

Abstract

Prostate cancer diagnostic algorithm

Aim: The aim of the study is to implement the latest scientific knowledge in the diagnosis of prostate cancer (PC). We focused on tumor markers, imaging methods, prostate biopsy methodology and we created a diagnostic algorithm based on a review of current literature in combination with our own experience.

Material and methods: The algorithm is divided into several branches, which have been individually subjected to clinical studies. Due to the low sensitivity and specificity of PSA, prostate health index (PHI) was added to the first line of patient stratification. 787 patients were primarily examined and these subsequently underwent radical prostatectomy. PHI levels were compared with definitive staging and grading. Cut-off values for PC detection and high-risk stratification, including locally advanced PC were determined. Next, 320 patients underwent prostate biopsy followed by radical prostatectomy. The cohort was further divided into two subgroups, patients with GS = 6 and patients with GS > 6. The ability of PHI to distinguish between insignificant and significant prostate cancer was evaluated. In a multicentric study with 395 patients, PHI with additional markers (tPSA, PSAD) and multiparametric magnetic resonance imaging of prostate (mpMRI) was assessed. In another study with 472 patients, the ability of PHI and other markers (tPSA, fPSA, fPSA / PSA ratio, [-2] proPSA / fPSA ratio) to predict the presence of significant PC, GS upgrading, extracapsular extension (pT3), and the presence of positive surgical margins was analyzed. Emphasis is placed primarily on performing mpMRI of the prostate before biopsy. Our attention was focused on PET / MRI with ⁶⁸Ga-PSMA-11. Our hospital is the only one in the whole Czech republic with access to this tracer. It was available for patients enrolled in a specific clinical trial treatment plan. 145 patients underwent ⁶⁸Ga-PSMA-11 PET / MRI examination. This highly-specialized imaging study had its specific place in our diagnostic algorithm - it was indicated for patients diagnosed with high-risk prostate cancer as well as for patients, in whom prostate cancer was not histologically confirmed yet, but who were in the highest-risk marker group. The last step in the algorithm is a prostate biopsy. The most effective prostate biopsy is MRI / TRUS fusion software-based targeted biopsy of the prostate. Thus, 495 patients were examined. In the case of biopsy naïve men systematic biopsy was added to targeted biopsy for comprehensive histological verification.

Results: The Ph.D. thesis is a collection of commented articles published in peer-reviewed journals, including journals with IF. The presented studies are a part of multicentric trials and of our own cohorts as well. In the first stratification of the patient, a cut-off value was set for PHI > 40 as suspected from PC and PSA according to age-specific levels, a PHI value > 100 as suspected for high-risk and locally advanced PC. We based these values on the results of our study with 787 patients after radical prostatectomy.

In a study with 320 patients for radical prostatectomy, the results of PHI were statistically significant for distinguishing between the GS = 6 and GS > 6 groups compared to other parameters, both after prostate biopsy (P = 0.0005) and in definitive histology (P < 0.0001). The best area under the curve (AUC) was achieved for PHI (0.7496) in the subgroup according to the definitive GS. In a study with 395 men undergoing prostate biopsy, combined PHI and mpMRI significantly increased the accuracy of predicting significant PC (p = 0.007). A result from a multicentric study in 472 patients undergoing radical prostatectomy found that the addition of PHI to a baseline multivariate model significantly increased the accuracy of pathological GS prediction by 4 % (p = 0.015) and GS upgrading by 5 % (p = 0.025). 88 out of 145 patients examined with ⁶⁸Ga-PSMA-11 PET / MRI were scheduled for radical prostatectomy, but only 60 (68 %) underwent the operation. This imaging study led to a change therapeutic approach in 18 patients (20.5 %). Pelvic lymphadenectomy was performed in 47 patients (78 %), lymph node metastases were histologically verified in two patients, ⁶⁸Ga-PSMA-11 PET / MRI detected only one N+ patient. In the group of patients undergoing ⁶⁸Ga-PSMA-11 PET / MRI before prostate biopsy, GS 6 was detected in 46 %, locally advanced PC in 33 % and metastatic PC in 25 %. In the group of patient undergoing MRI / TRUS fusion software-based targeted biopsy of the prostate, the detection of PC is high, 61.5 %, in biopsy naïve men 64.2 % and in re-biopsy 57.8 %.

Conclusion: The studies show that PHI can distinguish significant PC from insignificant, predict worse staging, upgrading in definitive GS and the presence of positive surgical margins after radical prostatectomy. The ⁶⁸Ga-PSMA-11 PET / MRI is a good staging examination. In our cohort, this examination led to a change in the therapeutic strategy in 20.5 %. Incorporating a MRI / TRUS fusion software-based targeted biopsy of prostate into the examination scheme leads to a high detection of PC and thus to a reduction of repeated biopsies. Based on these results, a diagnostic algorithm was created, enabling a fast and effective procedure in a patient with suspected PC according to the latest available methods.