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Original article

Tumor percentage but not number of tumor foci predicts disease-free survival after radical prostatectomy especially in high-risk patients

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Abstract

Objective: To evaluate the predictive value of tumor volume (TV), tumor percentage (TP), and number of tumor foci (NF) in patients with prostate cancer.

The prognostic relevance of TV, TP, and NF as predictors of biochemical recurrence (BCR) following radical prostatectomy (RPE) is controversial.

Patients and methods: The cohort consisted of 758 referred subjects who underwent RPE between 2000 and 2005 at the University of Muenster. The mean time of follow-up was 62 months. TV, TP, and NF were estimated visually with the assistance of a pathologic mapping grid for embedded whole-mount RPE specimens. In addition, TV and TP were assessed in a categorized fashion by using quartiles as cutoff points. Subgroup analyses for high- and low-risk patients using univariate and multivariate Cox proportional hazard analyses for BCR were performed.

Results: TV, TP, and NF were strongly related to tumor stage, Gleason score, surgical margin status, and preoperative prostate-specific antigen (PSA). In univariate analysis, all pathologic parameters including TV, TP, and NF were predictive for BCR. In multivariate analysis, only TP, tumor stage, and PSA level were independent predictors. In subgroup analysis, TP was an independent predictor for BCR in the high-risk group but not in the low-risk group.

Conclusions: TP, but not TV or NF, was found to be an independent predictor for BCR in patients after RPE. TP seems to be more relevant in high-risk patients (i.e., any of the following: >pT2, Gleason score >6, or PSA >20 ng/ml).

Keywords: prostate cancer; multifocal; prognosis; radical prostatectomy; tumor volume

1. Introduction

Several study groups have reported on the effect of tumor volume (TV) and associated parameters like tumor percentage ([TP], fraction of prostate infiltrated by tumor in percent) on the prognosis following radical prostatectomy (RPE). Most reports have shown a prognostic value of TV or TV-associated parameters, but the controversy remains whether TV provides additional information after correcting for standard prognostic parameters such as total preoperative prostate-specific antigen (PSA), tumor stage, Gleason score, and surgical margin status (SM). Studies that report an independent prognostic value of TV often consider populations with unfavorable tumor characteristics [1–3], whereas studies with more favorable tumor characteristics fail to find additional value of TV or related parameters [4–6].

Various methods of determining TV and associated parameters have been described. Computer-assisted measurement of TV seems to be the most accurate but also the most time-intensive method to assess TV. Simplified methods such as visual estimation [7–9] or measurement of the maximal tumor diameter [10] have been developed. Regardless of the method of assessment, the need to report TV remains a matter of debate. Its role as an independent predictor is not clearly defined. There are several studies confirming the independent

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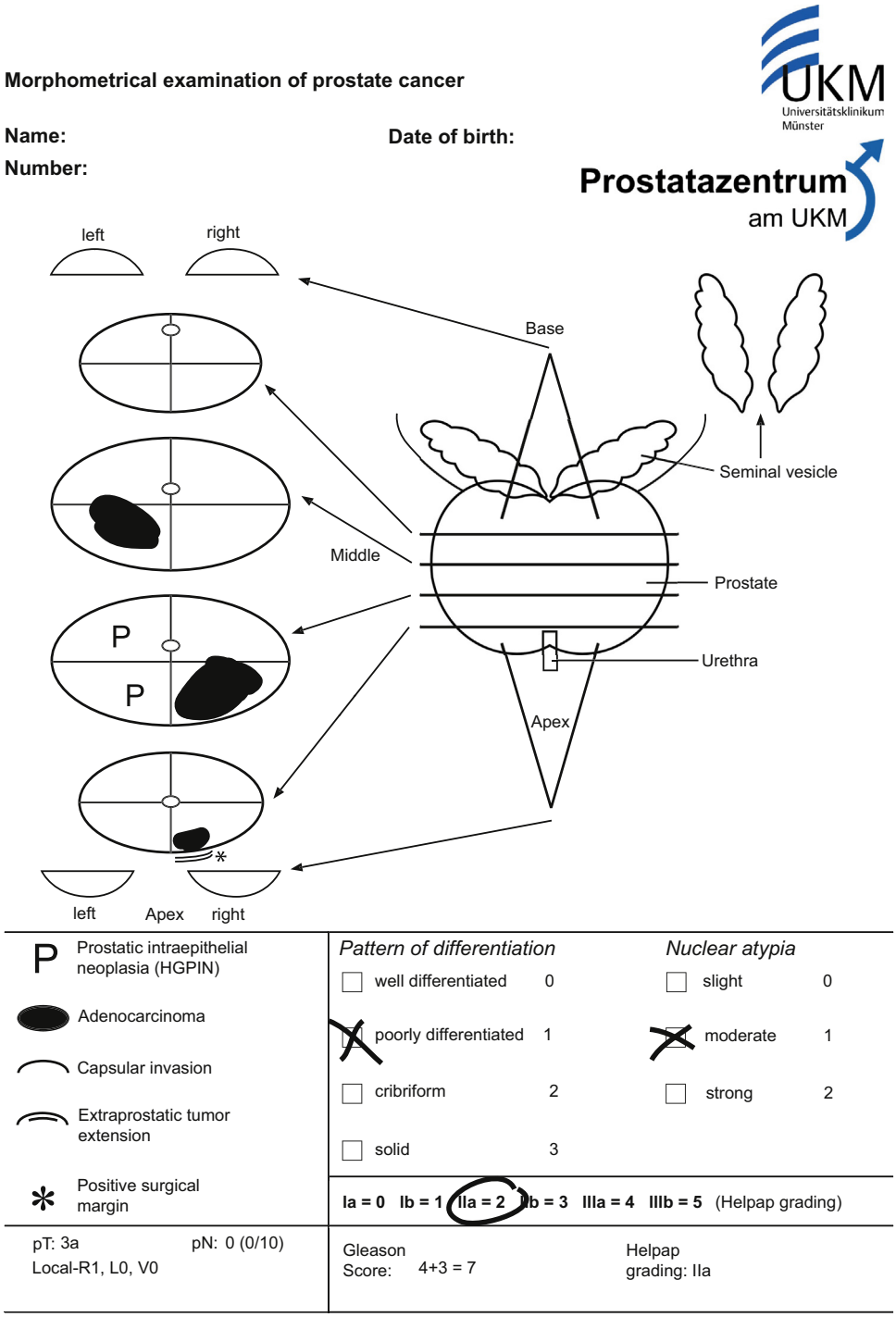

Fig. 1. Example of a mapping protocol including tumor extension, capsule, and surgical margin status.

prognostic value of TV [1,3,9,11–13], whereas other investigations did not support this assumption [4–6,8,14].

The tumor stage pT2 includes a large variety of tumors without capsular penetration, subclassified only by the involvement of both lobes of the prostate (pT2c) or more (pT2b) or less (pT2a) than half of the lobe. This means that very small tumors may be classified as pT2c if present in both lobes, and rather large tumors may be classified as pT2a if limited to 1 lobe, but occupying less than half of the lobe. Accordingly, there may be no relevant prognostic information derived from the pT2 subclassification [15]. We studied whether TV and related parameters could add independent prognostic information to the established histopathologic parameters and evaluated the role of TV in the subclassification of pT2.

There are only few studies considering the number of tumor foci (NF) in RPE specimens as a potential prognostic predictor [16–19]. Most investigations found no prognostic