

not observed any association for the studied variants when cases were stratified by age of diagnosis, family history, PSA, Gleason score and tumor stage.

Conclusions: Inherited variation in RNASEL, MSR1 and E-cadherin genes do not seem to contribute to PC development in Poland.

N3

Pelvic floor muscles evaluation in patients with erectile dysfunction after radical prostatectomy

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Introduction and Objectives: Evaluate bulbocavernosus and external anal sphincter muscles with needle EMG patients with neurogenic erectile dysfunction, 6–12 month after radical prostatectomy.

Material and Methods: The investigation of 14 patients with erectile dysfunction included vascular, hormonal, general and neurological examination, needle EMG analysis of pelvic floor muscles. In all patients MUPs mean amplitude and duration, muscle fibers spontaneous activity (FP and PSW) were evaluated.

Results: Motor and sensory deficit was revealed in 2 patients with herniated disc spondylotomy and 1 had spinal stroke; the rest 8 patients have no neurological disturbances. In 5 patients significant asymmetry of MUPs recruitment pattern and single-sided amplitude and duration decay accompanied by denervation activity (FP) was found. Spontaneous activity (FP and PSW) without signs of reinnervation was observed in 4 patients. In 6 patients moderate polyneuropathy with decreased limb and pudendal nerve conduction was found. In 1 patient the vegetative neuropathy was proved. In consideration of neurogenic dysfunction of pelvic floor muscles an additional active therapy was started. Erectile dysfunction symptoms (erection quality, rate of spontaneous erectile activity, sensitivity of external genitalia) were improved within 3–6 months.

Conclusions: Our results suggest the importance of pelvic floor muscles innervation status in patients with erectile dysfunction, from patients after RP. The pelvic floor muscles dysfunction should be considered an important component of erectile dysfunction pathogenesis and its improvement requires specific management.

N4

Phase II study of ketoconazole combined with weekly doxorubicin in patients with hormone-refractory prostate cancer

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Introduction and Objectives: Estramustine phosphate +/- vinblastine is an effective 1st line salvage treatment for hormone-refractory prostate cancer (HRPC). Nevertheless, the prognosis subsequent to progression after 1st line therapy is poor. We report the results with high doses of ketoconazole (KET) with hydrocortisone substitution and weekly doxorubicin (DOX). The principal end-point of the study was PSA response.

Material and Methods: The study comprised 40 patients (pts) with HRPC managed with KET 400 mg TID with replacement hydrocortisone (30 mg) per os DOX 35 mg/ sqm/ weekly, until progression. The pts were monitored clinically and with PSA measurement every 3 months (m). The pts with NR/PD are referred to chemotherapeutic regimens (docetaxel+pronisone).

Results: The median age was 71.5 years (y)(range 45–79), ECOG performance status 1 (range 0–2). All pts had PSA progression, 36 (90%) had bone metastasis (painful in 61% pts) and 16 (40%)

had measurable soft tissue metastasis. All pts have undergone bilateral orchiectomy at 1st line hormonal therapy. The median interval from diagnosis to the development of HRPC was 22.3 m (range 2.5–205.7). At beginning of therapy, the mean PSA value was 56.5 ng/ml (range 4.5–1580). The median number of courses administered was 7.5 (range 2–17). The median cumulative dose of DOX was 225 mg/sqm (range 50–600). The dose of KET was reduced in 14 pts (35%). With a median follow-up of 19.5 months (m), 9 pts (22%) were alive with no progression. In 31 pts (78%), their ds had progressed and they died of their ds. The median overall survival (OS) time was 13.05 m (95% CI, 8.7–17.3%) and the median time to progression was 3.9 m (95% CI, 2.0–5.9%). The overall PSA response was 45% (95% CI, 26–62%), 6 pts (15%) had no response and in 16 (40%), the ds progressed. Of 16 pts with measurable ds, the overall response rate was 37.5% (95% CI, 8–15%), with 2 complete (12%) and 4 partial (25%) response. 4 pts (25%) had no change and 6 (41%) their ds progressed. Using the PSA decline >50% the median survival time for responders was 24 m compared to 9 m for non-responders (p=0.0089). Toxicity was mild, with only 4 cases of non-hematologic grade 3 or 4 toxicity. The most frequent toxicity was nail changes (12), which was mainly grade 1 (8).

Conclusions: The combination of weekly DOX and KET is an effective, well-tolerated, 2nd line CT for HRPC accompanied with mild toxicity. A PSA decrease >50% appears to represent a significant marker in survival in a group of pts with apparently refractory, but still hormone sensitive PC. PSA response to KET+DOX can be identified within 1st 6–8 weeks of therapy allowing an early identification of responders and non-responders. Responders will benefit from continuation of therapy and non-responders might be recruited for salvage cytotoxic regimens at an early stage.

N5

The use of CT in the staging of prostate cancer

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Introduction and Objectives: According to current guidelines, patients at Herlev Hospital, Denmark, with intermediate or high risk prostate cancer (PC), who may be candidates for curative treatment, undergo pelvic lymphadenectomy (PLA) in order to detect lymph node metastases. Prior to this, an abdominal CT is performed in order to spare the patients with positive lymph nodes on CT unnecessary invasive PLA.

Objective: To assess the usefulness of CT in the staging procedure of PC.

Material and Methods: All patients with PC who had an abdominal CT in 2008 were reviewed. Furthermore, all patients with PC, who had a radical prostatectomy (RP) with PLA and patients who underwent PLA prior to external beam radiation (EBR) or brachytherapy (BT) were reviewed. The two groups were crossed, and the results from PLA were correlated to the CT findings.

Results: 171 patients had PLA. There were no patients who had CT that did not undergo PLA. The prevalence of lymph node metastases after PLA was 22.2%. In the group of patients who had RP or were scheduled for BT (85 patients with generally localized PC), the prevalence was 9.9%. In the group scheduled for EBR (generally locally advanced PC), the prevalence was 35.7%. 5 patients (2.9%) had positive CTs, 3 true positive and 2 false positive. The sensitivity, specificity, positive predictive value and negative predictive value of CT was thus 7.9%, 98.5%, 60% and 78.9%. Fine needle aspiration biopsy (FNAB) was only performed in 1 of the cases of positive CTs, showing no metastases. In none of the cases in this study did CT result

in avoiding PLA. In 17 patients (9.9%), CT revealed unexpected pathologic findings, which were succeeded by other invasive or non-invasive examinations.

Conclusions: The sensitivity of CT in this study is extremely low, corresponding to earlier findings. CT does not meet the demands of a meaningful diagnostic tool for this group of patients. The disadvantages are obvious: Exposition to unnecessary radiation, prolongation of the time of treatment and redundant expenses. We propose that CT should consequently not be performed in the staging of PC.

N6

BRCA2 gene mutation characterization in hereditary prostate cancer patients in Latvia

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Introduction and Objectives: Prostate cancer is one of the most commonly diagnosed tumors affecting men in Latvia. A significant factor in prostate cancerogenesis is genetic. The failure to identify highly penetrant genes in hereditary prostate cancer may result from the fact that multiple genes with a small to moderate effect are involved. Aim of the study is to evaluate the epidemiological features and BRCA2 gene mutation variations in hereditary prostate cancer in Latvia, as well as to consider association with other malignancies.

Material and Methods: In total 855 prostate cancer families were selected for our study that was identified from Nov-2003 to Jan-2009. Data were collected on their clinical characteristics; additionally blood samples were collected for DNA tests. Family cancer histories were analyzed according to clinical diagnostic criteria of hereditary prostate cancer, if at least one of the following criteria applied: (a) at least 3 affected blood relatives at any age; or (b) 2 affected blood relatives at age ≤ 55 years. Complete sequencing of the BRCA2 gene was performed for 9 probands from selected hereditary prostate cancer families.

Results: 855 family histories of prostate cancer patients were analyzed; from those 11 (1.3%, 95% CI: 0.7-2.3) families matched clinical diagnostic criteria of hereditary prostate cancer. The median age at diagnosis in this group was 65.4 (range 54-74) years. Besides BRCA2 polymorphisms in all analyzed cases, the novel missense mutation V2419D was detected in 73 years old proband with family history of 2 prostate, 1 lung and 1 stomach cancer. Along with prostate cancer at least 1 other localization malignancy was found among blood relatives in 9 (81.8%, 95% CI: 52.3-94.9) families of hereditary prostate cancer group. Distribution of the most frequent malignancies are: lung in 4 (36.4%) cases, uterine in 3 (27.3%) cases, stomach in 2 (18.2%) cases, breast in 2 (18.2%) cases, kidney in 1 (9.1%) case, leukemia in 1 (9.1%) case, unknown in 1 (9.1%) case.

Conclusions: Hereditary prostate cancer according to definitive clinical diagnostic criteria was found in 1.3% (95% CI: 0.7-2.3) of prostate cancer cases in Latvia. Further research of first degree family members and control group needed to confirm clinical significance of detected novel missense mutation V2419D in predisposition to hereditary prostate cancer and other localization malignancies.

N7

Trinucleotide repeat length polymorphisms of the androgen receptor gene – a step forward in understanding the pathogenesis of prostate cancer

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Introduction and Objectives: The pathogenesis of prostate cancer (PC) and the mechanisms responsible for progression of this tumor are not fully understood. The fact of androgen dependence of PC is known since 1940s. Action of androgens in prostate gland is mediated through the cytoplasmic molecule of androgen receptor (AR), which in turn stimulates expression of target genes correlated with regulation of cell cycle. Three regions of trinucleotide repeats were identified in the sequence of exon 1 of AR gene, namely (CAG)_n, (GGN)_n and (CCN)_n. Two former are characterized by repeat length polymorphisms, which influence the activity and protein yield of AR. Data from literature suggest that shorter (CAG)_n and (GGN)_n regions are associated with higher transactivation activity and higher protein yield of the AR and may therefore constitute a risk factor for PC. The aim of our study was to evaluate the correlation between (CAG)_n, (GGN)_n and (CCN)_n repeat length polymorphism of the AR gene and prostate cancer risk in polish population.

Material and Methods: The study was approved by local ethics committee. Written informed consent was obtained from 120 consecutive patients with pathologically confirmed prostate cancer, hospitalized in department of urology in Szczecin between 2004 and 2006. Population control group comprised genomic DNA samples isolated from umbilical cord blood samples of 120 male newborns born in the neonatology unit between 2004 and 2005. Amplification of polymorphic regions (CAG)_n, (GGN)_n and (CCN)_n was performed using PCR method with fluorochrome stained primers. Length of microsatellites was assessed by means of capillary electrophoresis and sequencing. Statistic analysis was performed with Statistica 7.0. software.

Results: There were repeat length polymorphisms identified in (CAG)_n and (GGN)_n regions. The number of CCN repeats remained constant in both groups. There was no significant correlation between number of CAG repeats and number of GGN repeats. In comparison with control group, patients with PC had a significantly ($p < 0.05$) higher frequency of shorter CAG ($n \leq 18$ repeats) and GGN ($n \leq 19$ repeats) regions.

Conclusions: Shorter variants of (CAG)_n and (GGN)_n microsatellites were already shown to be associated with higher biological activity of androgen receptor. Our current study demonstrated that they are more frequently found in patients with prostate cancer than in population control. These findings suggest their role in pathogenesis of prostate cancer, and make them candidates for future genetic models of PC risk assessment.