Youden's index increased at decreasing sperm concentration, with its maximum in the case of sperm concentration <1 M/ml (39.7). Likewise, as for CFTR polymorphisms the model performance was comparable (AUC: 51.9% vs. 52.2% vs. 51.5% vs. 51.8% vs. 51.9% vs. 51.3% vs. 49.9%). The Youden's index for CFTR polymorphisms was maximum in the case of sperm concentration <10 M/ml (4.3).
Conclusions: Current EAU guidelines for CFTR mutations testing (<1.5 ml) depicts an overall good performance in identifying both CFTR deletion and polymorphisms. However, given the greater prevalence of a reduced sperm concentration compared to a reduced semen volume in the everyday clinical practice, this newly-suggested cut-off appears to be more widely applicable while maintaining the same performance values.

SC24 Clomiphene citrate and FSH treatment in men with elevated sperm DNA fragmentation index: Findings from a cross-sectional study

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Introduction: Sperm DNA fragmentation index (SDF) has been associated with impaired spermatogenesis and infertility, with negative consequences on biological events such as fertilization and embryonic development. Clomiphene citrate (CC) and FSH treatment (either highly purified FSH (uhFSH) and recombinant human FSH (rhFSH)) have been used to empirically improved sperm quality, but their effect on SDF is relatively poorly studied. We cross-sectionally analyzed the effect of CC and FSH treatment on SDF in men presenting for primary couple's infertility.
Materials and methods: Data from 433 men treated with either CC (n = 370, 85.5%) or FSH (n = 63, 14.5%) for pathologic SDF were analyzed. Semen analysis, SDF (according to SCSA) and serum hormones were measured in every patient; health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI). Pre vs. post treatment semen analysis and SDF were evaluated with paired t-test. Logistic regression analysis was used to test potential predictors of SDF improvement after treatment.
Results: Overall, median (IQR) age, FSH and SDF were 37.5 (24, 64) years, 4.8 (2.8, 5.0) mUI/mL and 43.5% (33.2, 61.4), respectively. At first post-treatment (any) assessment, an improvement in terms of SDF, sperm concentration, percentage of progressive motility and of normal morphology was observed in 36 (60%), 167 (52.5%), 152 (54.9%), and 154 (57%) men, respectively. SDF rate was significantly reduced after treatment (any) (44.9 vs. 52.5%; mean post vs. pre change −7.6; p = 0.001). Conversely, sperm concentration (12.3 vs. 15.0 × 10^6/mL) and progressive motility (18.6 vs. 19.1%) were slightly but not significantly improved after treatment (any). Normal morphology (10.8 vs. 6.5%) was significantly reduced after treatment (any) (p < 0.001), particularly after CC treatment (10.9 vs. 6.9%, p < 0.001). Both CC (p = 0.001) and FSH (p = 0.04) therapy significantly improved SDF levels, with a higher improvement after CC compared to FSH treatment (−12.5 vs. −2.5; p = 0.01). ROC curves revealed that baseline SDF>35% could predict SDF improvement after treatment, with 97% sensitivity and 71% specificity. At multivariable logistic regression analysis, only a baseline SDF>35% was associated with SDF improvement after treatment, after accounting for age, BMI, serum FSH and smoking status.
Conclusions: Both CC or FSH treatment improved SDF in primary infertile men. Patients who benefit most are those with higher baseline SDF, with SDF>35% as a possible clinical cut-off.

SC25 Challenging the guidelines: Proposal of a new sperm concentration cut-off for Y chromosome microdeletions testing in primary infertile men

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Introduction: The 2019 EAU guidelines for male infertility suggest performing Y-chromosome microdeletion test if the sperm concentration is <5 M/ml. Recently, a systematic review showed that most microdeletions occur in men with sperm concentrations of ≤1 M/ml sperm. We evaluated the sensibility, specificity and predictive accuracy (PA) of the EAU guidelines sperm concentration cut-off in comparison with other sperm concentration values in identifying Y-chromosome microdeletions in a homogenous cohort of white-European men presenting for primary couple's infertility.
Materials and methods: Complete data from the last 823 primary infertile men were analyzed. Semen parameters were assessed based on 2010 WHO reference criteria. EAU guidelines for Y-chromosome microdeletion testing (sperm concentration <5 M/ml as for WHO criteria) were firstly adopted in our cohort; thus, the predictive performance and accuracy of different sperm concentration cut-offs (5 M/ml vs. 4 M/ml vs. 3 M/ml vs. 2 M/ml vs. 1 M/ml vs. azoospermia) was tested. Youden's index calculation was used to identify the best cut-off for sperm concentration. AUC curve was used to graphically display the correlation between sensibility and false positive rate (FPR) at different cut offs.
Results: Of 823, 524 (69.7%) patients had sperm count <5 M/mL; of them, 19 (3.5%) actually displayed a Y-chromosome microdeletion. Overall predictive accuracy, sensibility, specificity, FPR and AUC of EAU guidelines were 37.4%, 100%, 36%, 64% and 68%, respectively. Lowering the cut off of 1 M/ml each step (5 M/ml vs. 4 M/ml vs. 3 M/ml vs. 2 M/ml vs. 1 M/ml vs. azoospermia), model performance increased (PA: 41.9% vs. 45.6% vs. 49.4% vs. 56.2% vs. 66.1%; AUC: 70.1% vs. 72.2.6% vs. 71.5% vs. 72.5% vs. 77.5%). The Youden's index increased at decreasing sperm concentration, with its maximum in case of azoospermia (55.02).
Conclusions: Current EAU guidelines for Y-chromosome microdeletion testing (<5 M/ml) misclassify patients in two thirds of cases. The accuracy of testing increases steadily at decreasing level of sperm concentration with maximum predictive performance in the case of azoospermia. Therefore, in non-azoospermic infertile men, 1 M/ml should be used.

SC26 infertile men have higher PSA values than aged-matched fertile controls: Potential implications for personalized prevention strategies

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Introduction: Infertile men are at greater risk of oncologic and non-oncologic chronic disease than the fertile of comparable age. Thereof, male factor infertility (MFI) may be considered an identifiable early sentinel marker for the development of prostate cancer (PCa). We investigated serum PSA levels in a cohort of men presenting for MFI associated with primary couple's infertility compared to a cohort of aged-matched fertile controls, according to the EAU recommendation that a first PSA assessment should be obtained at 40–45 years of age.
Materials and methods: Data from 956 (90%) infertile men and 102 (9.6%) fertile controls were analysed. Comorbidities were scored with