Prognostic differences and survival outcomes in patients with papillary renal cell carcinoma subtypes – A comparison between type I vs. type II

Giuseppe Rosiello[1], Fabio Muttin[1], Alessandro Nini[1,2], Gianfranco Baiamonte[1], Carlo Bravi[1], Marco Bandini[1], Alberto Martini[1], Luca Villa[1], Francesco Trevisani[1], Francesco Montorsi[1], Andrea Salonia[1], Alberto Briganti[1], Roberto Bertini[1], Alessandro Larcher[1], Umberto Capitanio[1]

[1] Unit of Urology, Division of Experimental Oncology, Urological Research Institute, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy;
[2] Department of Urology, Universitätsklinikum Düsseldorf, Düsseldorf, Germany;

INTRODUCTION

Controversial findings have been shown regarding the prognostic value of papillary subtypes (papillary type I vs. II), in the context of renal cell carcinoma (RCC) patients. The aim of the study is to investigate differences between papillary type I and papillary type II RCC subtypes at pre-, post, and long-term follow-up patient evaluation using a large, prospectively maintained database with a long-term follow-up.

RESULTS

Overall, 163 (54%) papillary type I and 137 (46%) papillary type II RCC patients underwent nephrectomy between 1991 and 2017. Preoperatively, papillary type II was associated with higher clinical size (p<0.001) and smoking status (p<0.01). Postoperatively, papillary type II was associated with higher tumor grade (50 vs. 8.5%; p<0.001), higher pathological stage (27 vs. 12%; p<0.001), presence of tumor necrosis (63 vs. 32%; p<0.001) and lymph vascular invasion (16 vs. 3.6%%; p<0.001). Median follow-up was 59 months. At 5-year follow-up, 15 (9.2%) papillary type I vs. 24 (18%) papillary type II experienced regional or distant progression and 13 (7.9%) papillary type I vs. 17 (12.4%) papillary type II died due to cancer-related death (CSM). In multivariable Cox-regression models, papillary type II resulted independently associated with higher risk of clinical progression (HR: 2.16 %; p<0.001) as well as of cancer-specific mortality (HR: 2.82%; p<0.001).

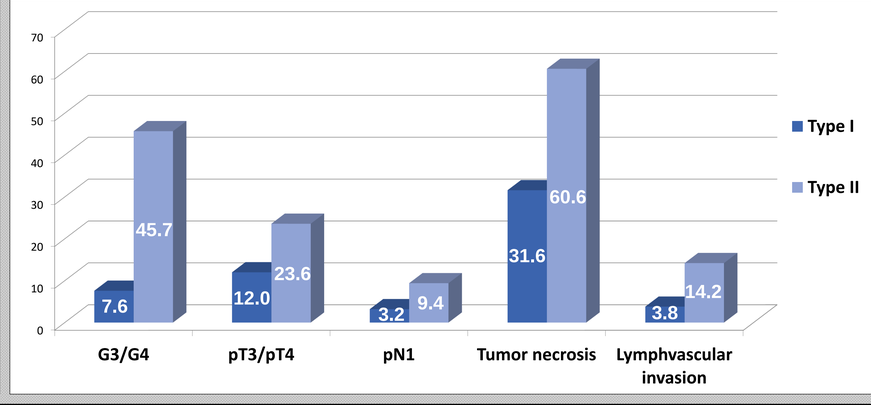
MATERIALS AND METHODS

Within a single institution database, we identified 300 patients with papillary type I (163; 54%) and papillary type II (137; 46%) renal cell carcinoma (RCC), treated with nephrectomy between 1991 and 2017. Kaplan-Meier plots and Cox-regression models were used to investigate clinical progression (CP), as well as of cancer-specific mortality (CSM) according to histology.

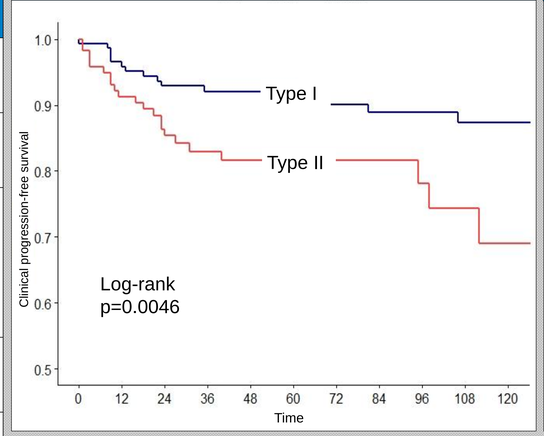
BASELINE

Variables		Papillary type I (n= 158; 55.4%)	Papillary type II (n= 127; 44.6%)	*p-value*
Age at surgery, years	Median	60	64	***<0.01***
	Range	52.2-69	55.5-70.5	
Gender, n (%)	Female	24 (15.2)	28 (22)	*0.2*
	Male	134 (84.8)	99 (78)	
Charlson Comorbidity Index, n (%)	0	82 (51.9)	61 (48)	*0.2*
	1	26 (16.5)	27 (21.3)	
	2	33 (20.9)	18 (14.2)	
	>3	17 (10.8)	21 (16.5)	
Clinical size, mm	Median	35	40	***0.02***
	Range	20-60	30-63	
Clinical N-stage, n (%)	cN0	146 (92.4)	109 (85.8)	***0.01***
	cN1	12 (7.6)	18 (14.2)	

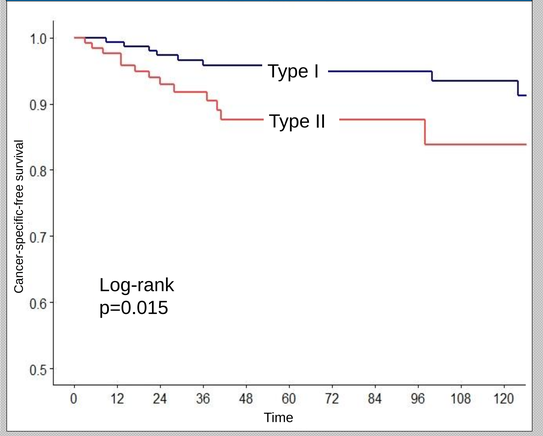
PATHOLOGICAL FINDINGS



CLINICAL PROGRESSION-FREE SURVIVAL



CANCER-SPECIFIC-FREE SURVIVAL



MULTIVARIABLE COX-REGRESSION MODELS

Predictors	CLINICAL PROGRESSION			CANCER-SPECIFIC MORTALITY		
	HR	95%CI	*p-value*	HR	95%CI	*p-value*
Type I	*Ref.*			*Ref.*		
Type II	2.41	(1.18-4.91)	***0.01***	3.33	(1.31-8.43)	***0.01***
Age	1.01	(0.98-1.04)	*0.3*	1.01	(0.97-1.05)	*0.5*
Clinical size	1.21	(1.13-1.31)	***<0.001***	1.25	(1.13-1.37)	***<0.001***
Year of surgery	0.98	(0.93-1.04)	*0.7*	0.91	(0.85-0.98)	***0.02***

CONCLUSIONS

Papillary type II subtype is associated with worse pathologic and oncologic outcomes compared to papillary type I subtype. Based on virtually the same rates of papillary type I and type II at histopathological examination, particular attention is needed in this unfavorable subgroup of RCC patients, which might deserve a more aggressive post-surgical surveillance. The very long follow-up represents a unique strength of this analysis.