## Pathological characteristics and prognostic impact of peritumoral capsule 93 penetration in renal cell carcinoma after tumor enucleation

Eur Urol Suppl 2013;12;e93

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INTRODUCTION & OBJECTIVES: To evaluate the pathological characteristics of peritumoral capsule and the prognostic impact of capsule penetration on tumor recurrence in patients treated by tumor enucleation (TE) for RCC.

MATERIAL & METHODS: Between January 2005 and June 2011, 304 consecutive patients with single sporadic intracapsular RCC had TE. Peritumoral capsule status was carefully analyzed by two dedicated uropathologists. The degree and the side of capsule penetration if present were evaluated.

RESULTS: According to the peritumoral capsule status, of the 304 RCCs, in 155 (51%) the peritumoral capsule was intact and free from neoplastic penetration (PC-) while in 149 (49%) there were signs of penetration within its layers. Overall, 34.9% had capsular penetration on the parenchymal side and of those 75

(24.7%) had penetration only (PCK+) and 31 (10.2%) had capsular penetration and invasion beyond it (PCK++). Whereas, 14.1% had peritumoral capsule invasion on the perirenal fat tissue side and of those 18 (5.9%) had capsular penetration (PCF+) and 25 (8.2%) had penetration and invasion beyond it (PCF++). None of the patients had positive surgical margins detected at the pathologic examination.

Mean (median, range) follow up was 49 months (46, 25-69). During the study period, 13 (4.3%) patients had progressive disease. The 5-year progression-free survival rate for RCC according to PC status was: PC- 97.5%, PCK+ 98.2%; PCK++, 92.8%; PCF+, 82.6%; PCF++, 74% (p<0.0001).

The multivariate Cox model showed capsular penetration on the perirenal tissue side (PCF) to be the sole significant independent predictor of progression-free survival. In particular, patients with PCF had a 6-fold higher risk of disease progression than patients with PC- (CI 0.966, 42.295; p=0.0543), while patients who had PCK did not present a significant increased risk in developing a relapse (CI 0.292, 7.216; p=0.6488). Tumor stage, imperative indications for surgery and tumor greatest dimension were not independent predictor of progression. Then, we created a subset of tumors by eliminating PCF++ and PCK++ with the aim to evaluate the prognostic role of capsular invasion without exceeding the peritumoral capsule by the tumor. At multivariate Cox model, PCF+ was confirmed to be the sole significant independent predictor of disease recurrence with a 7-fold higher risk of disease progression than patients with PC- (CI 1.0.94, 50.610; p=0.0401).

CONCLUSIONS: Peritumoral capsule invasion on the perirenal adipose tissue side is a significant predictor of worse outcome and is the sole independent prognostic factor at the multivariate analysis with a relative risk of disease progression nearly 6 times higher than in patients with an intact peritumoral capsule. PCF appears to be a prognostic factor more accurate than TNM staging system for risk stratification of localized RCCs.