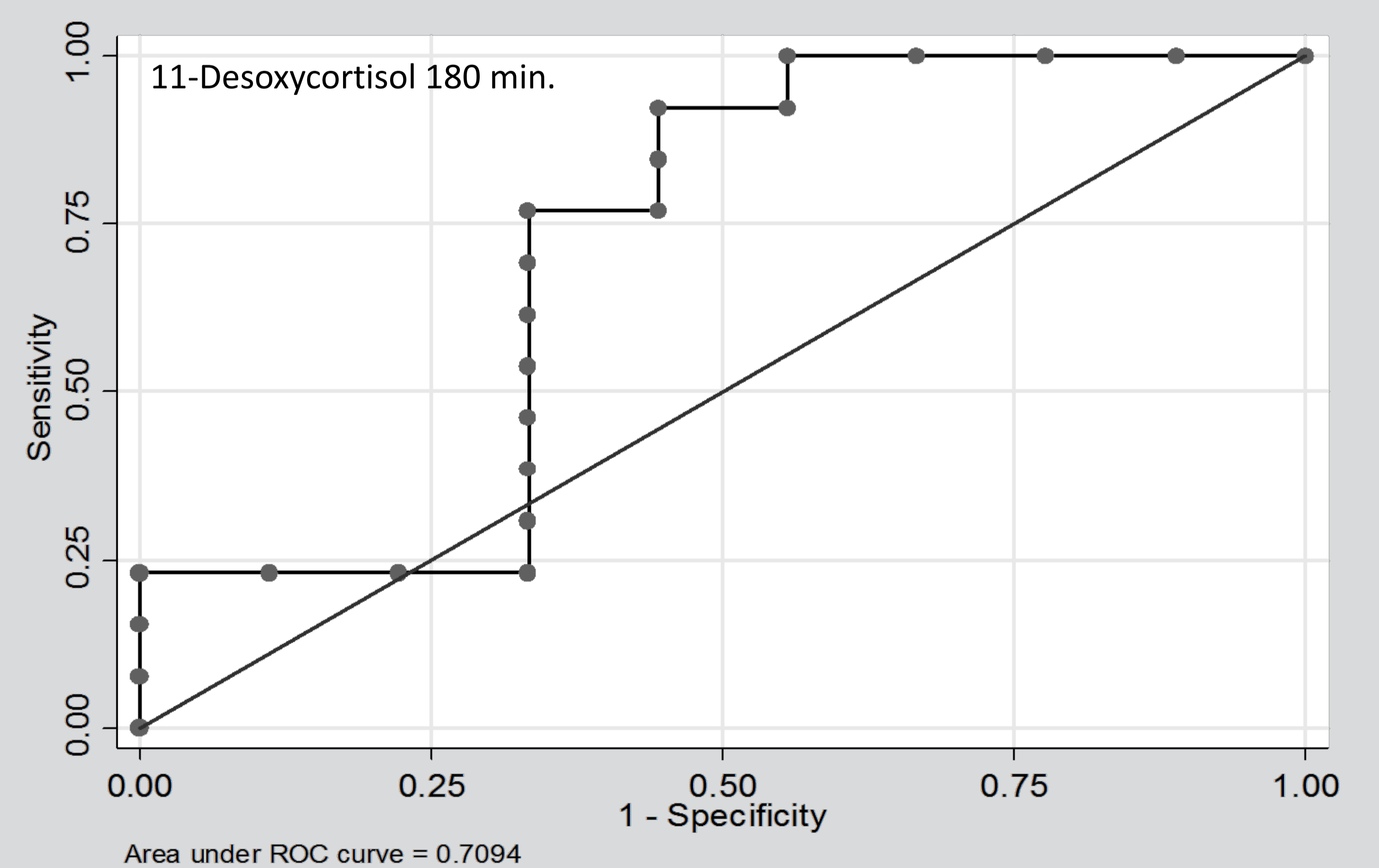
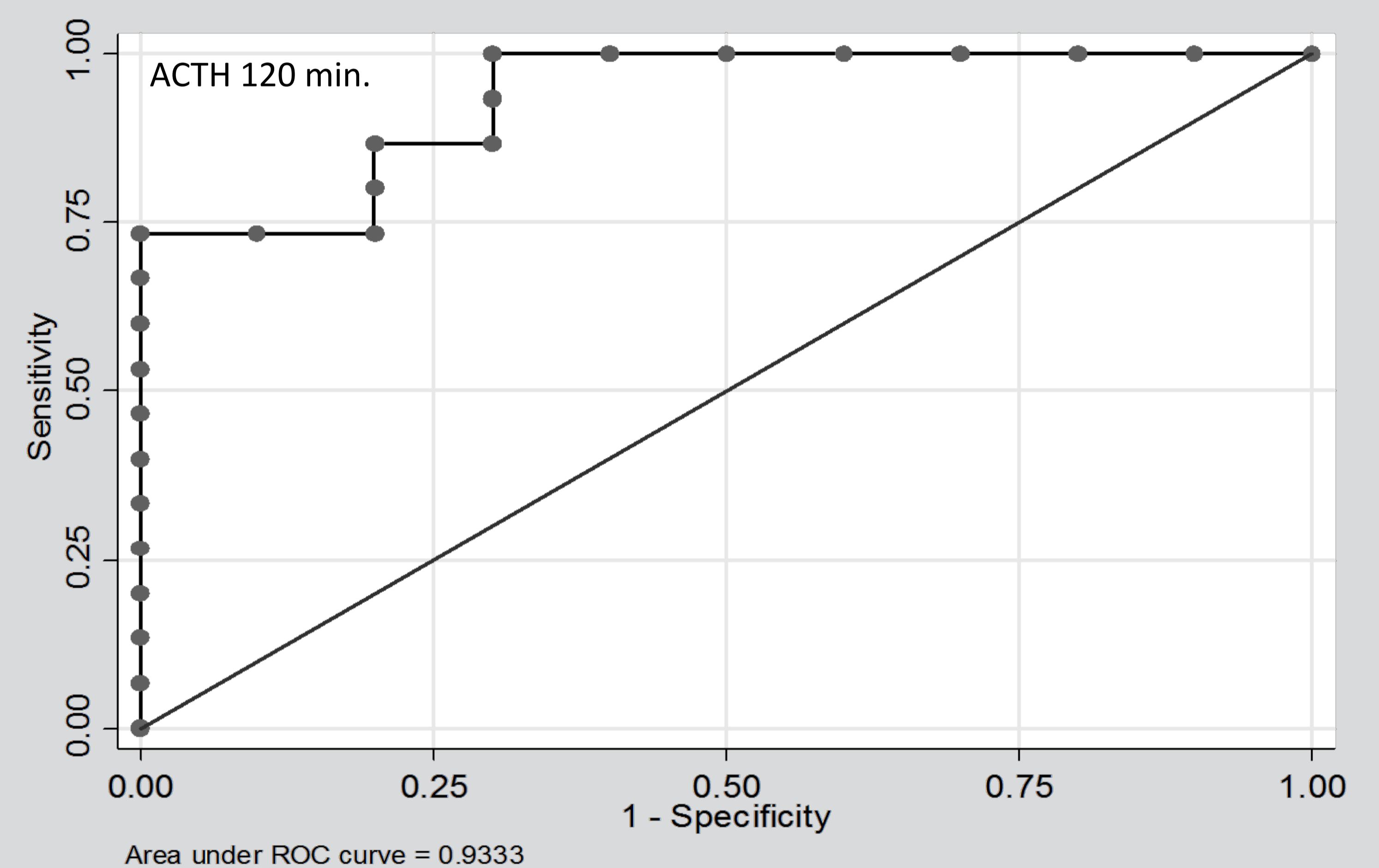


Figure 3: ROC analysis of ACTH concentration at 120 minutes as well as 11-Desoxycortisol concentrations at 180 minutes showed higher negative predictive value of high ACTH levels at 120 minutes.

## Conclusion

In contrast to previous reports, we found a significant rise in ACTH concentration as soon as one hour after oral Metyrapone administration. Early ACTH values seem to estimate the pituitary corticotrophic function.