Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

overall subjects [MD 5.77 (4.28-7.25), $p < 0.001$] and within each group [VR: MD 5.93 (3.44-8.42), $p < 0.001$; and nVR: MD 5.36 (3.71-7.02), $p < 0.001$], with non-significant between-group difference ($Q = 0.14$, $p = 0.7$). Similar results were obtained for progressive sperm motility [MD 7.21 (3.66-10.76), p< 0.001; VR: MD 3.36 (0.8-5.93), $p = 0.01$; nVR: MD 7.78 (3.86-11.7), $p < 0.001$] with non-significant between-group difference ($Q = 3.4$; $p = 0.06$) and total sperm motility [overall: MD 7.52 (3.11-11.94), $p = 0.001$; VR: MD 7.11 (4.12-10.11), $p < 0.001$; nVR: MD 7.7 (2.73-12.67), $p = 0.002$] with non-significant between-group difference ($Q = 0.04$; $p = 0.8$). Improved sperm morphology was similarly significantly demonstrated in overall subjects [overall: MD 3.28 (2.4-4.17), $p < 0.001$] and within each group [VR: MD 6.84 (5.33-8.34), $p < 0.001$; and nVR: MD 1.34 (0.13-2.56), $p = 0.03$]. However, the between-group analysis has shown a significant difference in improved morphology favouring VR ($Q = 31$, $p < 0.001$).

CONCLUSIONS: Apart from sperm morphology, treatment with AOX significantly improved conventional sperm parameters, independently from VR.

IMPACT STATEMENT: The results of this study suggest that men with varicocele and OAT should receive AOXs as their primary therapy, and additional benefit from VR is likely to be limited.

SUPPORT: None

P-473 6:45 AM Wednesday, October 26, 2022

EFFECT OF VARICOCELE REPAIR ON CONVENTIONAL SPERM PARAMETERS IN INFERTILE PATIENTS WITH CLINICAL VARICOCELE: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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OBJECTIVE: Varicocele is present in almost 35-40% of men presenting with primary infertility. Despite the significant role of varicocele in the pathogenesis of male infertility, the impact of varicocele repair (VR) on conventional semen parameters remains controversial. To the best of our knowledge, only a few systematic reviews and meta-analyses (SRMA) have evaluated the impact of VR on sperm concentration, total motility, and progressive motility using a before-after analytic approach for analyzing 22, 17, and 5 prospective uncontrolled trials, respectively. Indeed, the majority of SRMAs have focused on pregnancy rate as an outcome. This study aimed to evaluate the effect of VR on conventional semen parameters in infertile patients with clinical varicocele compared to untreated controls.

MATERIALS AND METHODS: Literature search was performed in Scopus, PubMed, Ovid, Embase, and Cochrane databases using the PICO model (Population: Infertile patients with clinical varicocele; Intervention: Varicocele repair; Comparison: No treatment; Outcomes: Sperm concentration, sperm total count, sperm progressive motility, sperm total motility, and semen volume). Both randomized-controlled trials (RCTs) and observational studies were included.

RESULTS: 1632 abstracts were initially assessed for eligibility. 16 studies were finally included with a total of 2420 infertile patients with clinical varicocele (1424 patients treated with VR vs. 996 untreated controls). The analysis showed significantly improved post-operative sperm parameters in the VR group compared to controls: sperm concentration [standardized mean difference (SMD) 1.87 (95% CI: 1.25, 2.48); $p<0.01$; $I^2=97.6\%$], total sperm count [SMD 1.89 (95% CI: 0.57, 3.22); $p<0.05$; $I^2=97.8\%$], sperm progressive motility [SMD 3.30% (95% CI: 2.16, 4.44); $p<0.01$; $I^2=98.4\%$], total sperm motility [SMD 0.89% (95% CI: 0.04, 1.74); $p=0.04$; $I^2=97.4\%$] and normal sperm morphology [SMD 1.68% (95% CI: 0.88, 2.47); $p<0.05$; $I^2=97.4\%$]. All the outcomes had a high level of inter-study heterogeneity, but sensitivity analysis showed that no study was sensitive enough to change these results. Publication bias was present only in the analysis of sperm concentration and progressive motility. No significant difference was found in semen volume [SMD 0.13 ml (95% CI: -0.24, 0.87); $p=0.27$; $I^2=89.7\%$].

CONCLUSIONS: This study provides evidence in favor of a positive effect of VR in improving conventional semen parameters in patients with clinical varicocele and infertility.

IMPACT STATEMENT: To the best of our knowledge, this is the first SRMA evaluating the impact of VR on conventional semen parameters in controlled studies in the largest population, the highest number of RCTs, and the broadest publication period. Therefore, our study provides a higher level of evidence compared to that derived by other SRMAs on uncontrolled studies. Our findings strengthen the available evidence and have a potential to upgrade the societies' practice recommendations favoring VR to improve conventional semen parameters in infertile patients.

SUPPORT: None

P-475 6:45 AM Wednesday, October 26, 2022

COVID-19 IS UNLIKELY TO AFFECT MALE FERTILITY: RESULTS OF HISTOPATHOLOGIC AND RT-PCR ANALYSIS.

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OBJECTIVE: Male sex is an independent risk factor for death from COVID19. The ACE2 receptor is a known entry mechanism of SARS-CoV-2 into cells and is present within testicles. There is limited and conflicting data as to whether COVID19 infects the testes. We sought to identify evidence of COVID19 within the testes of men who died with active COVID19 infection.

MATERIALS AND METHODS: We performed autopsy of 8 consecutive men who died of COVID19 pneumonia and whose families provided consent to harvest testicle tissue. Lung and testis tissue of all men were stained for SARS-CoV-2 nucleocapsid, ACE2 receptor IHC. H&E IHC was performed to assess for spermatogenesis and evidence of testicle tissue damage. RTPCR analysis for SARS-CoV-2 was performed on matched lung and bilateral testicular tissue samples from all men.

RESULTS: Patient age ranged 50 to 79 years. The average time from COVID19 diagnosis to death was 21 days. SARS-CoV-2 viral RNA was detected by RTPCR in testis tissue in one man, and in pulmonary tissue of all men. The man with RTPCR positivity in testis tissue (left testicle: CT 39.23 in 1/5 runs; CT 39.63 in 2/5 runs) had the highest RTPCR positivity in lung (CT 37.55 in 3/5 runs). All 8 testicle specimens that underwent ACE2 IHC showed uniformly strong immunoreactivity against all testicle cell populations. By H&E, no testis specimens showed inflammation, vascular thrombosis, vasculitis, or morphologic evidence of viral changes. One case showed diminished but present spermatogenesis, consistent with patient age (Table 1).

CONCLUSIONS: Our RTPCR results suggest that while SARS-CoV-2 is not common in testes at time of death, it can infect the testes. We believe our IHC results were similar to others' findings, but inconclusive based on a lack of a standardized control. Contrary to all prior histologic studies, our results showed no evidence of damage to reproductive tissues that might impair fertility.

IMPACT STATEMENT: Our results suggest that SARS-CoV-2 infection likely does not adversely affect male fertility.

P-476 6:45 AM Wednesday, October 26, 2022

EVALUATION OF ANDROGEN SATURATION IN HUMAN CORPUS CAVERNOSUM. Kajal Khodamoradi, PhD,[1] Alexandra Dullea, MS,[1] Roei Golan, BS,[2] Daniel E. Nassau, MD,[1] Jesse Ory, MD,[1] Himanshu Arora, B.SC., M.SC., PH.D.,[1] Ranjith Ramasamy, M.D.[1] [1]University of Miami Miller School of Medicine, Miami, FL; [2]Florida State University College of Medicine, FL, USA, Tallahassee, FL.

OBJECTIVE: Testosterone (T) plays an essential role in properly developing and maintaining male reproductive tissues (1). The normal serum testosterone levels can vary between 300 to 1000 ng/dL. However, it is unclear whether androgen receptor signaling can vary based on serum T levels. What remains unknown is whether there is a consistent serum T level above which androgen receptor signaling within the tissue remains similar. Therefore, we evaluated whether varying serum levels of T alter androgen receptor (AR) signaling in human penile tissue.

MATERIALS AND METHODS: We obtained human corpus cavernosum (CC) tissue biopsies during penile implant surgery from 17 men. We recorded their serum T levels one week before surgery. After mechanical dispersion of CC tissue with a homogenizer, the total protein was extracted using RIPA buffer, and quantitative detection of vascular endothelial growth factor (VEGF) was evaluated by western blot.

RESULTS: The mean age of participants was 64 $\pm$ 10, and the mean T level was 487 ng/dL $\pm$. 377. The western blot results showed that all corpus cavernosum samples in men with T >200ng/dL expressed similar levels of VEGF in men. However, men with a low serum T level (<200 ng/dL) had decreased expression of VEGF.

CONCLUSIONS: Even with a wide range of serum T levels (200-1594 ng/dl), androgen receptor signaling was similar in penile tissue. This data suggests that the saturation value for penile androgen receptors could be approximately 200ng/dL.

IMPACT STATEMENT: Understanding the androgen receptor saturation hypothesis provides the vital context necessary for appropriately prescribing exogenous T to optimize patient outcomes.

P-477 6:45 AM Wednesday, October 26, 2022

DYSREGULATION OF THE HUMAN B-DEFENSIN 128 GENE IMPACTS SPERM FUNCTION. Shruti Kane, B.SC., M.SC.,[1] Sarah Martins da Silva, M.B.B.CH., M.D.,[2] Sean Brown Dr, PhD[3] [1]University of Abertay Dundee, Dundee, Angus, United Kingdom; [2]University of Dundee, NHS Tayside; [3]University of Abertay.

OBJECTIVE: Male infertility is a global issue and many of the cases of male infertility have unknown causes. Genetic mutations may be a causative factor in a significant number of idiopathic cases. We conducted Whole Exome Sequencing (WES) analysis in men undergoing assisted conception and identified a genetic mutation in the β-defensin 128 (DEFB128) gene. The DEFB128 gene is explicitly expressed in the male reproductive tract, where it forms part of the sperm glycocalyx and protects sperm cells in the female reproductive tract.

MATERIALS AND METHODS: DNA was extracted from the blood of 26 men attending the assisted conception unit and sequenced using WES. A pathogenic variant in the β-defensin 128 gene was identified using bioinformatics analysis and validated using Sanger sequencing. Enzyme-linked immunosorbent assay (ELISA) was used to detect the presence of the DEFB128 protein on sperm cells. wtDEFB128 recombinant protein was brought commercially and anti-microbial assays against a range of control strain Gram-positive and Gram-negative bacteria commonly found in the female reproductive tract were performed.

RESULTS: Based on bioinformatics analysis, we identified a novel pathogenic homozygous frame-shift insertion causing a premature stop codon in the DEFB128 gene from one patient. Sanger sequencing was used to confirm the pathogenic mutation in the patient. DEFB128 has been shown in literature to be highly and exclusively expressed in the male tissue, presence of DEFB128 on sperm was investigated using ELISA assays. In order to identify the functional significance of this protein, antimicrobial assays were performed using the commercially available DEFB128 recombinant protein.

Based on our results, we hypothesise that the loss of the DEFB128 protein reduced the competence of the patients sperm cells by making them more prone to infections in the female reproductive tract.

CONCLUSIONS: The identified DEFB128 mutation (rs11396059) has not been associated with any disease to date. Reduced antimicrobial activity due to the pathogenic mutation may render sperm cells with less protection against pathogens in the female reproductive tract. As the patient with the DEFB128 mutation has no other medical condition we predict that it is the cause of infertility. However, the exact physiological impairment in-vivo needs to be confirmed.

Furthermore, like the human DEFB126 protein, the DEFB128 may contribute to the formation of the sperm glycocalyx and hence it may be involved in the efficient movement of sperm in the female reproductive tract. Sperm penetration assays will need to be performed on affected patients sperm cells to provide further evidence of functional failure.

IMPACT STATEMENT: Many cases of idiopathic male infertility remain a mystery. This may be in-part due to the lack of understanding of the physiological regulation of sperm cells. The DEFB128 gene is exclusive expressed in the male reproductive tract and forms part of the sperm glycocalyx. Understanding the sperm glycocalyx and its functional significance will help in understanding the cause of dysfunction in many cases of idiopathic male infertility.

P-478 6:45 AM Wednesday, October 26, 2022

IMPACT OF COMORBIDITIES ON MALE TESTOSTERONE LEVELS WITH AGE: RESULTS FROM THE BALTIMORE LONGITUDINAL AGING STUDY. Joshua Theodore White, MD,[1] Chase Carto, BS,[2] Maria Camila Suarez Arbelaez, MD,[2] Ranjith Ramasamy, M.D.[2] [1]Dalhousie University, Halifax, NS, Canada; [2]University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To evaluate the longitudinal impact of additive comorbidity burden on testosterone levels in aging males. We hypothesized that age alone in the absence of comorbidities would not predict a significant decline in testosterone level, but development of comorbidities would lead to testosterone decline with aging.