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Changes in Renal Cell Carcinoma Features: A Comparison Between Two Periods

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Abstract

Objectives

The aim of this work is to assess the changes that had occurred in epidemiological and clinical features of renal cell carcinoma in tunisian adults and how its topographic, therapeutic, pathological and prognostic specificities had become. This study is based on data collected over the three last decades with a comparison between two 15-year periods.

Methods

We carried out a comparative, retrospective, descriptive and analytical monocentric study on 208 files of patients with renal cell carcinoma treated and monitored in the urology department over a period of 30 years spanning January 1990 to December 2019. These patients were divided into two groups: the first group concerns the period from 1990 to 2004 and the second group covers the period from 2005 to 2019. This collect was carried out because of different Data sources: medical hospitalization records, follow-up of patient consultations, pathological examinations and operative reports.

Results

The average age was 58 years (ranges: 20 and 89 years) with a male predominance (sex ratio = 1.39) with decrease in the sex ratio during the second period (1.1) whereas it was 2 during the first period. Hypertension and smoking were the most found risk factors and we found a statistically significant increase in obesity during the second period of the study. Renal cell carcinoma is increasingly discovered incidentally during an imaging study (32.2%). In addition, we saw an increase in incidental cases during the second period (34.8%) compared with the first period (29.1%), with a decrease in tumor size at time of diagnosis. In fact, this latter was 6.83 cm for the period from 1990 to 2004, whereas it was only 5.94 cm for the period from 2005 to 2019. The majority of renal cell carcinomas were classified pT1-T2 (84.1 %) during the two study periods. Over the whole study period, 152 patients had to undergo an enlarged total nephrectomy. Whereas 51 patients were offered a partial nephrectomy. Hence, the performance of this conservative surgery had statistically increased since 2009. Histologically, renal cell carcinoma was largely dominated by clear cell carcinoma (71.6%) and low nucleolar grade (77.8%) and we found a statistically significant increase in the number of cases of chromophobic cell carcinoma and multilocular cystic renal cell carcinoma during the second study period. The average follow-up duration was 37.6 months (ranges were 1 and 277 months). The 5-yr overall survival was 80.9%. Multilocular cystic renal cell carcinoma and chromophobic cell carcinoma had the best prognosis with a 5-yr overall survival rates of 100% and 93%, respectively.

Conclusion

By comparing the results of the two study periods, renal cell carcinomas were shown to be increasingly discovered incidentally at a younger age, with a widening use of conservative surgery. Clear cell carcinoma is still the most frequent histological type. The number of obese patients, of chromophobic cell carcinoma type cancers and metastatic disease cases had statistically increased during the second period.

Keywords: Renal cell carcinoma; Epidemiology; Risk factors; Treatment; Prognostic

Introduction

Kidney cancer, and particularly Renal Cell Carcinoma (RCC), dominates solid adult kidney tumors, and accounts for about 3% of all adult malignant tumors. It ranks third among urological cancers in adults after prostate and bladder cancers [1].

Kidney cancer features has deeply changed over the last decades. While we still see 15 to 20% of advanced forms [2], we also observe 40% of asymptomatic forms, discovered incidentally, with smaller tumors of less than 4 cm [3]. Eighty percent of these tumors are limited to the kidney [4]. The standard treatment for these tumors is enlarged nephrectomy, but conservative surgery has been increasingly used [5]. The prognosis of these tumors depends on several clinical, histological, and therapeutic factors.

Our study, based upon data collected over two periods of 15

years each and covering 208 cases collected over the total period of 30 years, aims to review the changes in epidemiological, clinical, topographical, therapeutic, anatomopathological and prognostic features of renal cell carcinomas in adults.

Materials and Methods

We carried out a retrospective, descriptive, analytical, and single-center study of 208 cases of patients with renal cell carcinomas, all collected in the urology department over a period spanning 30 years from January 1990 to December 2019.

We excluded benign tumors, secondary malignant tumors, sarcomas, and patients under 20 years. During the period from 1990 to 2004 (G1), 96 patients were included versus 112 patients during the period from 2005 to 2019 (G2).

The diagnosis of kidney cancer is radiological and was confirmed by the pathological study of the surgical specimen or the biopsy sample. This study was carried out in the anatomopathology services of Farhat Hached hospital in Sousse (from 1990 to 1996), and Fattouma Bourguiba hospital in Monastir.

We analyzed in all patients the following data: age, sex, risk factors, onset symptoms, surgery, histological types, nucleolar grade, TNM classification, duration of follow-up, analysis of survival related to different histological types. Then, we compared the results of 2 study periods: the first period lasts from 1990 to 2004 and the second period lasts from 2005 to 2019.

Data processing was performed using SPSS software version 19.0.

Survival analysis was performed according to the Kaplan-Meier model.

Results

Our survey included 208 patients which ages ranged from 20 to 89 years and the average age was 58 years. The average age at diagnosis for the period 1990-2004 was 59.17 years for 96 patients, while the average age from 2005 was 56.73 years for 112 patients.

The sex ratio for the period from 1990 to 2004 was 2 for renal cell carcinoma, against 1.1 for the period from 2005 to 2019 with an average sex ratio for the two periods of 1.39.

High blood pressure and active smoking were the most prominent risk factors in our series, at 34.6% and 20.2% rates respectively. We found a statistically significant increase in the number of obese patients during the second period of the study compared with the first period.

The various risk factors found are presented in Table 1.

Table 1: Risk factors variation between the two periods of the study.

Risk factors n (%)	Number of patients			Percentage	P
	1990-2004	2005-2019	Total		
High blood pressure	35 (36.4)	37 (33)	72	34.6	0,16
Smoking	20 (20.8)	22 (19.6)	42	20.2	0,13
Obesity	8 (8.3)	22 (19.6)	30	14.4	0,008
Hemodialysis	2 (2)	2 (1.7)	4	1.9	0,1
VHL* disease	1 (1)	2 (1.7)	3	1.4	0,18

*VHL : Von Hippel Lindau

Specific symptoms revealed renal tumors for 141 patients in our series, i.e 67.7%. And it was incidental on imaging studies for 67 patients, i.se 32.2%, including 28 cases before 2005 out of 96 patients, i.e. 29.1%. Since 2005, the rate of incidental cases had increased up to 34.8 % i.e. 39 patients out of 112.

The majority of kidney cancers were staged T1-T2 during both periods of the study. In 175 cases the tumor was staged T1-T2, in 31 cases staged T3, and 2 patients were staged T4. For node involvement, 191 cases of kidney cancers were staged N0. Regional metastatic lymph node involvement was noticed in 17 cases. For eight patients, metastatsis were present (3 lung metastasis, 1 hepatic metastasis and 4 bone metastasis) and we observed a statistically significant increase in metastatic RCC during the second period of the study (Table 2). The tumor size was 6.83cm for the first period, while it was 5.94cm for the second period.

Table 2: Renal tumors pTNM variation between the two periods of the study.

pTNM ; n (%)	Number of patients			Percentage	P
	1990-2004	2005-2019	Total		
T1 – T2	79 (82.2)	96 (85.7)	175	84.1	0,1
T3	16 (16.6)	15 (13.3)	31	14.9	0,8
T4	0	2 (1.7)	2	0.96	0,32

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N0	90 (93.7)	101 (90.1)	191	91.8	0,1
N+	6 (6.25)	11 (9.8)	17	8.1	0,13
M0	95 (98.9)	105 (93.7)	200	96.1	0,09
M1	1 (1)	7 (6.25)	8	3.8	0,008

Two hundred and two patients had unilateral tumor, the tumor was bilateral in three cases, one of which was part of Von Hippel Lindau's disease. Three of our patients had an anatomically or functionally unique kidney.

One hundred and fifty-two patients or 73% had an enlarged total nephrectomy. Partial nephrectomy was performed for 51 patients, 6 partial nephrectomies were performed during the first period and 45 partial nephrectomies were performed during the second period of the study (Figure 1).

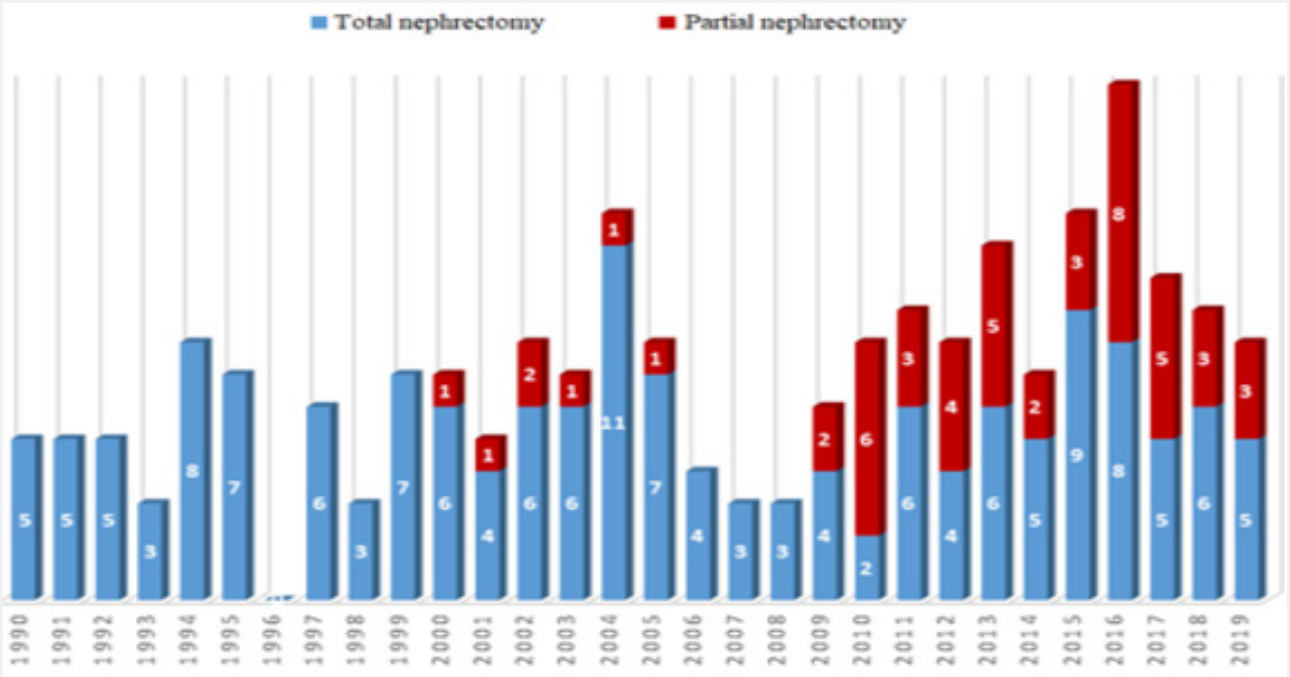

Figure 1: Evolution of the type of nephrectomy over the years.

Among the 8 metastatic patients, 5 had a renal biopsy.

In our series, as reported by other authors, the average age of patients at time of RCC onset is 58 years. M. Benjelloun et al. [6] found an average age of 60 years. In addition, another study published by Poisson et al agree with the fact that the average age is 59.6 years [7].

We found that for the last years, the age at time of kidney cancer diagnosis had been lowering. Indeed, in our series, the average age for the second period had become 56.73 years. A recent Indian study showed that up to 18% of patients are under 40 at the time of diagnosis [8].

An American study showed a male predominance with an incidence of 4.88 / 100,000 inhabitants [9]. There is also a male predominance in European countries, noticed in the study published by Ljungberg et al. [10]. In our series, a male predominance was found, i.e. 58.2% of the headcount with a sex ratio of 1.39. Benjelloun et al. [6], in their study, found the sex ratio to be 2.1. We found almost the same sex-ratio value as the series published by Poisson et al. [7] and which is 2.1. Pal et al. [8] found a sex ratio of 0.89 for patients under 40 and a sex ratio of 2.8 for patients after the age of 40.

High blood pressure and active smoking were the most common risk factors found for our patients, at 34.6% and 20.2% respectively. Other studies showed that the two main risk factors are smoking and obesity [10-12].

The use of imaging studies has increased incidental discovery of kidney tumors. In fact, in the series published by Poisson et al [7], the incidental discovery was noticed in nearly half of cases. O'connor et al [13] found that 14% of kidney tumors were discovered incidentally among 3001 asymptomatic patients having a colonoscan. In our study, we found that incidental discovery of the tumor was in 1/3 of cases (32.2%) (Figure 2).

When technically feasible, a partial nephrectomy should be performed [5]. Many studies showed a widening place of partial nephrectomy since 1990s [7]. In our study, partial nephrectomy had become more widely performed since 2009.

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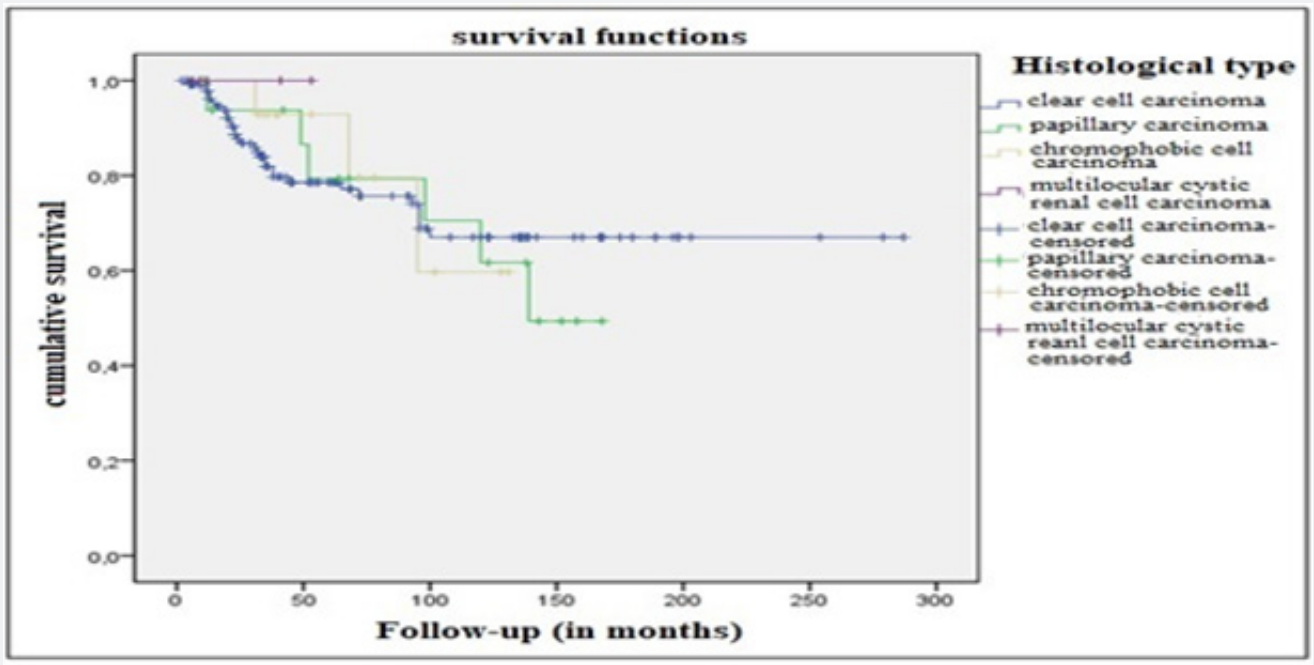

Figure 2: Survival analysis for main histological types of RCC.

The three main types of RCC are: clear cell carcinoma, papillary carcinoma (type 1 and 2) and chromophobic cell carcinoma. Referring to several published series, Clear Cell Carcinoma is the most common histological subtype among all RCC and represents 70 to 83% [6-8,14,15].

In our series, clear cell carcinoma represents 71.6% of all renal cell carcinoma. For chromophobic cell carcinoma, we found that in the different published series it is found between 2.5 to 6% of cases [6-8,14,15], while in our series it represents 10% of all RCC.

The anatomopatological examination allows the evaluation of tumors according to the nucleolar grade histo-prognosis. The various published series have shown that grades 1 and 2 are more represented, i.e., around 70% of cases with a 5-yr survival percentage between 80 and 90% (Table 2 & 3).

Table 3: Comparison of the histological types of RCC for the two periods of the study.

Histological type, n (%)	Number of patients		Total	Percentage	P
	1990-2004	2005-2019			
Clear cell carcinoma	78 (81.2)	71 (63.3)	149	71.6	0.16
Papillary carcinoma	12 (12.5)	18 (16)	30	14.4	0.13
Chromophobic Cell Carcinoma	5 (5.2)	16 (14.2)	21	10	0.001
Multilocular cystic renal cell carcinoma	0 (0)	6 (5.3)	6	2.8	0.01
Bellini duct carcinoma	1 (1)	0 (0)	1	0.48	0.32
Xp11 Translocation Renal Cell Carcinoma	0 (0)	1 (0.89)	1	0.48	0.32

In our series, grade 1 and 2 represent 77.8%. This correlates with a better prognosis for the majority of our operated patients, i.e, a survival rate of 93.8% for grade 1 and 92% for grade 2. Our patients presented with mainly good prognosis pT1and pT2 stages (84.1%). These two stages 5-year survival rates were 94% and 81% respectively. In other published series, the most presented stages were the pT1-T2 with 5-year survival rates close to ours [6-8,16].

In our study, the 5-year overall survival was 80.9%, while in other published series, the overall survival varied between 67% and 77% (Table 4). This difference can be explained by the high incidence of chromophobic cell carcinoma and multilocular cystic renal cell carcinoma in our series compared with the others and which have a very good prognosis.

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Table 4: Comparison of the pathological nuclear grades for the two study periods.

Nuclear grade n (%)	Number of patients			Percentage	P
	1990-2004	2005-2019	Total		
I et II	76 (79.1)	86 (76.7)	162	77.8	0,15
III et IV	20 (20.8)	26 (23.2)	46	22.1	0,12

In the majority of published series, chromophobic cell carcinoma has the best 5-year survival rate, which is higher than 90% [7,17-20]. In our series, this survival rate is 93%. Furthermore, multilocular cystic renal cell carcinoma in our series has the best survival rate, which is 100%. In the series of Li et al. [21], 76 cases with multilocular cystic renal cell carcinoma showed 100% survival for a median follow-up period of 52 months. Only one patient died of colorectal cancer with no recurrence or metastasis of renal cell carcinoma. For metastatic forms, the prognostic models of MSKCC and IMDC (or Heng's model) should be used to establish the prognosis of patients and choose the appropriate therapy. In our series, only one patient with metastatic clear cell carcinoma received palliative treatment with Sunitinib.

Conclusion

Renal cell carcinoma has been increasing over the last decades. Its discovery is increasingly incidental thanks to advances in imaging studies. The average age of discovery is getting lower. There had been a male dominance that is narrowing over the last years and the sex Ratio is approaching 1. The most implicated risk factors are smoking and hypertension. In our series, the majority of patients had an enlarged total nephrectomy. However, the number of partial nephrectomies had been increasing since 2009. Renal cell carcinomas are, in the majority of cases, stage T1-T2N0M0. The histological forms of renal cell carcinomas are still dominated by clear cell carcinoma and ISUP Grade 1 and 2 which are still the most prevalent and still have the best survival rates.

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