Endocrine profiling and association with testicular volume and biometrics in a cohort of Norwegian boys

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Conflicts of interest: None

BACKGROUND

Puberty in boys is mediated by pituitary release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) which stimulate gonadal production of sperm and testosterone, respectively[1]. Attainment of testicular volume (TV) 4 ml measured by orchidometer is the common definition of puberty onset. Whereas Prader orchidometry is limited to an ordinal scale, testicular examination by ultrasound provides a continuous measure of TV which enables new possibilities for data analyses. Recent studies indicate a secular trend of earlier puberty timing[2,3] that may be associated with obesity and health risk[3,4].

OBJECTIVES

- From our cross-sectional Bergen Growth Study 2 (2016-) we aimed to evaluate the clinical usefulness of establishing "endocrine profiles" from principle component analysis of pituitary-gonadal hormones.

- To investigate associations between hormone levels and biometrics related to overweight and obesity.

METHODS

Blood samples from 414 healthy boys, aged 6 – 16 years and living in Norway were analyzed by LC-MS/MS (testosterone) and Siemens IMMULITE 2000xpi (FSH, LH and sex hormone-binding globulin, SHBG). Ultrasound TV was calculated into equivalent orchidometer TV based on the mathematical formula established in our test-retest study[6].
Data were analyzed using R/RStudio and GraphPad Prism.

RESULTS

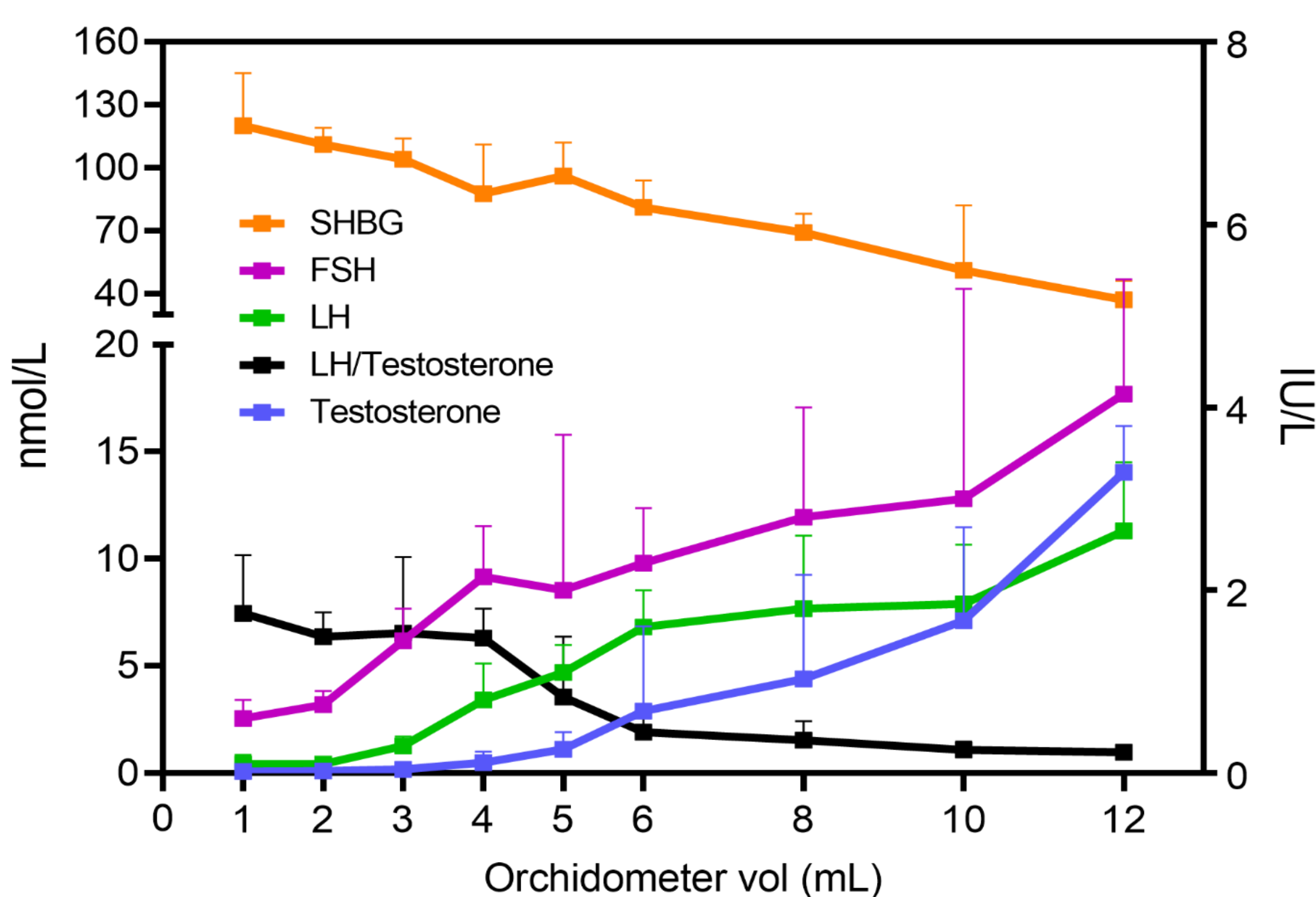### Hormone levels in relation to testicular volume throughout puberty

Figure 1. Median hormone profile during pubertal development Levels of indicated hormones were plotted against calculated orchidometer volumes throughout puberty. Dots and error bars represent the cohort median and upper limit of the 95% confidence interval of the median for each ordinal on the orchidometer scale. Total testosterone and SHBG refer to nmol/L and FSH and LH were counted in international units per liter (IU/L). Pediatric hormone reference intervals were constructed from these data (manuscript in review).

REFERENCES
1. Abreu AP et al., Pubertal development and regulation, Lancet Diabetes Endocrinol (2016)
2. Sørensen K et al., Recent Changes in Pubertal Timing in Healthy Danish Boys: Associations with Body Mass Index, J Clin Endocrinol Metab (2010)
3. Aksglaede L et al., Recent decline in age at breast development: the Copenhagen Puberty Study, Pediatrics (2009)
4. Day FR et al., Puberty timing associated with diabetes, cardiovascular disease and also diverse health outcomes in men and women, Sci Rep (2015)
5. Maule M et al., Age at puberty and risk of testicular cancer: a meta-analysis, Int J Androl (2012)
6. Oehme NHB et al., Ultrasound-based measurements of testicular volume in 6- to 16-year-old boys - intra- and interobserver agreement and comparison with Prader orchidometry, Pediatr Radiol (2018)

RESULTS CONT'D

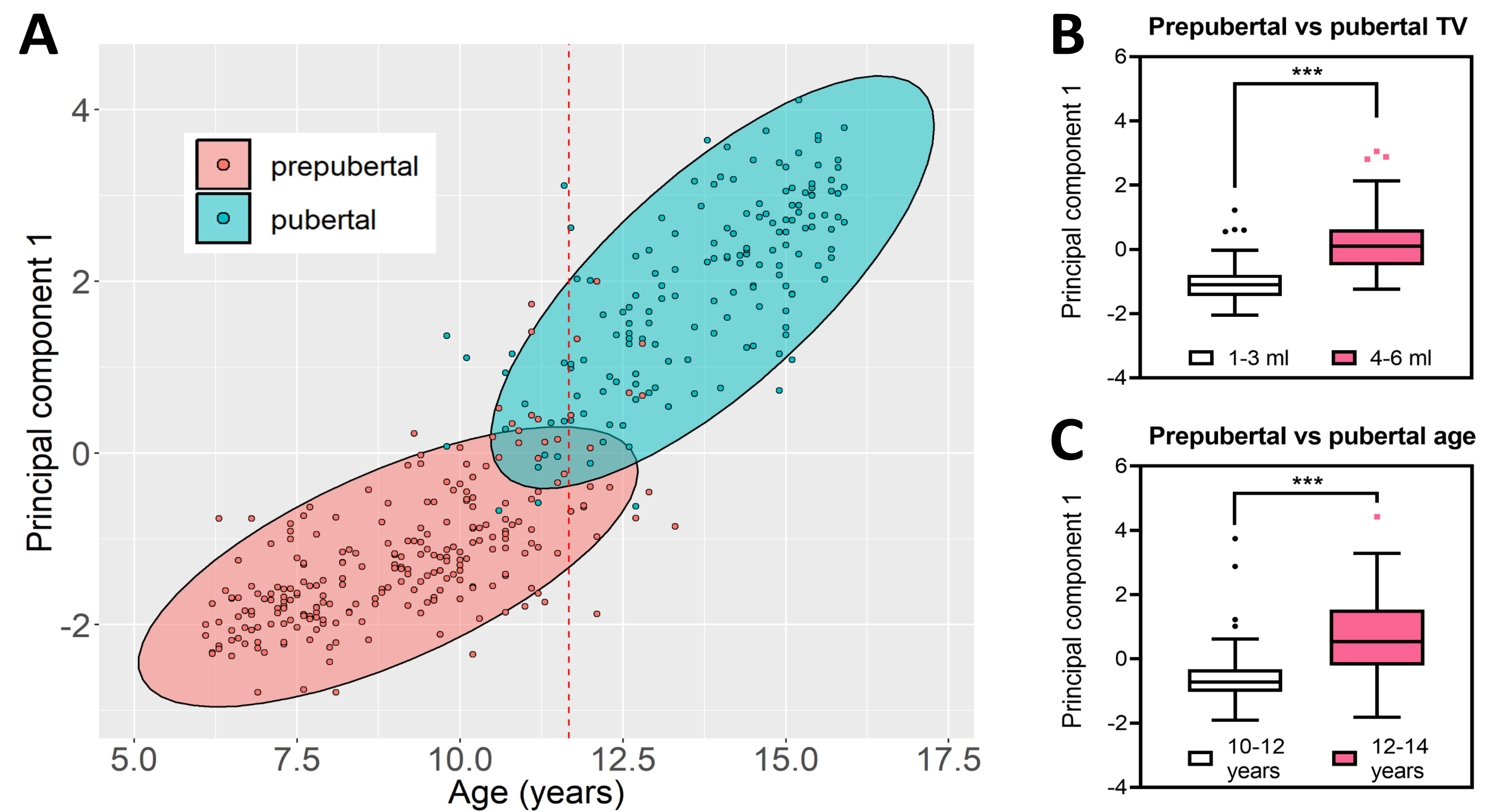### Endocrine profile principal component analysis (PCA)

Figure 2. Dimension reduction of cohort participant serum levels of testosterone, FSH, LH and SHBG. A) The primary principal component (PC1) endocrine profile vector exhibited the following variable rotation: testosterone (0.519); FSH (0.485); LH (0.527) and SHBG (-0.467) and accounted for 76.0% proportion (Eigenvalue 3.0) of data variance. Ellipses represent geometric 95% confidence intervals. Endocrine profiles provided by the PC1 differed significantly between **B)** prepubertal (1-3 ml) and pubertal (4-6 ml) orchidometer testicular volume groups and **C)** between prepubertal and pubertal age groups. Differences marked *** indicates p<0.001 (Welch t-test).

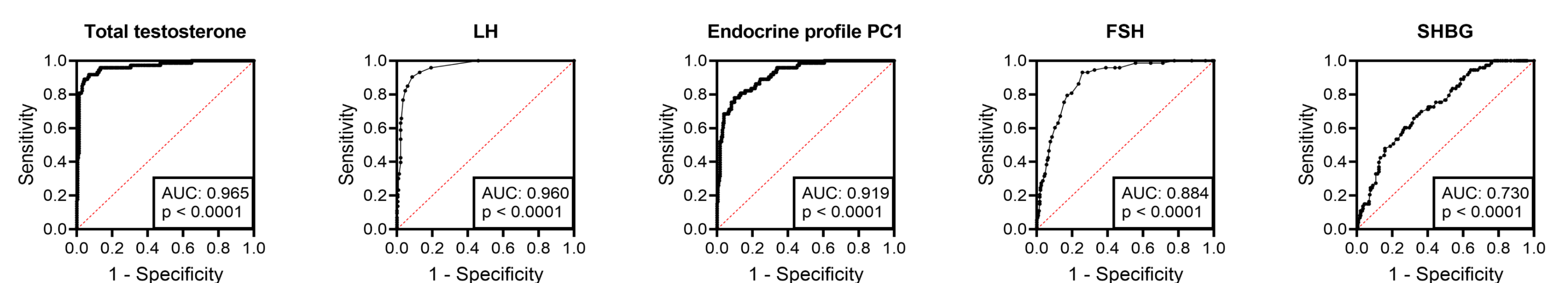### Leveraging endocrine profiles to predict puberty onset

Figure 3. Receiver operating characteristic (ROC) curves for indicated endocrine variables with respect to predicting the binary transition from prepubertal (1-3 ml) to pubertal (4-6 ml) testicular volume. In decreasing order of predictive value, the probability of having attained pubertal testicular volume was predicted by serum levels of circulating testosterone (96.5%), LH (96.0%), the endocrine profile PC1 (91.9%), serum FSH (88.4%) and SHBG (73.0%).

Associations between hormone levels and overweight anthropometrics

Biometric, corrected for age	Total testosterone	Circulating SHBG	Free androgen index
Body mass index (BMI)	r = 0.04 (n.s)	r = **-0.31 (***)**	r = **0.19 (*)**
Weight	r = 0.09 (n.s)	r = **-0.29 (***)**	r = **0.21 (**)**
Waist circumference	r = 0.02 (n.s)	r = **-0.24 (**)**	r = 0.14 (n.s)
Subscapularis skinfold	r = -0.04 (n.s)	r = **-0.24 (**)**	r = 0.11 (n.s)

Table 1. Spearman correlation table. Hormone levels were correlated with standard deviation scores (SDS) for pubertal boys' BMI, weight, waist circumference and skinfold thickness. Free androgen index was defined as total testosterone/SHBG*100. Not significant (n.s); *(p<0.05); **(p<0.01); ***(p<0.001).

CONCLUSIONS

- Ultrasound assessments of TV provide objective data on a continuous scale, allowing for more precise analyses and additional statistical modeling e.g. LMS.

- The endocrine profile vector was able to model the relationship between hormones but its predictive value for clinical evaluation of puberty was inferior to testosterone.

- Key biometrics of overweight were associated with decreased serum SHBG and increased bioavailable testosterone that may accelerate pubertal development.

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