TISSUE AND URINARY KIM-1 RELATE WITH TUMOR CHARACTERISTICS IN PATIENTS WITH CLEAR RENAL CELL CARCINOMA

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Objectives:

Clear renal cell carcinoma (cRCC) is the most common and aggressive form of RCC, often characterized by lack of early symptoms, signs and laboratory abnormalities. Recently, elevated uKIM-1 was recognized as a specific and sensitive marker for the early detection of cRCC. Also, KIM-1 represents a tissue and urinary marker which distinguishes clear cell from chromophobe RCC and oncocytoma at the molecular level. The objective of this prospective follow-up trial was to ascertain if the urinary kidney injury molecule-1 (uKIM-1) associates with tumor tissue (tKIM-1) expression and with the pathological characteristics of cRCC in radically nephrectomized (RN) and/or in partially nephrectomized (PN) patients with cRCC.
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Methods:

This clinical study included 40 patients subjected to RN/PN (cRCC group) and 30 healthy volunteers (control group). Urinary KIM-1 was determined by ELISA TIM-1/KIM-1 kit and normalized by urinary creatinine. Immunohistochemical staining (monoclonal anti-human anti-TIM-1/KIM-1/HAVCR antibody) was used for semiquantitative analysis of the tKIM-1 expression and expressed as a score (% KIM-1 positively stained tubules). Both markers were interpreted in terms of the tumor characteristics comprising tumor size, Fuhrman gradus, pathological (pT) stage, tumor/nodes/metastasis (TNM) stage, lymphovascular invasion and type of surgery RN/PN.

PATIENTS -PH caracteristics-		uKIM-1.0 (ng/mgU$_{cr}$)		p
		AVERAGE VELUES (SD)	MEDIAN (range)	
TUMOR SIZE	≤4 cm	0.37 (0,32)	0.282 (0.109-1.404)	0.003
	4.1-7 cm	0.28 (0.16)	0.23 (0.076-0.565)	
	>7 cm	2.2 (3,02)	0.662 (0.337-9.8)	
TUMOR GRADUS	G2	0.42 (0.53)	0.257 (0.076-2.92)	0.002
	G3	2.74 (3.57)	0.783 (0.342-9.8)	
pT STADIUM	pT1a	0.27 (0.11)	0.25 (0.109-0.401)	5.42*10^{-5}
	pT16	0.25 (0.15)	0.21 (0.07-0.56)	
	pT2a	0.38 (0.08)	0.34(0.34-0.47)	
	pT3a	2.07 (2.8)	0.8 (0.26-9.8)	
TNM STADIUM	I	0.26 (0.13)	0.22 (0.076-0.565)	0.0001
	II	0.38 (0.08)	0.31 (0.147-0.873)	
	III	1.45 (1.78)	1 (0.144-5)	
	IV	5.15 (6.58)	2.76 (0.529-5)	

y = 0.40922x - 1.33680
p=0.541

Diffuse cytoplasmatic immunoreactivity 3+

Results:

Preoperative uKIM-1 was significantly higher in the cRCC group compared to controls (p=0.0015), such as uKIM-1 was statistically higher in RN than PN patients (p=0.003). Postoperatively, uKIM-1 decreased to control values. Urinary KIM-1 values were significantly associated with tumor dimension, Fuhrman grade, pt and TNM stage (p=0.003, p=0.002, p=5.42*10^{-5}, p=0.0001, respectively). Expression of tKIM-1 was documented in all nephrectomized patients. We demonstrated significant associations between concentrations of uKIM-1 and KIM-1 tumor expression (p=0.041). The sensitivity and specificity of uKIM-1 concentrations to identify patients with kidney cancer was assessed by ROC curve analysis . Based on this, the area under the curve for KIM-1 was 0.73 (p=0.008).

Conclusions:

Based on the accomplished associations, we found uKIM-1 as a highly sensitive marker for cRCC diagnosis.

References:

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