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Clinical and histopathological characteristics of Finnish familial prostate cancers

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Introduction and Objectives: Prostate cancer (PrCa) is the most common malignancy in men in many industrialized countries and positive family history of the disease is one of the strongest known risk factors of this disease. However, clinical features of familial PrCa are still poorly known. Families with PrCa have been collected in Finland since 1995. The aim of this study was to describe clinical characteristics of PrCas in the Finnish PrCa families using detailed analysis of patient records and histopathological samples.

Material and Methods: 202 Finnish families with 617 PrCa cases with confirmed histology and genealogy was collected. The mean number of affected men per family was 3.1. Complete clinical data including age and PSA at diagnosis, stage, grade and primary treatment was collected from hospital records. All the diagnostic biopsy samples, which were available (n=323) were collected, reviewed and re-graded by the same experienced uropathologist.

Results: The mean year of diagnosis was 1993 (range 1962–2006) and the mean age at diagnosis was 68 (range 43–98). The median value of primary PSA was 16 (range 0.8–11000). In clinical staging 49% had local T1–2 disease, 39% advanced, stage T3–4 disease and 17% of the patients had metastases at the time of diagnosis. In original histological grading 11% of the PrCa cases had WHO III, 56% had WHO II and 33% WHO I. After re-grading the grade distribution was: 22% WHO III, 65% WHO II and 13% WHO I. In original Gleason grading (available of 204, 63% of the samples) the distribution was 72% of Gleason score under 7, 18% of Gleason score 7 and 11% of Gleason score over 7. And after re-evaluation 38% of Gleason score under 7, 37% of Gleason score 7 and 25% of Gleason score over 7, respectively. The changes were statistically significant ($p=0.0015$ in WHO grading and $p=6.9 \times 10^{-8}$ in Gleason grading). The most common primary treatments were surgical castration (27%), radical prostatectomy (24%), chemical castration (11%) and radiation therapy (10%).

Conclusions: Familial PrCa has a slightly earlier age of onset than the mean age of diagnosis of PrCa in Finland. However, the criteria for Gleason grading has changed remarkably during the 14 years of collection. Therefore, preferably re-evaluation and re-grading by the experienced uropathologist is needed when comparing pathological grading of tumours from a long time period.

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Impact of Neoadjuvant Hormonal Therapy (NHT) on prostate cancer Gleason score and staging based on the comparison of TRUScoreBx and post radical prostatectomy specimens

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Introduction and Objectives: NHT is being applied in patients scheduled for operative treatment of prostate cancer due to reported by some authors potential; advantages as decrease of the size of the tumor and prostate facilitating surgery, rarer positive surgical margins, possibility to postpone surgery

and reduction of cancer cells spread into blood vessels. Nevertheless, NHT nowadays is not recommended by EAU (class A recommendation) due to lack of evidence of long term benefit, high costs of therapy, possibility of histological assessment alteration and suppression of PSA levels which makes this factor useless in post surgical evaluation of the patient. Objectives: The authors assess the influence of NHT on histopathological findings in prostate comparing specimens from TRUScoreBx and after radical prostatectomy.

Material and Methods: We retrospectively analyzed 215 radical prostatectomies performed in two reference centers (1, n=84 and 2, n=131) in the period 2007–2008. Only patients who had TRUScoreBx and radical prostatectomy performed in the same center were included (n=117; centre 1, n=44, centre 2, n=73). In the centre 1, all patients after TRUScoreBx received NHT (n=44). The LH-RH analog and antiandrogens were used. We compared both groups with respect to age, PSA levels, Gleason grading of biopsy specimens, timing of surgery after first diagnosis, Gleason score and staging (pT) after radical prostatectomy.

Results: We found no significant difference in age and PSA levels in both groups in the moment in first diagnosis of prostate cancer. There were no significant difference in Gleason score of TRUScoreBx in both groups. Timing of surgery was similar, median 73 days (18–568) in NHT group and median 65 days (27–331) in non-NHT group. The number of Gleason score <7 in NHT group was significantly lower than in non-NHT group (72.73% vs 90.41%). We found in post prostatectomy specimens pT3 stage in 41 (40.17%) cases and in this group we found significant difference between NHT and non-NHT group (pT3 11.36% in NHT group vs pT3 49.32% in non-NHT group).

Conclusions: The Neoadjuvant Hormonal Therapy applied after TRUScoreBx results in higher Gleason score and lower staging of the tumor in post radical prostatectomy specimens. Long NHT causes fibrosis and atrophy of gland epithelium.

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Volume and localization of the prostate tumor as the predictive factors of the prostate cancer stage

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Introduction and Objectives: Tumor volume (TV) is one of the most important prognostic factors in the tumor characteristics and prognosis for the prostate cancer (CaP) patient. Nevertheless, the value of TV as an independent prognostic factor still remains unclear (Bostwick D.G. et al., 2000). To define correlation between the TV, localization and the stage of the CaP analyzing prostate after the radical prostatectomy.

Material and Methods: During the last five years in the Federal State Institution Russian research center for radiology and surgical technologies – Petersburg 58 prostates obtained after the radical prostatectomy because of the CaP were analyzed pathomorphologically. Correlation between the prostate gland volume, peripheral zone (PZ) volume and transitory zone (TZ) volume was issued by the definition of appropriate linear coefficients (rxy). Using correlation analysis the data about absolute and relative tumor volume in a prostate gland were compared with pathological stage frequency (pT3).

Results: Correlation between the percentage of PZ volume and prostate gland volume is significant and inverse ($rxy=-0.58$), and between the percentage of TZ volume and prostate gland volume is significant and direct ($rxy=0.61$). In all patients with adenocarcinoma in TZ the tumor was limited by prostate gland (pT2) in contrast to the patients with adenocarcinoma in PZ (16 from 47 patients had pT3), in spite of less tumor volume

in patients with main tumor node in PZ ($1.87 \pm 0.38 \text{ cm}^3$) then in patients with main tumor node in TZ ($9.55 \pm 8.03 \text{ cm}^3$). For adenocarcinoma occupying the 1% of prostate gland volume, probability of pT3 stage is 18%, and in greater tumor volume 10% of probability of pT3 stage increases till 54% (correlating equation $y = 0,0289x + 0,0885$; $R^2 = 0,5434$).

Conclusions: Frequency pT3 stage depends on tumor volume predominantly in patients with adenocarcinoma in PZ, because pT3 stage is connected not only with the tumor volume, but also with its localization – more centrally tumor is localized, less probability of pT3 stage it would have. That is why the main role in staging has tumor volume in PZ. PZ volume in prostate gland is the least variable in older men. Risk of pT3 stage is higher in patients with small prostate gland volume. Results of current research could serve as a base for studying a prognosis of a pathological stage by the biopsy results before patients' distribution on the treatment group.

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Preventive role of postoperatively early introduced intracavernosal PGE1 injections on the development of blood flow disturbances in penis after radical prostatectomy

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Introduction and Objectives: Erectile dysfunction (ED) is a natural sequel of radical prostatectomy (RP). The operation results in apraxia of cavernosal nerves and development of impaired blood flow in penis; these changes tend to progress with time and lead to loss of spontaneous erections and irreversible vascular disturbances in cavernosal bodies. Application of the nerve sparing RP technique and early commencement of pharmacotherapy for ED may limit the development of the above mentioned pathologies. The aim of the study is to evaluate: 1) The incidence and characteristics of hemodynamic changes in penis after RP. 2) The influence of early started pharmacotherapy after RP on blood flow in cavernosal bodies.

Material and Methods: The prospective study comprised 67 preoperatively potent men. The preoperative diagnostics of potency consisted of anaemnesis, IIEF-5 questionnaire and Power Doppler evaluation of blood flow in penis following intracavernosal injection (ICI) of 10 ug of Alprostadil (only potent men – with normal results were enrolled). The Power Doppler study was repeated at 6 weeks and at 6 months after the surgery. At 6 weeks after operation all patients were offered to start the therapy with intracavernosal injections of 10 ug of PGE1 done twice a week, and were trained how to perform the ICI. The ICI-therapy was started and continued by 29 men (43.3%) – group 1. The remaining patients refused or stopped ICI within the study period – group 2.

Results: At 6 weeks after RP correct vascular blood flow, arterial, venous and mixed type of vascular disorders were found in 34 (50.75%), 18 (26.87%), 8 (11.94%) and 7 (10.45%) patients respectively. At this timepoint a significant decrease of mean PSV and RI values was found whereas mean EDV value increased slightly in comparison to the preoperative results. At 6 months after the surgery statistically significant differences of PSV, EDV and RI values were noted between group 1 and group 2. Mean results of Doppler examination for group 1 and group 2 were: PSV – 36.09 cm/s vs. 25.78 cm/s ($p = 0,000001$), EDV – 1.96 cm/s vs. 9.72 cm/s ($p = 0,000001$) and RI – 0.926 vs. 0.613 ($p = 0,000001$) respectively. Correct blood flow was diagnosed in 27 patients (93.1%) treated with ICI (group 1) and 4 (10.5%) men not treated with ICI (group 2). The frequencies of cavernosal vascular disorders in group 1 and group 2 were: arterial – 3.45% vs. 5.26%, venous 3.45% vs. 44.74% and mixed 0% vs. 39.47% respectively. The frequencies of correct blood

flow, venous and mixed vascular disorders in penis differed significantly ($p < 0,05$) between both groups.

Conclusions: 1. In the early postoperative period dominate arterial disturbances, and with the time venous leakage becomes more intense. 2. Early start of ICI-therapy seriously limits the development of hemodynamic dysfunctions in penis after radical prostatectomy

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Minimal-invasive surgery – what do we mean by this? Radical perineal prostatectomy (suprasphincteric) RPP and Transperineal Lymphadenectomy (TPL) as minimal-invasive method of the treatment of prostate cancer. Technique of the procedure and own experience

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Introduction and Objectives: Radical perineal prostatectomy (RPP) was introduced in 1905 by Young. Transperineal Lymphadenectomy (TPL) was introduced by HJ. Keller. Recently there is increasing interest in transperineal approach. The reasons for new interest in this procedure are: better knowledge of pelvic and perineal anatomy, development of new surgical techniques. Radical perineal prostatectomy (suprasphincteric) is characterized by: a very small surgical incision, omitting and preservation of large groups of muscles and blood vessels. RPP provides excellent access to prostate, urethra and neurovascular bundles, very quick postoperative recovery and good cosmetic effect. Operation time is short and performance of vesicourethral anastomosis is very precise, watertight and fast. Procedure is performed successfully even at "difficult" patients (obese, after large abdominal operations, after transurethral prostatic procedures, have large prostatic volume). In addition there is possible to perform lymphadenectomy through perineal incision simultaneously during radical perineal prostatectomy, as is presented in additional movie. The aim of the study is to present results of the radical suprasphincteric perineal prostatectomy and technique of transperineal lymphadenectomy and in addition a schemes, photos and film.

Material and Methods: Authors present the course of the operation and early postoperative period of patients with localized prostate cancer who were submitted to radical perineal prostatectomy. Av. age of patients: 62.5 years (48–75 years), initial PSA: av. 16.2 ng/ml (0.69–76.48), Gleason 5 (1+2 – 4+5), T1-T2b. There was no pathological changes in local lymph nodes.

Results: Operation parameters: time – av. 110 min, median blood loss – 350 ml, % of the nerve-sparing procedures – 23%, Postoperative period: Patient mobilization and oral nutrition – 1th day after operation. Median total hospital stay – 3.8 days. Removal of the urinary catheter – 7–10th day (in ambulatory). Removal of sutures – 10th day (in ambulatory).

Conclusions: Radical Perineal Prostatectomy (suprasphincteric) and Transperitoneal Lymphadenectomy is a valuable treatment method of locally advanced prostate cancer with advantages of low morbidity and short hospitalization. RPP with TPL certainly fulfills requirements of minimal invasive procedure and is characterized by short operating time, good cosmetic results and low percentage of side effects, early patient mobilization and quick start of oral nutrition in comparison to other methods. In opposition to other prostatectomy methods, RPP needs strict cooperation between patient and staff – patient should be profoundly informed about wound hygiene. According to the medical data, proportion of patients with postoperative erectile dysfunction and urinary incontinence is very similar to other methods.