

# Serum 17-hydroxyprogesterone is a potential biomarker for evaluating intratesticular testosterone (MP78-02).



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### Introduction

- Intratesticular testosterone (ITT) is essential for spermatogenesis and can only be reliably measured with invasive testicular sampling.
- At present, there is no serum biomarker for ITT and as such, serum testosterone, which is highly variable, is often used as a surrogate.
- Amory et al previously demonstrated good correlation between ITT and 17-OHP in men treated with human chorionic gonadotropin (hCG).
- Serum 17-hydroxyprogesterone (17-OHP) is an intermediate in the production of testosterone (T) from cholesterol through the steroid biosynthesis pathway.

### Aims

- 1) To evaluate effects of exogenous testosterone (TRT) or hCG and clomiphene citrate (CC) on 17-OHP levels.
- 2) To compare baseline and follow-up 17-OHP values in men receiving medications that alter ITT levels with fertile men (controls).

### Method

- We performed a 2-stage study to evaluate 17-OHP and T levels in men presenting to our clinic between July 2018 – November 2019.
- First, on the cross-sectional analysis, we included men seen in clinic and had 17-OHP and testosterone levels recorded between July 2018 - March 2019.
- We compared men receiving TRT or hCG/CC to fertile men (T > 300 ng/dL).
- We then prospectively followed men between July 2018 - November 2019 and compared pre- and post-treatment values of T and 17-OHP in the men that received hCG/CC or TRT with fertile controls.
- All patients went through full clinical evaluation, including measurement of testicular size with Prader orchidometer at baseline and follow-up. For all men, blood was drawn at the same lab from 6:00 am – 10:00 am.
- Exclusion criteria: receive therapies that alter ITT during the baseline, lose follow-up or change therapy before follow-up evaluation.
- Comparison of numerical variables between groups was performed using the Kruskal-Wallis, ANOVA, U Mann-Whitney, or Wilcoxon rank test as required.

### Results

- Cross-Sectional analysis: 30 men received hCG/CC, 21 men TRT and 42 men were used as control. All men showed normal range (300 – 1000ng/dL) levels of T, but serum 17-OHP was found to be lower in the men that received TRT. (Figure 1)

### Results

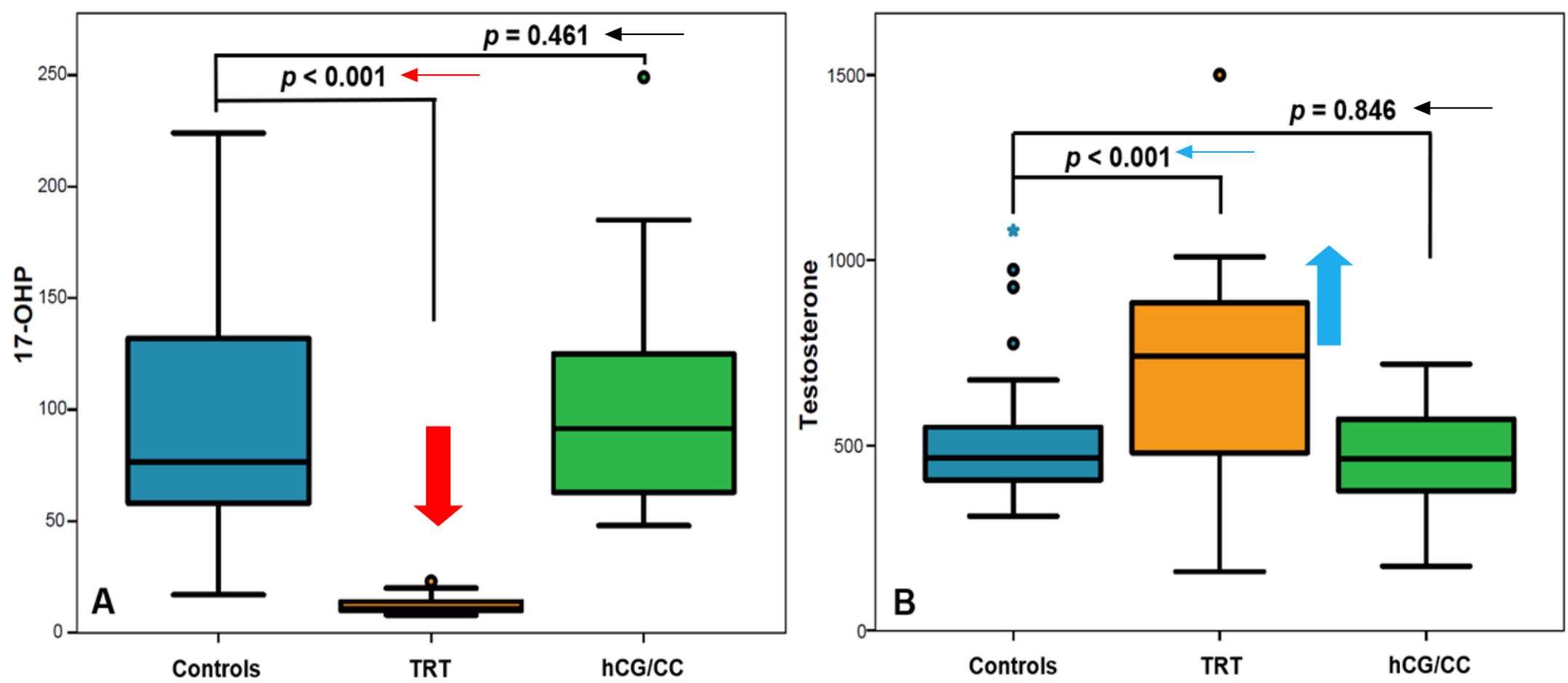


Figure 1: Cross-sectional analysis of serum 17-OHP and T in 93 men.

- Power Calculation: sample of size n=20 patients with hypogonadism will ensure that a two-sided test with  $\alpha = 0.05$  has 80% power to detect a difference in 17-OHP level before and after treatment.
- Prospective analysis: 140 men were analyzed. Clinical and demographics characteristics in Table 1. Median follow-up visit occurred within 105 [91 – 133] days for men receiving hCG/CC and 139 [92 – 204] for those receiving TRT.
- Men that received TRT had a reduction of 17-OHP from 47.5 [21 – 70] ng/dL to 13.5 [10 – 23] ng/dL ( $p < 0.001$ ), while those treated with hCG/CC presented with an increase from 42 [24 – 72] ng/dL to 88 [61 – 135] ng/dL ( $p < 0.001$ ). (Figure 2)
- Men receiving TRT had lower 17-OHP levels than fertile controls ( $p < 0.001$ ), whereas those receiving hCG/CC had similar serum levels ( $p = 0.705$ ). (Figure 2)
- All groups had comparable levels of T in the follow-up ( $p > 0.05$ ). (Figure 3)

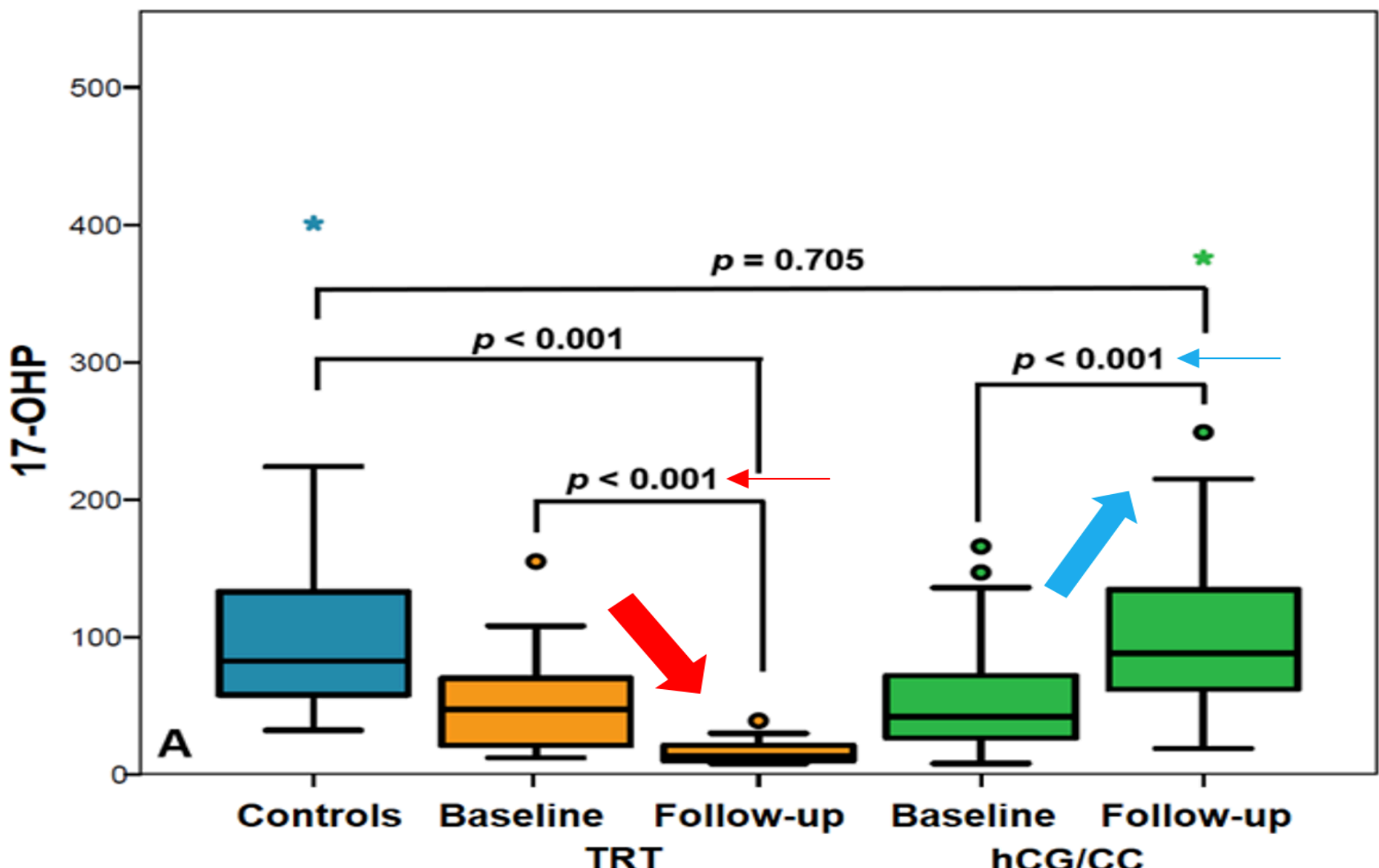


Figure 2: Prospective Cohort of 140 men. Changes in 17-OHP between Baseline and follow-up.

Table 1. Clinical and demographic characteristics of the analyzed men.

Variables	Control n = 64	TRT n = 22	hCG/CC n = 55	p-value
Age in years	37.2 ± 12.8	47.14 ± 12.3	40 ± 8.7	0.002
BMI (kg/m <sup>2</sup> )	25.5 [23.2 – 29]	32.3 [27.9 – 34.8]	28.5 [26 – 32.9]	< 0.001
Test abuse (%)	1 (1.6%)	10 (45.5%)	14 (25.5%)	< 0.001
Mean testicular Volume (cc)	15 ± 3.1	12.6 ± 3.1	13.9 ± 3.9	0.034

Mean ± SD, median [IQR 25-75]

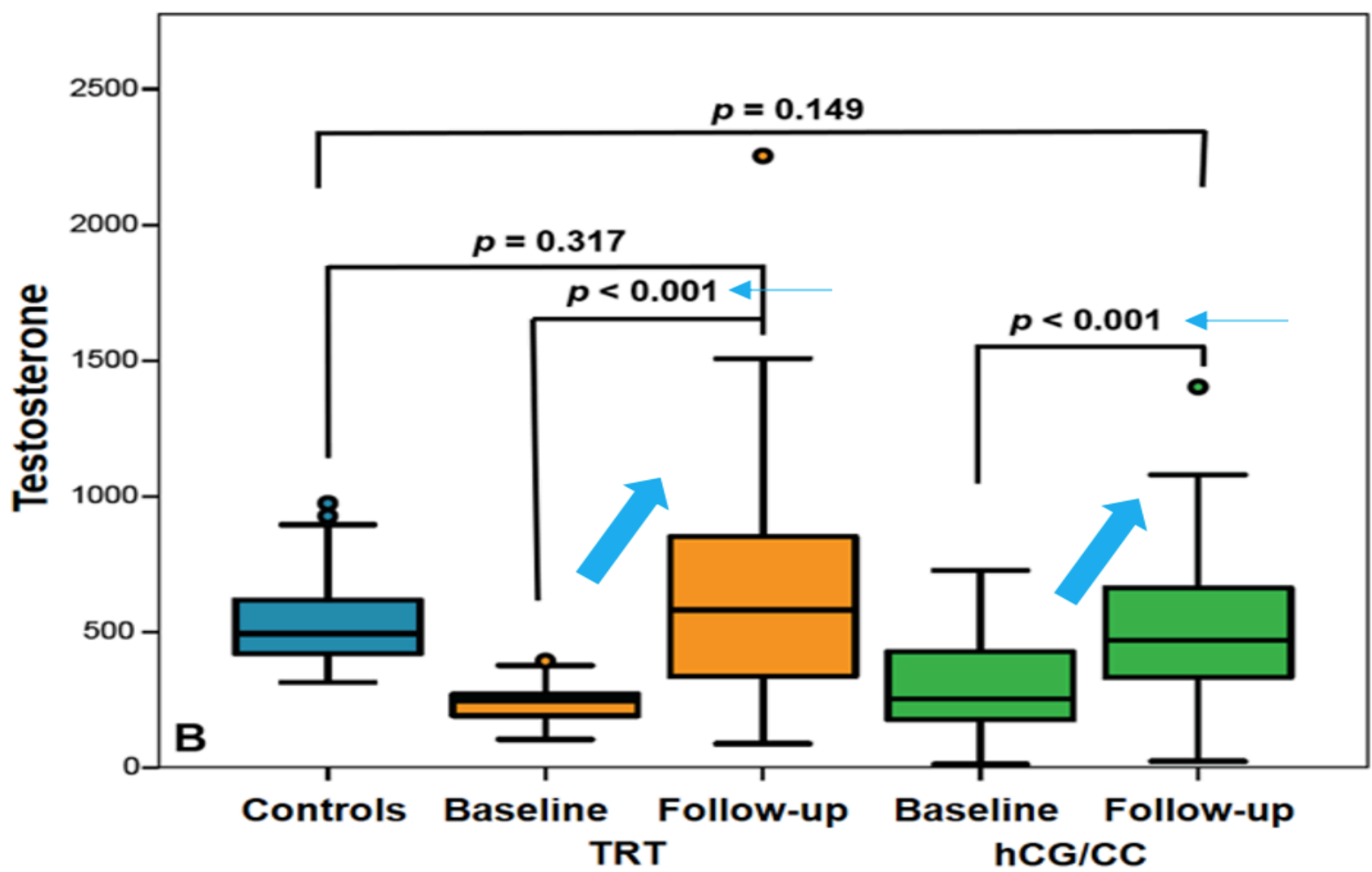


Figure 3: Prospective Cohort of 140 men. Changes in T between baseline and follow-up.

### Conclusions

- TRT resulted in nearly undetectable levels of serum 17-OHP, while hCG/CC therapy improved 17-OHP levels in hypogonadal men.
- Serum 17-OHP was a reliable marker ITT levels in follow-up therapy.
- 17-OHP may be used to guide therapies that alter ITT
- Future studies will need to evaluate what levels of 17-OHP are necessary for spermatogenesis to occur and what levels of serum 17-OHP should be considered normal in the fertile male population.

### Contacts and Reference

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- Lima, T.F.N., Premal Patel, P., Blachman-Braun, R., Madhusoodanan, V., Ramasamy, R. Serum 17-hydroxyprogesterone is a potential biomarker for evaluating intratesticular testosterone. J Urol. 2020, Mar 13;101097JU0000000000001016. PMID: 32167868.