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COMPARISON OF PROGNOSTIC INDICATORS HA, HYAL1, CD44V6 AND MICROVESSEL DENSITY FOR PROSTATE CANCER: A 5-YEAR RETROSPECTIVE STUDY

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INTRODUCTION & OBJECTIVES: Despite the development of nomograms designed to evaluate a prostate cancer (CaP) patient's prognosis, the information has been limited to prostate specific antigen (PSA), clinical stage and Gleason score. We compared the prognostic potential of 4 histologic markers, hyaluronic acid (HA), HYAL1 type hyaluronidase (HAase), CD44v6 and microvessel density using immunohistochemistry. HA is a glycosaminoglycan that promotes tumour metastasis. CD44 glycoproteins serve as cell surface receptors for HA and CD44v6 isoform is associated with tumour metastasis. HAase is an enzyme that degrades HA into angiogenic fragments. We have previously shown that HA and HYAL1 type HAase levels are diagnostic markers for bladder cancer. Tumour angiogenesis, evaluated as microvessel density (MVD), has some prognostic potential for CaP.

MATERIAL & METHODS: Archival CaP specimens were obtained from patients who underwent radical retro pubic prostatectomy for clinically localized CaP. Group 1 (n = 25): Patients who showed biochemical recurrence within 64 months (PSA > 0.4 ng/ml; mean recurrence: 21.3 mos). Group 2: no clinical or biochemical recurrence patients in 64 months (n = 44, mean follow-up: 80.9 mos). For HA, HYAL1 and CD44v6 staining and MVD determination, a biotinylated HA-binding protein, an anti-HYAL1 IgG, an anti-CD44v6 IgG and an anti-CD34 IgG were used, respectively. HA and HYAL1 staining was evaluated on the basis of intensity and then grouped as low- and high-grade. For CD44v6 and MVD the staining was evaluated quantitatively and then grouped as low- and high-grade staining.

RESULTS: In CaP specimens, while HYAL1 and CD44v6 were exclusively expressed in tumour cells, HA was localized both in tumour stroma and cells. HA, HYAL1, combined HA-HYAL1, CD44v6 and MVD staining predicted progression with 96%, 84%, 84%, 68% and 76% sensitivity, respectively. The specificity was, 56.8% (HA), 81.8% (HYAL1) and 88.6% (HA-HYAL1), 54.5% (CD44v6) and 61.4% (MVD), respectively. In univariate analysis, preoperative PSA, Gleason sum, margin, seminal vesicle, extra-prostatic extension (EPE), HA, HYAL1 and HA-HYAL1 and MVD were significant in predicting progression ($P < 0.05$). However, CD44v6, age and clinical stage were not significant in predicting progression. In the multivariate analysis, only EPE (odds ratio (OR) = 33.264; P, 0.0024), HYAL1 (OR =12.37; p = 0.0095)/HA-HYAL1 (OR = 18.698; P = 0.003) and margin (OR = 26.948; P = 0.006) were significant.

CONCLUSIONS: In this 5-year retrospective follow-up study, HYAL1 together, with EPE and margin was found to be an independent prognostic indicator.

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P6 SEXUAL DYSFUNCTION: PREVALENCE, DIAGNOSIS AND TREATMENT OUTCOMES
Thursday, 25 March, 12.00-13.30, Hall C/ Red level

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THE EFFICACY OF SERTRALINE HYDROCHLORIDE AND LIDOCAINE CREAM IN PATIENTS WITH PREMATURE EJACULATION: A RANDOMIZED, PLACEBO CONTROLLED STUDY

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INTRODUCTION & OBJECTIVES: Sertraline hydrochloride (selective serotonin re-uptake inhibitor) and lidocaine cream (local anesthetic) are alternatives in treatment of premature ejaculation. In this study, we compared the efficacy of sertraline and lidocaine cream with each other and placebo.

MATERIAL & METHODS: The study included 60 men with intravaginal ejaculation latency time less than 60 seconds. Three groups were enrolled by randomization for sertraline, lidocaine cream and placebo, and each groups had 20 patients. Mean age for sertraline, lidocaine cream and placebo were 35.7 years (22-62), 34.9 years (24-47) and 38 years (22-53), respectively. Patients took one capsule of sertraline (50 mg) and placebo in a day. Patients applied lidocaine cream 5 minutes before coitus. These patients were also recommended for use of condom. The intravaginal latency times before and after 4 weeks treatment determined by averaging last two latency times obtained from patient information. Side effects of drugs and complaints of patients also evaluated. Wilcoxon Signed Ranks and Mann-Whitney U tests were used for statistical analysis.

RESULTS: After 4 weeks of treatment, sertraline, lidocaine cream and placebo increased mean intravaginal ejaculation latency time significantly from 42.5 to 579.5 seconds (p=0.000), 41.8 to 385.5 seconds (p=0.000) and 37.0 to 66.3 seconds (p=0.008), respectively. The efficacy of sertraline and lidocaine cream was found significantly higher than placebo (p=0.000, p=0.001). Efficacy of sertraline was also found higher than lidocaine cream (p=0.013). Only two patients had anorgasmia and one patient had nausea in sertraline group. Sertraline was used day after day and anorgasmia was disappeared in these 2 patients. In lidocaine cream group most of the patients complained from decreased sensation.

CONCLUSIONS: Sertraline and lidocaine cream increased intravaginal ejaculation latency times significantly and their efficacy were significantly higher than placebo. Efficacy of sertraline was also significantly higher than lidocaine cream. Side effects of sertraline were minimal, and lidocaine cream had disadvantage of decreased sensation.

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THE EXPRESSION OF N-ACETYLTRANSFERASE1 IN THE HUMAN BENIGN AND MALIGNANT PROSTATE

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INTRODUCTION & OBJECTIVES: N-Acetyltransferase1 (NAT1) is involved in the activation of many human promutagens and procarcinogens including heterocyclic amines. Enzymatic activation is crucial for forming the "ultimate" carcinogen capable of reacting with DNA and initiating the carcinogenesis process. The mRNA expression of NAT1 enzyme in the prostate is well documented. However, to our knowledge, NAT1 protein expression in human prostate has not been reported previously.

MATERIAL & METHODS: A polyclonal antibody raised against the c-terminal of NAT1 protein was used to determine the NAT1 activity in 31 samples of benign human prostatic tissue obtained from transurethral resection of prostate. Cytosols were prepared from all 31 samples and enzymatic activity of NAT1 was determined using western blotting with equal amounts of cytosolic protein. Immunohistochemical staining was used to characterise the distribution of the NAT1 protein within the prostate in 12 benign and 4 histologically proven prostate cancer specimens. A section of human breast tissue known to express NAT1 was used as a positive control.

RESULTS: Twenty two out of 31 benign prostate samples showed positive activity of NAT1 protein when tested using western blotting. Positive bands showed variation in intensity reflecting variable levels of expression. Positivity was confirmed in 8 out of 12 samples using immunohistochemistry. All 4 prostate cancer specimens were positive. Cytoplasmic staining of benign and malignant prostate epithelial cells, but not stroma, was observed in all positive samples.

CONCLUSIONS: This is the first report describing the distribution of NAT1 enzyme in the human benign and malignant prostate. This suggests that the human prostate is capable of locally activating environmental carcinogens and individual variation in the level of expression may play a role in predisposition to prostate cancer.

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PREVALENCE OF EJACULATORY DISORDERS AND THEIR BOTHERSOMENESS IN THE AGEING MALE: ASSOCIATION WITH LUTS SEVERITY AND THE IPSS BOTHER SCORE

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INTRODUCTION & OBJECTIVES: The association between LUTS severity and sexual dysfunction has been confirmed in a large multinational survey (MSAM-7) conducted in Europe and in the USA. In contrast to erectile dysfunction, ejaculatory disorders are often neglected in the ageing male population presenting with LUTS and other urogenital disorders.

MATERIAL & METHODS: 14,254 men aged 50-80 years completed a mail survey including validated symptoms scales (IPSS, DAN-PSS and IIEF), and questions on demographic and health characteristics.

RESULTS: 12,815 questionnaires were evaluated. The overall prevalence of ejaculatory problems (47%) was similar to erection difficulties (50%). The ejaculatory disorders are bothersome for a majority of the population (59%), even for those in the oldest age group (70-80 years). Multivariable analysis including age, IPSS class severity, IPSS bother score, co-morbidities confirmed that IPSS class severity (mild, moderate, severe) and the IPSS bother score are the strongest predictors of bothersomeness of the ejaculatory dysfunction. Nocturia, obstructive or irritative symptoms did not appear to play a specific role in this association.

CONCLUSIONS: The high prevalence of ejaculatory disorders was similar in each of the cohorts of aging men, and was bothersome for the majority of men in each age cohort. The severity of LUTS and IPSS bother scores should be considered as important risk factors for ejaculation disorders in older men.