TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2013) 43: 459-463
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doi:10.3906/sag-1207-83

Is renal cell cancer stage migration valid throughout the world?

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Received: 23.07.2012 • **Accepted:** 11.09.2012 • **Published Online:** 29.05.2013 • **Printed:** 21.06.2013

Aim: To investigate changes in tumor sizes and pathological tumor stages in patients undergoing surgery for renal mass between 2000 and 2011.

Materials and methods: The data of 157 patients who underwent surgery for renal mass, including TNM stage, size, and Fuhrman grade at final pathology, were evaluated retrospectively.

Results: The mean pathological size of the tumor in the whole population of the study was 6.97 cm. The mean size of the renal mass was 7.22 cm, 7.05 cm, and 6.91 cm in group 1, group 2, and group 3, respectively, and the difference was not statistically significant. Of the renal cell carcinomas, 57.2% were stage I, 22.7% were stage II, 10.3% were stage III, and 9.6% were stage IV. Differences between groups in terms of changes in tumor stage were not statistically significant.

Conclusion: We observed that there was no downward stage migration in renal cell carcinoma during the 12-year study period.

Key words: Renal cell carcinoma, stage migration, histology, grade

1. Introduction

The incidence of renal cell carcinoma (RCC) is globally more than 200,000 cases every year (1). RCC is the most common malignant tumor of the kidney (2). RCC is more prevalent in men than in women, and it occurs most frequently at 50–70 years of age (3). The incidence of RCC has increased by 3%–4% on average per year since the 1970s. The changes in prevalence are associated with potential risk factors such as hypertension, smoking, and obesity, as well as being largely related to the more widespread use of abdominal imaging modalities for the diagnosis of a variety of abdominal and pelvic problems (4).

Depending on the prevalence of the use of ultrasonography and computerized tomography (CT), there are different results for downward stage migration over time (5). The detection rate of tumors at lower stages and smaller sizes has been reported to have increased in US and European publications (6–8).

On the other hand, a retrospective study from Australia showed a different and striking result, which was that there was no significant stage and size alteration between 1993 and 2007 (9).

Since our clinical observations are not different from the results of the Australian study, we intended to investigate the changes in renal tumor size and pathological tumor stage in patients undergoing surgery at our center between 2000 and 2011.

2. Materials and methods

All patients undergoing partial or radical nephrectomy with a renal mass diagnosis performed by 4 surgeons at Cumhuriyet University Medical Faculty, Department of Urology, between January 2000 and December 2011 were included in the study. The recorded data of 174 consecutive patients were examined, including patient demographics, TNM stage, size, and Fuhrman grade at final pathology, and the data of 157 patients with accessible complete information were evaluated retrospectively.

Tumors were staged according to the 2004 edition TNM classification system, and cases diagnosed before 2004 were restaged using 4th edition criteria (10). T stage, or tumor size, was recorded the largest tumor diameter (cm) reported in the final pathology report. Table 1 illustrates the clinicopathological parameters of 157 patients.

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Table 1. Clinicopathological parameters of the entire study cohort (n = 157).

	Number	%
Sex		
Male	89	56.7
Female	68	43.3
Age (years)		
	61.46 ± 12.09	
Tumor size (cm)		
	6.97 ± 3.718 Median (interquartile range): 6 (1–20)	
Pathologic stage		
pT1	83	57.2
pT2	33	22.7
pT3	15	10.3
pT4	14	9.6
Histology		
Clear cell RCC	121	83.4
Papillary RCC	15	10.3
Chromophobe RCC	8	5.5
Mucinous tubular and spindle cell	1	0.6
Benign tumors		
Oncocytoma	8	66.6
Angiomyolipoma	4	33.3
Nuclear grade (Fuhrman)		
G1	1	0.6
G2	67	46.2
G3	46	31.7
G4	31	21.3

The data were divided into 3 equal time periods: group 1, from 1 January 2000 to 31 December 2003; group 2, from 1 January 2004 to 31 December 2007; and group 3, from 1 January 2008 to 31 December 2011. The significance of trends in histological subtype, Fuhrman nuclear grade, tumor size, sex distribution, and benign lesions were also assessed.

The results were analyzed using SPSS 14. The chi-square test and analysis of variance were used, and a P-value of less than 0.05 was considered significant. All procedures were performed in accordance with the ethical guidelines of the Cumhuriyet University Medical Faculty.

3. Results

No reliable staging record was available in the data of 18 patients. We were able to fully evaluate the data of the remaining 157 patients.

The average age of the patients was 61.6 years (ranging between 10 and 86 years). Overall, there were 23 cases in group 1 (2000–2003), 40 cases in group 2 (2004–2007), and 94 cases in group 3 (2008–2011). With respect to age, there was not a significant difference at the diagnosis during the study period; the average ages of the patients at operation time were 63.30 years for group 1, 60.31 years for group 2, and 62.50 years for group 3 (P = 0.484).

The male-to-female ratio in the study population was 1.32 (89 men and 68 women). The between-group sex ratio was similar, and changes over time were not statistically significant (P = 0.319).

The mean pathological size of the tumor in the whole study population was 6.97 cm (1–20 cm). The mean size of the renal mass was 7.22 cm, 7.05 cm, and 6.91 cm in group 1, group 2, and group 3, respectively, and the difference was not statistically significant

(P = 0.45).

During the 12-year period, 57.2% of RCCs were stage I, 22.7% were stage II, 10.3% were stage III, and 9.6% were stage IV. The difference between groups in terms of changes in tumor stage was not statistically significant (P = 0.424) (Table 2; Figure 1).

Table 2. RCC stage percentage distribution by time period: n (%).

Groups	pT1	pT2	pT3	pT4
2000–2003	13 (56.5)	5 (21.7)	2 (8.7)	3 (13.0)
2004–2007	20 (60.60)	8 (24.24)	3 (9.09)	2 (6.06)
2008–2011	50 (56.17)	20 (22.47)	10 (11.23)	9 (10.11)

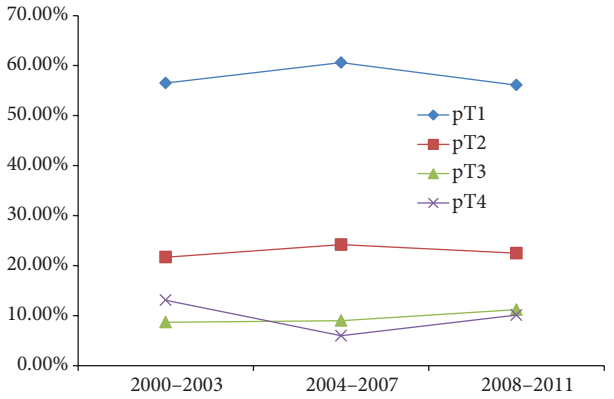

Figure 1. RCC pathological stage distribution by diagnosis year groups.

The most frequent histologic subtype of kidney cancers was clear cell renal carcinoma, in 119 out of 157 patients, followed by 14 papillary, 10 chromophobe, and 1 mucinous tubular and 1 spindle cell. Tumors were reported to be benign in 12 cases; 8 of these were oncocytomas and 4 were angiomyolipomas. Table 1 illustrates the distribution of the histology types of all cases, and Table 3 illustrates the distribution of the histology types for groups. Although the difference was not statistically significant, a decreasing trend was observed in the number of clear cell conventional carcinomas (P = 0.207) (Figure 2). It was observed that there was an increase in the papillary renal cell cancer rate from 4.3% in group 1 to 7.5% in group 2 and 11.7% group 3; however, the difference was not statistically significant (P = 0.207).

Fuhrman nuclear grade, which is considered to be another prognostic factor for RCC, was assessed in 145 out of 157 cases, and 0.6% were Fuhrman grade I, 46.2% were Fuhrman grade II, 31.7% were Fuhrman grade III, and 21.3% were Fuhrman grade IV. When changes between the groups were evaluated, a statistically significant increase was observed in the rate of Fuhrman III and Fuhrman IV (P = 0.03) (Table 4; Figure 3).

Table 3. RCC histological subtype* percentage distribution by time period: n (%).

Groups	Clear cell RCC	Papillary RCC	Chromophobe RCC
2000–2003	22 (95.65)	1 (4.37)	0 (0)
2004–2007	27 (81.81)	3 (9.09)	2 (6.06)
2008–2011	72 (80.89)	11 (12.35)	6 (6.74)

*Mucinous tubular and spindle cell carcinoma not included.

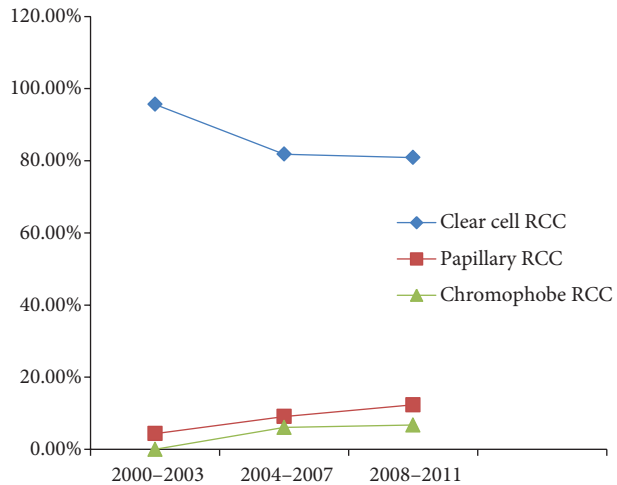

Figure 2. RCC histological distribution by diagnosis year groups.

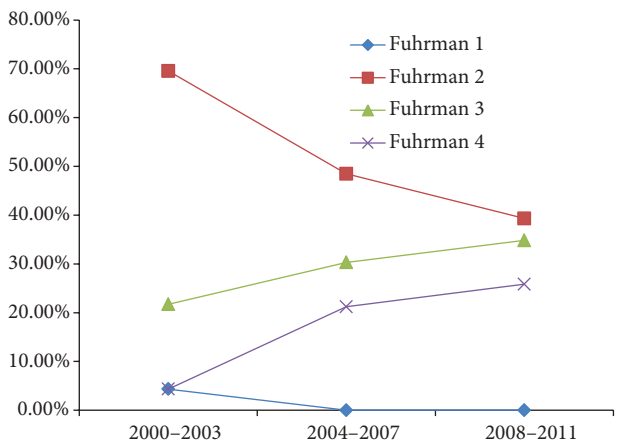

Figure 3. RCC Fuhrman grade distribution by diagnosis year groups.

4. Discussion

RCC constitutes 3% of all adult solid tumors (11). The incidence of RCC increases by about 3% per year (4). The results of this study revealed an upward migration in

Table 4. RCC Fuhrman grade percentage distribution by time period: n (%).

Groups	Fuhrman 1	Fuhrman 2	Fuhrman 3	Fuhrman 4
2000–2003	1 (4.34)	16 (69.56)	5 (21.73)	1 (4.34)
2004–2007	0 (0)	16 (48.48)	10 (30.30)	7 (21.21)
2008–2011	0 (0)	35 (39.32)	31 (34.83)	23 (25.84)

Fuhrman grade from I–II to III–IV, whereas no migration in stage existed in patients with RCC who underwent surgery in our institution during the last 12 years.

Luciani et al. reported that the proportion of clinical stage T1–T2 tumors increased from 49% to 74%, while the percentage of patients with M1 disease decreased from 20% to 10%. Similar patterns have been noted for pathologic stage (6). In a retrospective study conducted on a great number of patients undergoing surgery between 1993 and 2004, researchers found an increasing representation of stage I tumors, from 51 to 60%, and decreasing proportions of stage II and III disease (7). The results of another study from Europe, in which 2333 RCC cases were evaluated retrospectively within a period of 25 years, showed a downward stage migration towards organ-confined tumors, with an increasing representation of pT1–pT2 tumors and decreasing proportions of pT3–pT4 tumors (8). In this study, there was no stage migration, in contrast to Europe- and US-based studies. In another study from Australia, Doeuk et al. evaluated the pathological results of 547 patients undergoing radical or partial nephrectomy between January 1993 and December 2007, and they reported that they did not observe any migration towards earlier-stage and smaller RCCs, in line with this study (9). However, in both studies, the assessment of downward stage migration at presentation cannot be fully achieved in terms of study design. Although cases were appropriately stratified by stage according to year at diagnosis, a significant limitation in interpreting the results of both studies is the inclusion of only surgically treated cases, with no mention of the incidence of renal mass lesions on imaging criteria alone or the numbers of patients included in active surveillance programs. It is obvious that all informative data regarding the change in the proportions of stages, grades, mass sizes, and histologic subtypes should have included not only operated cases but also the proportion of biopsy-confirmed cases of RCC managed by active surveillance or by probe-ablative therapies. In addition to these tangible limitations, we think that general belief about the widespread use of abdominal imaging techniques is not applicable in the world as a whole, and the failure of providing health care may be responsible for this contradiction.

Pichler et al. reported that the clear cell RCC rate was 82%, the papillary RCC rate was 10.9%, and the chromophobe RCC rate was 3% (8). The rates determined in this study were 77.6% for clear cell RCC, 9% for papillary RCC, and 5.1% for chromophobe RCC. The histology types in this study showed patterns of frequency similar to those in other studies (7,9).

Another finding in this study was that an upward migration of Fuhrman grade towards III–IV tumors was determined in course of the time. The rates of Fuhrman III and IV increased from 21.7% and 4.3% to 33% and 24.5%, comparable to the findings of Doeuk et al., who reported that the rates of Fuhrman III and IV increased from 17.6% and 6.8% to 30.8% and 8.3% (9). However, Pichler et al. reported no change in Fuhrman grade in a 25-year period at a European center (8). The reason for this is not so obvious; however, the Fuhrman nuclear grade is not objective, and the prognostic role of the Fuhrman grading system is restricted by its subjective nature and observer instability because of the poor characterization of nuclear and nucleolar characteristics. We think that it could represent changing patterns of scoring by pathologists.

The greatest frequency of benign lesions in renal tumors is smaller than 3 cm, as previously published (12–14). This study concludes that benign lesion sizes are much larger than those reported in other studies. According to our findings, the mean sizes of oncocytoma and angiomyolipoma were 5.25 cm and 6.50 cm, respectively. This difference may be associated with the assessment of only masses that were removed by radical or partial nephrectomies. Cases diagnosed by biopsy and monitoring of small sizes were not included in this study.

In conclusion, we observed that there was no downward stage migration in RCC during the 12-year study period at our institution. Although it remains valid only for operated cases, which themselves are subject to surgeon selection bias, we think that shifts in stages and other parameters of diseases may show regional differences throughout the world.

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