872 Prospective comparison of molecular and histopathologic detection of lymph node metastases in prostate cancer patients undergoing radical prostatectomy with extended pelvic lymph node dissection: Prediction of biochemical recurrence

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Heck M.[1], Retz M.[1], Bandur M.[1], Souchay M.[1], Vitzthum E.[1], Weirich G.[2], Schuster T.[3], Autenrieth M.[1], Kübler H.[1], Maurer T.[1], Thalgott M.[1], Herkommer K.[1], Gschwend J.[1], Nawroth R.[1]

[1]Klinikum Rechts Der Isar, Technical University of Munich (TUM), Dept. of Urology, Munich, Germany, [2] Klinikum Rechts Der Isar, Technical University of Munich (TUM), Dept. of Pathology, Munich, Germany, [3]McGill University, Dept. of Family Medicine, Montreal, Canada

INTRODUCTION & OBJECTIVES: Molecular examination of lymph nodes (LN) using quantitative polymerase chain reaction (qPCR) promises a higher detection rate of LN metastases compared to standard histopathology. To prospectively compare both methods for prediction of biochemical recurrence-free survival (bRFS) in intermediate and high risk prostate cancer (PCa) patients treated with radical prostatectomy (RP) and extended pelvic lymph node dissection (ePLND).

MATERIAL & METHODS: Between 2010-2013 we prospectively enrolled 111 patients with intermediate or high risk PCa who were scheduled for RP. Patients with previous neoadjuvant hormonal therapy or primary radiation therapy were not included. A template ePLND was performed including obturatoric fossa, internal, external and common iliac vessels. LNs ≥3mm were bisected and examined by standard histopathology as well as qPCR for expression of Kallikrein 3 (KLK3). A threshold for unspecific baseline expression of KLK3 was determined in a control group (143 LNs of 25 male patients with histopathologic exclusion of PCa). Biochemical recurrence was defined by a postoperative prostate-specific antigen (PSA) increase > 0.2 ng/ml.

RESULTS: In 111 patients (29% intermediate and 71% high risk), 3173 LNs (median 27 LNs per patient) were dissected, of which 2411 LNs with a diameter ≥3mm were examined by both methods. Histopathology detected 68 LN metastases in 28 (25%) patients. Molecular LN analysis additionally detected 224 LN metastases and identified 32 (29%) patients harbouring LN metastases despite negative histopathology. PSA follow-up was available in 109 patients. At a median follow-up of 47 months (range 3-60) 43 of 109 (39%) patients developed biochemical recurrence. Biochemical recurrence occurred in 9 of 51 (18%) patients without LN metastases (pN0/molN0), 19 of 32 (59%) patients with exclusively molecular LN metastases (pN0/molN1) and 15 of 26 (58%) patients with LN metastases detected by histopathologic and molecular analysis (pN1/molN1). Patients with exclusively molecular LN metastases as well as patients with both histopathologic and molecular LN metastases had a significantly shorter bRFS (median bRFS pN0/molN0 (not reached) vs. pN0/molN1 (36.0 months [95%CI 17.4-54.6]) vs. pN1/molN1 (48.0 months [95%CI 36.1-59.9]); log-rank p-value<0.001). Using multivariate analysis adjusting for PSA level, postoperative Gleason score, tumor stage, margin status and histopathologic LN metastasis, detection of molecular LN metastases in pN0-patients was confirmed as an independent risk factor (Hazard ratio 5.1 [95%CI 2.2-12.0); p<0.001).

CONCLUSIONS: In intermediate and high risk PCa patients treated with RP and ePLND molecular LN

analysis showed a higher detection rate than standard histopathology and identified pN0-patients with a high risk for biochemical recurrence.