Testosterone Levels Among Non-Obstructive Azoospermic Patients 2 Years *After* Failed Bilateral MicroTESE Procedures Compared *to* Pre-MicroTESE

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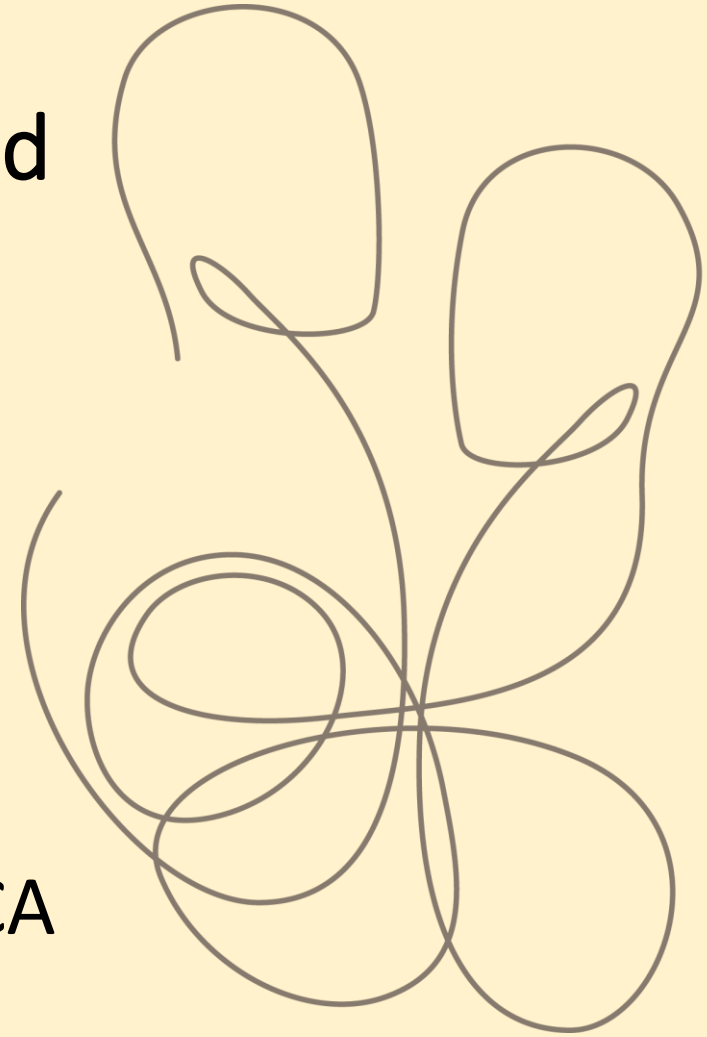

THE TUREK CLINIC

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Introduction-1

- Testicular sperm retrieval procedures are now almost **30 years** old
- Men with non-obstructive azoospermia (NOA) may undergo open testicular sperm extraction (TESE) to obtain sperm for IVF-ICSI
- Due to their invasive surgical nature, TESE procedures are associated with an increased risk of **scarring, atrophy,** and **hypogonadism**
- However, there is scarce literature examining the **health consequences** of surgical sperm retrieval procedures

Schlegel & Su. *Hum Reprod* 1997 **12:** 1688

Tash & Schlegel. Urology. 2001 **57**:334

Eliveld et al. *Hum Reprod Update* 2018 **24**: 442

Introduction-2

- The safety of TESE procedures has been measured as **“devascularization”** and **“scar”** (by ultrasound) and changes in **“seminiferous tubule diameter”** (by histology). However, these outcomes lack clinical correlates to health
- The most relevant health outcome of “invasiveness” of a testicular surgical procedure is **surgically-induced hypogonadism** or **low testosterone levels** following procedures

Schlegel & Su. *Hum Reprod* 1997 **12:** 1688
Tash & Schlegel. Urology. 2001 **57**:334
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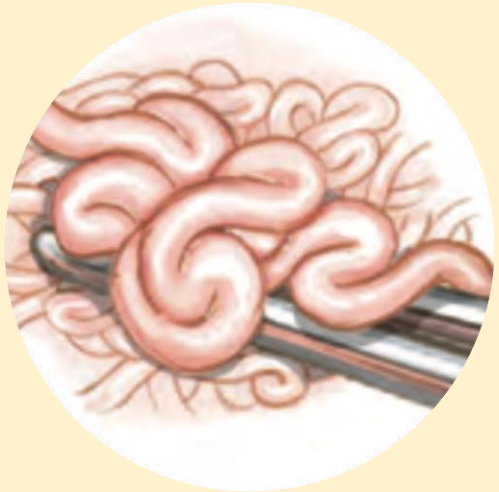
Introduction-3

- A recent systematic review and meta-analysis of **15** non-randomized, retrospective, uncontrolled studies of testosterone levels before and after TESE procedures examined hypogonadism
- Among men with both obstructive azoospermia (OA) and NOA, a **statistically significant decrease in testosterone levels** occurred for up to **12 months** after TESE procedures
- Full (> 95%) recovery of mean testosterone levels was noted at **18 months**
- Limitations of this analysis:
  - Heterogeneous procedures (i.e. TESA, TESE and microTESE)
  - Patients had different risk profiles (OA and NOA) for hypogonadism
  - Mean cohort testosterone levels analyzed and not individual T levels
  - Analysis didn’t exclude possibility that individuals did not recover T levels

Eliveld et al. *Hum Reprod Update* 2018 **24**: 442

Objective

To compare testosterone profiles of **surgically naïve NOA** controls with **microTESE patients** with differing risks for hypogonadism before and after surgery to better understand the true risk of surgically-induced hypogonadism



Methods – Design

- Case-controlled, retrospective study of community acquired NOA patients referred to a single clinic after failed bilateral microTESE
- Each microTESE patient was **age- and BMI-matched** to 2 non-surgical NOA controls
- All cohorts were further subdivided by risk of hypogonadism:
  - **High risk**: cancer, metabolic risk, orchitis, solitary testis, testicular trauma, and cryptorchidism
  - **Low risk**: No history of above conditions, comorbidities, or testicular surgery.

Methods – Patient Selection

Inclusion criteria:

- Complete history, physical exam and laboratory testing
- MicroTESE cohort: Laboratory testing before and > 6 months after a failed bilateral microTESE procedures

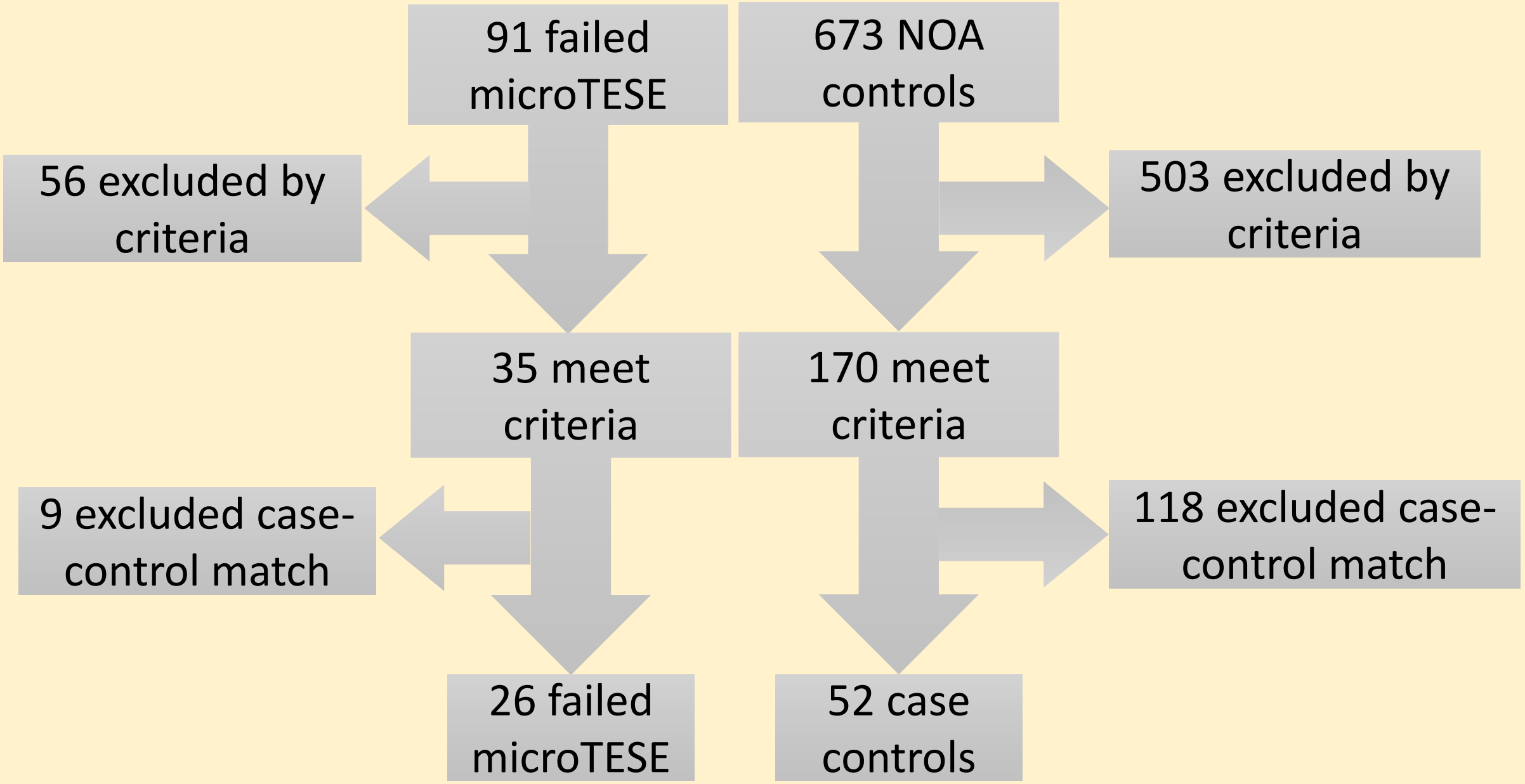
Exclusion criteria:

- Use of aromatase inhibitors, hCG, or T replacement within 3 months of laboratory testing
- Control cohort: Prior testicular surgery

Methods – Analysis

- Serum hormone levels were compared before and > 6 months after microTESE procedures.
- **Paired and non-paired student's t-tests** were applied to analyze differences among low and high risk microTESE patients.
- Hormones assessed:
  - total testosterone (T)
  - follicle stimulating hormone (FSH)
  - luteinizing hormone (LH)

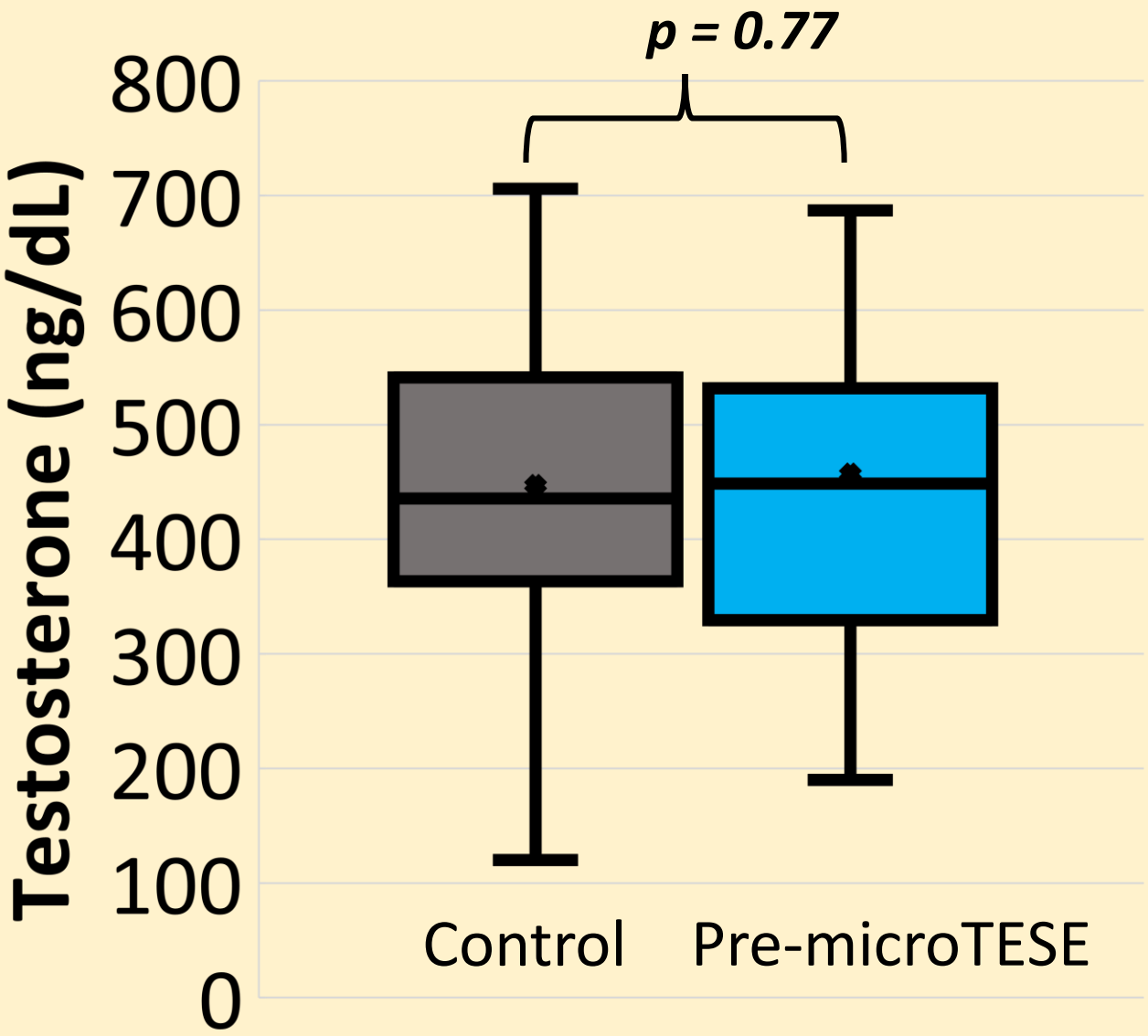
Results I – Patient Flow



Results II- Demographics

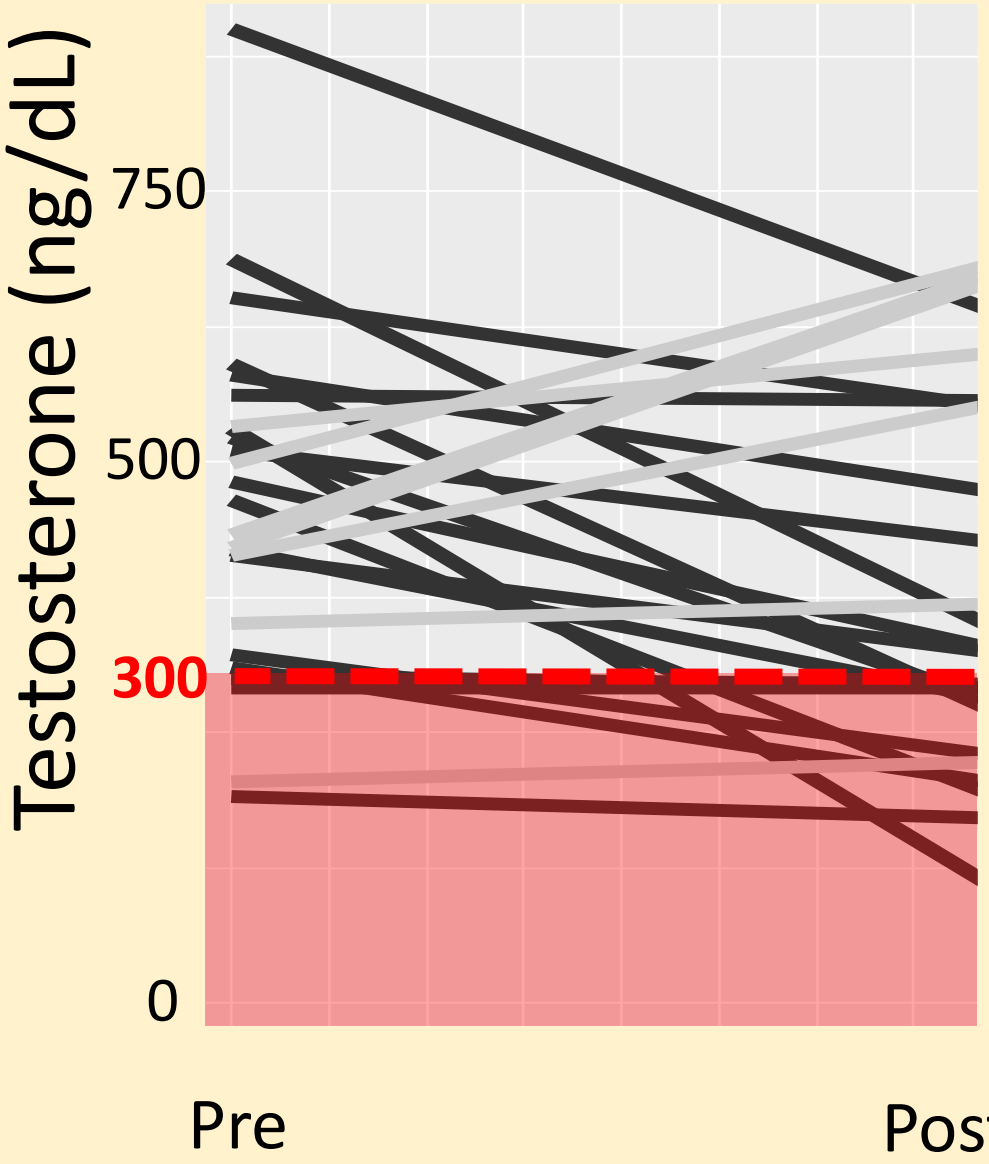
Patient Demographics		*Age	*BMI
MicroTESE n = 26	Average ± S.D.	33.3 ±5.5	28 ±5.6
	Range	25.3-47.7	22.2-44.2
Control NOA n = 52	Average ± S.D.	34.2 ±4.1	26.7 ±3.7
	Range	26.7-45.7	21.4-37.6
*No statistically significant difference in age or BMI			

Results III- Baseline and Postop T in Control NOA vs MicroTESE



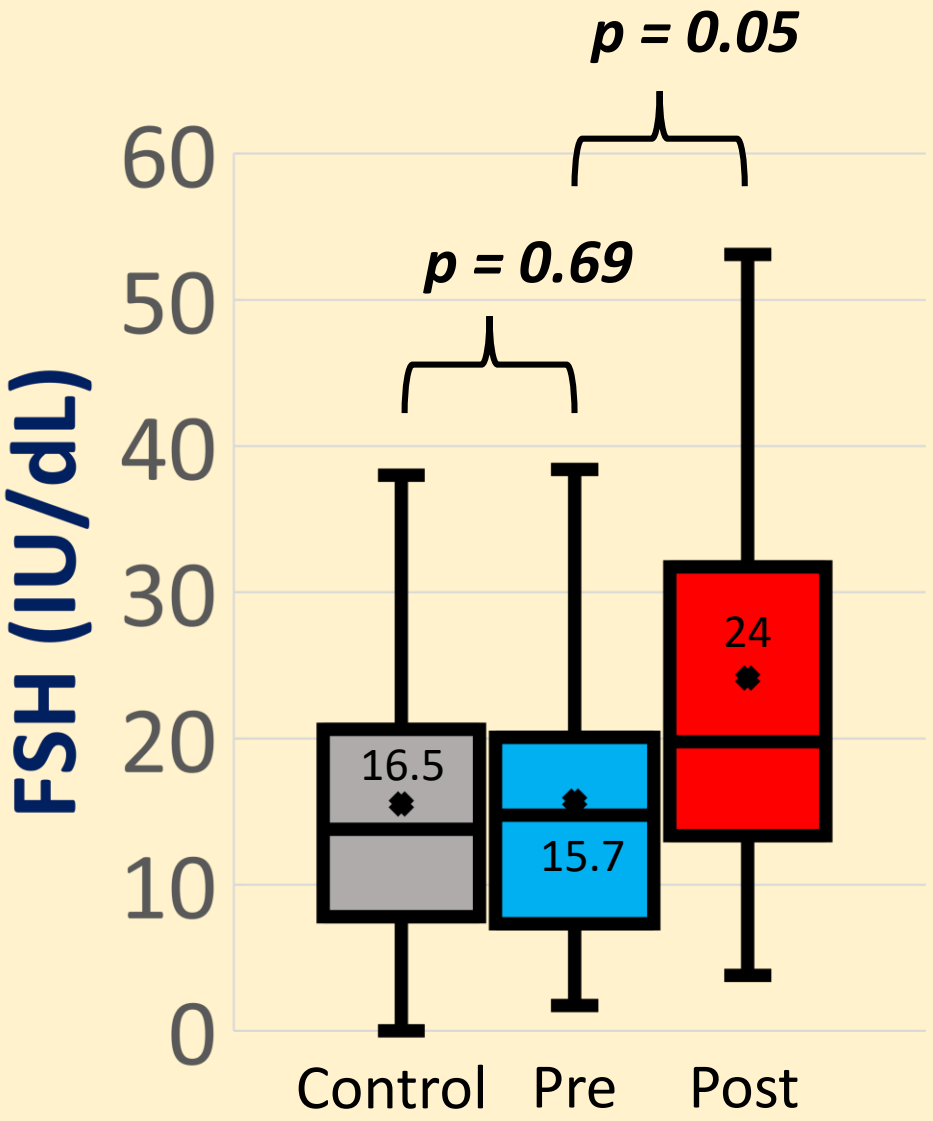
Descriptor	Testosterone (ng/dL ±SD)
Control NOA (n=52)	447 ±116
Pre-microTESE (n=26)	457 ±158
Post-microTESE (n=26)	384 ±178
Time to postop T check	26 months

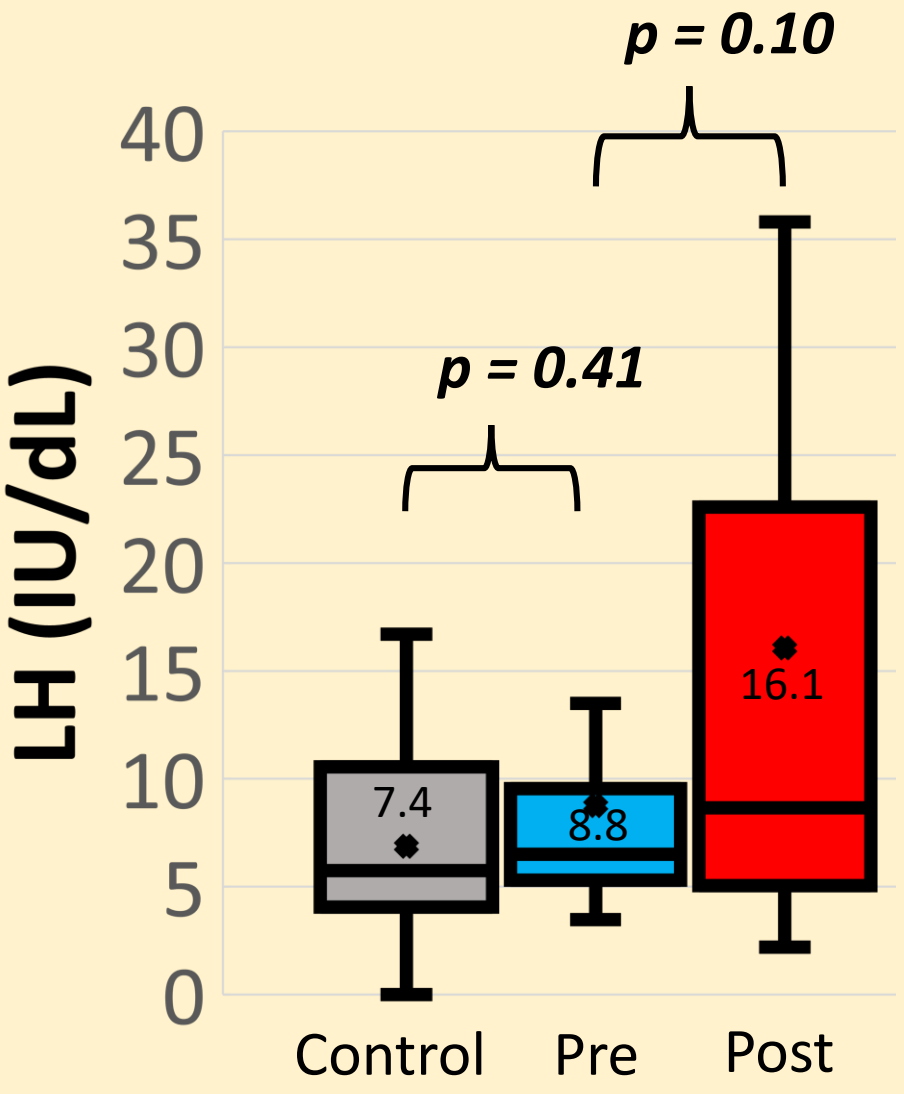
Results IV- Eugonadal to Hypogonadal Conversion *after* microTESE



- All microTESE patients
- Mean change in T levels= -**73.4 ng/dL**
- Confidence interval **(-27, -166)**
- p value, paired samples: ***p<0.01***
- **44%** of eugonadal men became hypogonadal after microTESE

Results V- Change in Gonadotropins *after* MicroTESE

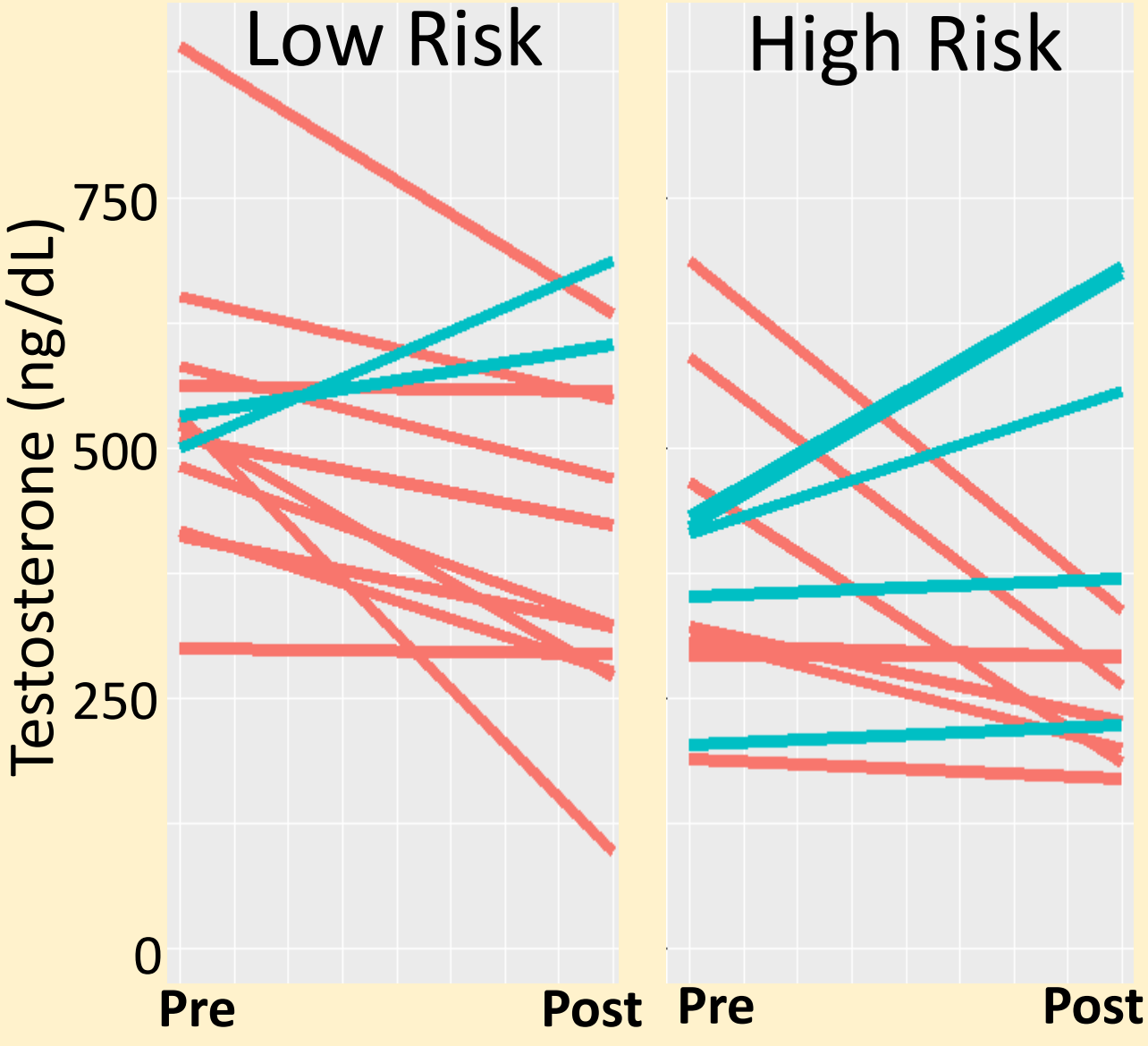




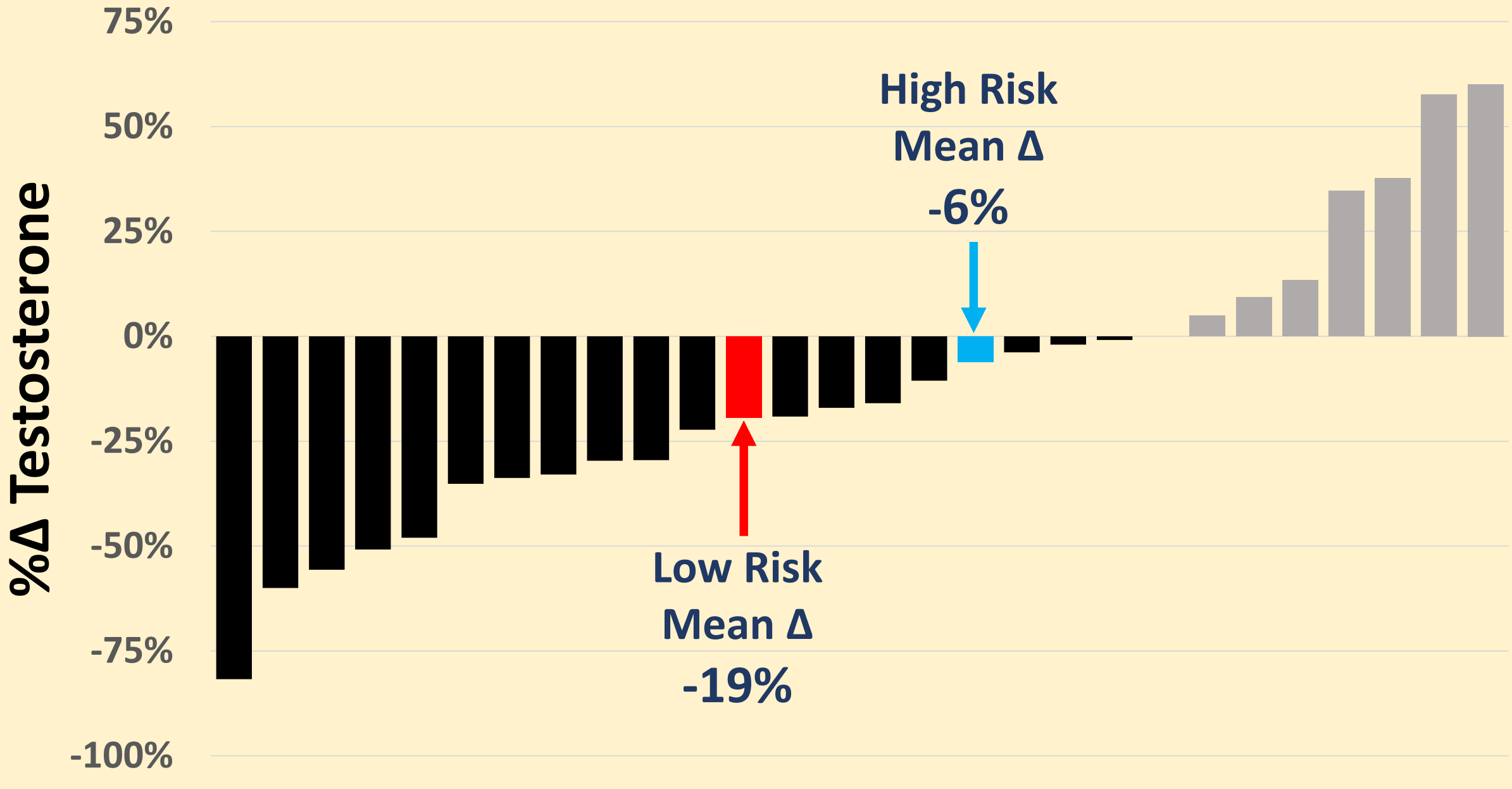
p value:
sample
means
t test

Results VI- Risk Stratified Change in Testosterone *after* microTESE

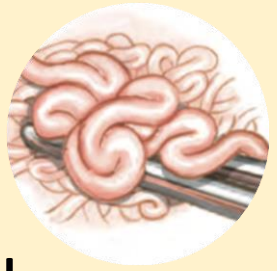
Risk Group	Mean Δ T (ng/dL)	Confidence Interval	p value
Low	-108	(-12.5, -203)	***p < 0.05**
High	-39	(-157, 79)	p = 0.48



Results VII- Percent Change in Testosterone *after* MicroTESE



Conclusions



- Men undergoing failed bilateral microTESE procedures have:
  - a **significant and durable decrease** in testosterone levels
  - a significant **increase in FSH** and upward **trend in LH** levels

- **44%** of eugonadal men (T > 300 ng/dL) become hypogonadal after failed bilateral microTESE procedures

- It appears that **low-risk** patients are at **greater risk** of **decreased testosterone levels** post microTESE than high risk patients

- There are **significant health implications** related to failed microTESE procedures in men with NOA