

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 × 10⁶/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. Therefore, 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

the Charlson Comorbidity Index (CCI). According to EAU recommendations, patients were segregated as younger (group 1) and older >40 years (group 2). Serum hormones, serum PSA and semen parameters were investigated in every man. Descriptive statistics and logistic regression models tested potential associations with PSA levels.

Results: Patient's age and BMI were comparable between fertile and infertile group. Median (IQR) age, BMI and total PSA were 38 (35, 43) years, 25.0 (23.3, 26.9) kg/m² and 0.7 (0.5, 1.1) ng/mL in the whole cohort, respectively. Median PSA (0.7 vs. 0.6 ng/ml, $p = 0.03$), CCI (0.8 vs. 0.1, $p = 0.03$) and FSH (6.0 vs. 4.0 mIU/ml, $p < 0.001$) values were higher and total testosterone (4.4 vs. 4.9 ng/ml, $p = 0.003$) was lower in infertile than fertile group. Overall, a PSA value >1 ng/mL was found in 318 (30.1%) men. A higher rate of PSA >1 ng/ml was found in infertile than fertile men (32.0% vs. 20.0%, $p = 0.01$). Among infertile men, sperm concentration (19.5 vs. 28.3 mil/ml, $p = 0.008$) was lower in patients with PSA >1 ng/mL than those with PSA <1 ng/mL. Among fertile patients, no differences were observed according to PSA levels. Of all, 176 (27.0%) group 1 patients had PSA >1 ng/mL. More group 1 infertile men than fertile controls had PSA >1 ng/ml (28.0% vs. 17.0%, $p = 0.03$). At MVA logistic regression analysis infertility status (OR 1.7, $p = 0.04$) was the only independent predictor for serum PSA >1 ng/mL in group 1, after accounting for testosterone level.

Conclusions: This case-control analysis showed that infertile men have higher PSA values than age-matched fertile controls. Of all, almost one out of three infertile men younger than 40 years have a first total PSA value greater than 1 ng/mL.

SC27

The relationship between isolated teratozoospermia, sperm DNA fragmentation and inflammatory biomarkers: Findings from a cross-sectional study

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Introduction: According to 2010 WHO reference values for human semen characteristics, teratozoospermia is defined when spermatozoa with morphologically normal forms are <4%. Isolated teratozoospermia (iTERATO) is frequently associated with infertility, fertilization success at ART and increased markers of sperm damage (i.e., sperm DNA fragmentation index (SDF) or reactive oxygen species). We aimed to assess the prevalence of and the clinical and hormonal characteristics of men with iTERATO seeking first medical help for primary couple's infertility.

Materials and methods: Data from 1857 primary infertile men (median (IQR) age 37 (21–41) years) were analyzed. Health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI). Semen analysis, serum hormones and SDF (with SDF $\geq 30\%$ at SCSA = pathologic) were investigated in every patient. A complete blood count was requested for every man and the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the monocyte-to-eosinophil ratio (MER) were calculated. Data from a cohort of 103 age-matched fertile men was also collected. Descriptive statistics tested the association between clinical and hormonal characteristics in patients with iTERATO, and either isolated oligozoospermia (iOLIGO) or asthenozoospermia (iASTHENO).

Results: Of 1857 patients, 223 (12%), 83 (4.5%) and 258 (13.9%) had semen parameters suggestive for iTERATO, iOLIGO and iASTHENO, respectively. Of 103 fertile men, iTERATO was found in 37 (35.9%) cases. Patient's age, BMI and CCI were comparable between groups. iOLIGO patients reported both higher median FSH (7.8 vs. 4.3 vs. 4.5 mIU/mL; $p = 0.001$), LH (4.6 vs. 3.4 vs. 3.9 mIU/mL; $p = 0.001$), but lower Inhb levels (106.4 vs. 167.1 vs. 153.4 pg/mL; $p = 0.001$) compared to iTERATO and iASTHENO, respectively. Total testosterone and SHBG were similar

among groups. Higher median SDF values (37.5 vs. 19.8 vs. 26.4%; $p = 0.001$) and higher rates of pathologic SDF (44.0% vs. 20.5% vs. 34.0%; $p = 0.04$) were more frequently observed in iTERATO than in both other groups. Median C-reactive protein (0.9 vs. 0.3 vs. 0.4 mg/L), NLR (2.1 vs. 1.6 vs. 1.8) and PLR (120.2 vs. 109.5 vs. 115.1) values were higher in patients with iTERATO than iOLIGO and iASTHENO, respectively. At Spearman's correlation, sperm morphology was inversely associated with SDF ($\rho = -0.25$; $p = 0.001$) and NLR ($\rho = -0.14$; $p = 0.02$). In the fertile cohort, NLR, PLR and MER were comparable between iTERATO vs. non iTERATO individuals.

Conclusions: One out of ten men seeking medical help for primary couple's infertility reported semen parameters suggestive for iTERATO. iTERATO is even more prevalent in fertile men. Infertile patients with iTERATO had increased levels of SDF and inflammatory serum markers compared to those with iOLIGO and iASTHENO. Our findings suggest a significant link between sperm morphology and oxidative balance in infertile men.

SC28

Treatment of erectile dysfunction using a nutraceutical mix. Preliminary data in a randomized, single-blind, placebo-controlled study

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Introduction: Approximately 50% of men aged 40–70 years report suffering from some degree of erectile dysfunction (ED). PDE5-i is the first line treatment for this condition. Many patients search for a different treatment, with less side effects. Use of food supplements is common and more patients are seeking for alternative treatment for ED. This study investigated the efficacy of a new supplement to improve male sexual function.

Materials and methods: In this randomized, single-blind, placebo-controlled study, 92 men with mild to moderate ED were enrolled. The mean age was 56.4 ± 15.9 years. Group A (56 pts) received the active treatment containing a mix of L-citrulline 2500 mg, Moringa oleifera 1500 mg, Tribulus terrestris 400 mg (45% saponins), Panax ginseng 400 mg, Lepidium Meyenii 200 mg, Trigonella Foenum-Graecum 200 mg, Zinc 15 mcg, Vitamin D3 7.5 mcg, Vitamin B6 1 mg. This treatment was administered twice a day for two months. Group B (36 pts) received a placebo. Patients were investigated by using the International Index of Erectile Function (IIEF-5) questionnaire, the Sexual Encounter Profile (SEP) diaries, SEP Question 2: "Were you able to insert your penis into your partner's vagina?" and SEP Question 3: "Did your erection last long enough for you to have successful intercourse?" In addition, patients underwent further evaluation with the Global Assessment Question (GAQ) by answering the two yes/no questions of the test: (GAQ-Q1) "Over the past four weeks has the treatment you have been taking improved your erectile function?" and (GAQ-Q2) "If yes, has the treatment improved your ability to engage in sexual activity over the past four weeks."

Results: At one month follow-up 10 pts drop-outs (11%): consisting of 6 pts from Group A and 4 pts from Group B. 4 pts (8%) reported mild gastrointestinal symptoms. 6 pts (12%) reported mild insomnia. Group A showed a statistically significant improvement of the IIEF mean scores compare to the control group, from a baseline total score of 14.7 ± 4.0 to 20.2 ± 3.4 Vs 15.6 ± 3.4 to 17.2 ± 2.6 . 42 pts (84%) answered 'yes' to SEP Q2 vs 30 pts (60%) pre-treatment. SEP Q3 was answered positively by 36 pts (72%) vs 27 pts (54%). For the GAQ questions, 30 pts (60%) answered "Yes" to the GAQ-Q1 while 29 pts (58%) answered "Yes" to the GAQ-Q2. When reviewing the change in SEP scores, a significant increase was noticeable between the baseline and follow-up data.

Conclusions: The combination of these composite improves male sexual function.