

University of Medicine and Pharmacy Tîrgu Mureş
Doctoral School

PhD Thesis Summary:

**MANAGEMENT OF THE PATIENTS WITH SUSPECTED PROSTATE CANCER IN
PROSTATE BIOPSY**

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Introduction: Prostate cancer is a common urological pathology whose diagnosis is based on prostate biopsy and histopathologic examination. But not all histopathological examinations are conclusive. This thesis deals with aspects of patient management with suspicion of prostate cancer, from the etiological aspects, risk factors, to the final therapeutic decision of various prostate pathologies, evidenced by histopathologic examination after ultrasound guided prostate biopsy. In the literature was observed that approximately 50% of the patients were confirmed with prostate cancer at rebiopsy. Thereby, the question arises whether or not these patients should receive a rigorous observation and rebiopsy?

Study objectives: The main aim of the study was to determine the efficiency and the diagnostic value of transrectal ultrasound-guided prostate biopsy considered the "gold standard" in the diagnosis of prostate cancer, and the effectiveness of the used prostate biopsy nomograms. The secondary endpoints were the following: to determine a strategy of follow up for the patients with ultrasound- guided prostate biopsy and uncertain diagnosis, to identify the optimal time for rebiopsy of these patients, and to determine the optimal number of core necessary to confirm a definitive diagnosis. The study aimed also to evaluate the effectiveness of active follow up using PSA and digital rectal examination in these patients, and to increase awareness of the patients against this "uncertain" diagnosis and the need for close cooperation between physician- patients. By questionnaires we evaluate the efficiency of local anesthesia in prostate biopsy. We try the evaluation of the criteria for histopathologic diagnosis on the pathological results (length of modified tissue, the number of affected cores, the number of suspicious glands on biopsy, specific stains used for diagnosis), and evaluate the patients compliance against the present prostate pathology.

Materials and methods: The thesis is based on two retrospective and one prospective study including results of prostate biopsies performed in a total of 1627 men. The majority of the patients were admitted in the Clinic of Urology Tîrgu Mureş as follow 848 men between 2009-2012, 102 patients between 2013-2015. The third study included also 677 men who underwent prostate biopsy at Clinic of Urology, Iaşi. The inclusion criteria for this study were the following: suspicious local clinical examination (DRE), and/ or increased PSA. The indication for the prostate biopsy was according to European Urology guidelines. All the patients followed a well- established investigational protocol before ultrasound-guided prostate biopsy (DRE, PSA, and TRUS), and signed informed consent. In order to analyze and quantify the risk factors of prostate cancer we studied the following: age, race, positive family history / genetic, elevated PSA level, smoking, and obesity in a prospective study. Each patient enrolled in the study after signing the informed consent and completing the survey questionnaire, underwent a prostate biopsy.

Results: In total were studied data of 1627 patients with suspicion of prostate cancer. The mean age of patients included in the study was approximately 70 years (min. 21, max 90 years). The value of

total PSA ranged between 0.49- 3,899 ng / ml, with a mean value of 66.51 ng / ml, the median 13.5 ng / ml. PSAt value analysis showed that 98.11% of our patients with prostate biopsy had values above 4.0 ng / ml (normal maximum value admitted by laboratory). The risk factors were analyzed in the first study as increased age, hypertension, and diabetes, history of neoplastic disease, a family history of prostate cancer and the increasing number of risk factors were significantly associated with increased diagnosis of prostate cancer at prostate biopsy. At statistical analysis on age and PSAt we observed weak correlation (Spearman $r = 0.24$), but a statistically significant difference ($p = 0.02$) between the analyzed parameters. In the second study the statistical analysis of PSAt value and histopathological confirmed CP we have highlighted a statistically significant correlation between these parameters ($p = 0.001$). Studying the number of punctures performed and prostate volume (less than 40 cm³ or more than 40 cm³), we showed a statistically significant difference regarding positive diagnosis at initial biopsy with more cores ($p < 0.011$, $p < 0.0001$). The diagnostic efficacy of PC after the first set of biopsy was studied in the third study, and it was about 48%. The diagnosis has been improved to about 70% after rebiopsy. The most important complications after procedure were hematuria at 12.85%, rectorrhagy at 5.3% of the patients (minimal rectal bleeding presented all patients, which disappeared during the first 24 hours), acute urinary retention appeared at 3.06%, fever / chills at 9.31 % patients that required parenteral antibiotic treatment, and 2.47% of the patients developed urosepsis. Histopathologic diagnosis of ASAP was identified in approximately 3% ($n = 52$) of the studied cases. The detection rate of prostate cancer after rebiopsy in these cases was 41%.

Conclusions: Transrectal ultrasound-guided prostate biopsy is currently the main method of diagnosis in prostate cancer. PSA is still, in addition to clinical examination, the most important investigation with predictive role in the diagnosis of prostate cancer. The sextant prostate biopsy, described by Hodge is no longer adequate in the diagnosis of prostate cancer. To improve the detection rate of the prostate cancer is necessary to use protocols accepted in the literature. The optimal number of cores must take into account the prostate gland volume, patient age, local clinical examination, and the PSA level. It becomes necessary to introduce a national register for reporting cases of prostate cancer in Romania for improving therapy and for clear evidence on the incidence of prostate cancer, patient outcomes, and data regarding specific death. By increasing the number of cores and their peripheral orientation increase the detection of prostate cancer rate and decrease the need of rebiopsies. In order to have the maximum value detection and staging and in order to influence as little as possible morbidity, the number of biopsies should be dependent on the volume of the prostate gland, patient's age, clinical (DRE) and biochemical (PSA) suspicion. Prostate cancer diagnosis is the result of a complex algorithm that includes DRE, PSAt, transrectal ultrasound and ultrasound-guided prostate biopsy. Ultrasound-guided prostate biopsy is the key step of this algorithm because it is the only minimally invasive intervention which can finally confirm the diagnosis of prostate cancer. The presence of ASAP in a sample of prostate biopsy is a significant predictor for prostate cancer. Rebiopsy is mandatory in these cases, even outside of a solid clinical suspicion of prostate cancer. Patient awareness to the outcome of ASAP is obligatory to increase its adherence to rebiopsy.

Keywords: prostate cancer, prostate biopsy, cancer, prostate, risk factors, transrectal ultrasound, visual analogue scale.