



# Renal Cell Carcinoma: 10-Year Clinical-Pathological Behaviours Report in Cuban Hospital

Aguirrechu CI<sup>1\*</sup>, Oca MD<sup>1</sup>, Yera EDC<sup>2</sup>, Rojas SI<sup>1</sup>, Lopez AC<sup>3</sup>, Garcia AG<sup>2</sup>, Matos E<sup>2</sup>, Rodriguez VLM<sup>1</sup>, Perez DRM<sup>1</sup> and Carvajal M<sup>1</sup>

<sup>1</sup>Clinical Oncology Service, Cuba

<sup>2</sup>Urology Service, Cuba

<sup>3</sup>Pathology, Hermanos Ameijeiras, Hospital (HHA), Havana, Cuba

\*Corresponding author: Aguirrechu CI, Oncologist specialist, Auxiliary professor and Investigator, Uro-oncological group, Postal code 10 200. Havana, Cuba; Email: [iraida.caballero@infomed.sld.cu](mailto:iraida.caballero@infomed.sld.cu)

## Abstract

**Background:** Introduction: Renal cell carcinoma (RCC) represents about 4% of the total adult malignant tumors and 90% of all renal tumors, all with different clinical evolution. Surgery is a gold standard of treatment in all stage and almost 95% of overall survival at 5 years in localized illness.

**Objective:** to characterize the clinical-epidemiological behavior of the patients, and identify the possible associated variables.

**Methods:** was conducted an observational, retrospective and longitudinal study to collected all the information recorded of the 336 surgical patients with RCC at the Cuban Hospital, over a 10 year period (2006-2015). A Cox regression model was adjusted to study the influence of demographic, anatomical, clinical-histological and laboratory variables on survival, with the consequent estimation of the risk ratios with their 95% confidence interval.

**Results:** The patients was represent to males in 67.9% and white skin color predominated in 77.1% of them, with a median age of 57 years. The most frequent associated comorbidities were arterial hypertension (59.2%) and diabetes mellitus (36%). The majority of patients (64%) were asymptomatic. The classic RCC had the highest frequency (72.9%). High erythrocyte sedimentation and anemia were the laboratory parameters associated with more than 75%. In multivariate analyses survival according to the presence of thrombus in the renal vein, high grade, and capsule infiltration was significantly lower ( $p < 0.01$ ), 95% confidence interval.

**Conclusions:** unilateral disease, male and young patients characterized the main study populations. Overall survival was high and the risk of individual stratification established from laboratory variables as haemoglobin and erythrocyte sedimentation is an independent and significant predictor of survival in Cuban patients with RCC.

**Keywords:** Renal carcinoma; Clear cells; Nephrectomy; Predictor

## Background

Renal cell carcinoma (RCC) represents 4% of total cases of neoplasms globally and 90% of renal tumors, with a higher frequency of incidence between the fifth and seventh decades of life. The incidence varies between different regions and is more frequent in Scandinavia and North America and infrequent in Africa [1].

RCC affects more than 400,000 people annually worldwide, resulting in 175, 098 deaths each year. Incidental diagnosis by images is frequent in asymptomatic patients, most with localized tumors smaller than 4 cm (50% to 70% of RCC) [1,2]. It is more common in terms of sex in the risk of RCC for men of 1:69 and women of 1: 116 [2]. It is a predominant tumor in old age, although the number of new cases has a tendency to increase in young patients [3]. At the time of the diagnosis, approximately 40% of patients have an already disseminated regional or distant

**Received date:** 01 April 2021; **Accepted date:** 13 April 2021; **Published date:** 17 April 2021

**Citation:** Aguirrechu CI, Oca MD, Yera EDC, Rojas SI, Lopez AC, Garcia AG, et al. (2021). Renal Cell Carcinoma: 10-Year Clinical-Pathological Behaviours Report in Cuban Hospital. SunText Rev Med Clin Res 2(1): 126.

**DOI:** <https://doi.org/10.51737/2766-4813.2021.026>

**Copyright:** © 2021 Aguirrechu CI, et al., This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Citation:** Kooma EH, Masaninga F, Lungu C, Kafula S, Zinyengere D, Sande S, et al. (2021). Indoor Residual Spraying Community-Based Delivery Model and Community Empowerment for Malaria Elimination. Lessons Learnt, Best Practices and Approach Methods in Zambia. SunText Rev Med Clin Res 2(1): 125.

pathology. The locations and frequency of invasion are as follows: lung (multiple nodules) (67-76%), lymph nodes (40-66%), bone (lytic lesions, rarely blastic) (42%), liver (41%), contralateral kidney (23%), ipsilateral adrenal (17%), opposite adrenal (11%), brain (11%) [3,4]. The main therapeutic option in the treatment of localized disease has been open radical nephrectomy, now the use of partial nephrectomy begins to be more frequent by minimal access techniques. The progress of medical technology in the last decade has led to the discovery of genetic bases and molecular pathways, which has enabled the implementation of novel therapies aimed at these discoveries. The identification of prognostic factors help to propose the most appropriate therapeutic strategy, to direct future treatments and develop specific follow-up schemes. They are divided into anatomy-pathological elements (tumour size, vascular invasion, Fuhrman's degree, adrenal invasion, tumor necrosis, lymphadenopathy, metastases); clinical (Karnofsky, systemic symptoms), laboratory (serum calcium, haemoglobin and LDH values); histological (histological subtype, presence of sarcomatoid pattern) and molecular (HIF, PTEN, p53, ki-67) [5]. RCC, although it is not one of adult's malignant tumors with the highest incidence rate, it constitutes a real challenge for its diagnosis and treatment. In most cases, the diagnosis is incidental and radical surgery is the strongest basis for treatment, multiple drugs have been added to the therapeutic drugs list approved by the FDA in recent years with a high cost and little benefit [6]. There are not enough related reports in our country on the characterization of renal cell tumors, so its study is important for a future identification of related prognostic factors and identified risk groups. In order to identify the behaviour of the RCC and the prognostic elements associated with its evolution, the present study was carried out to characterize the clinical-epidemiological behaviour in patients operated in the institution according with their prognostic factors.

## Methods

We conducted an observational, retrospective, and longitudinal-cut study of patients with a diagnosis of RCC, with surgical and the following, was carried out at the "Hermanos Ameijeiras" hospital in the period from January 2006 to December 2015. From the universe of Kidneys Tumors hospital was included a sample of 336 patients who received kidney tumours surgery and with availability of data in primary sources of hospital records. Statistical analysis. We used descriptive statistics to analyze our data set. Qualitative variables were summarized through arithmetic means, standard deviation, median, interquartile range and minimum and maximum values. For the qualitative variables, absolute frequencies and percentages were calculated. A Cox regression model was adjusted to study the influence of demographic, anatomical, clinical-histological and laboratory

variables on survival, with the consequent estimation of the risk ratios with their 95% confidence interval. The study was conducted in accordance with the provisions of the Helsinki Declaration of the World Medical Association, taking into account the latest update at the 64th General Assembly in Fortaleza, Brazil, October 2013, on research in human beings. The privacy, reliability and integrity of the data obtained from the patients was respected with the responsibility and obligation of not disclosing their identity.

## Results

Regarding the demographic characteristics of the patients, more than 65% were male and with white skin color (77.1%). The median age was 57.8 years, with 65% of patients concentrated in the range between 50 and 69 years of age. Only significant is the impact on the median survival in terms of sex with  $p = 0.023$  95% CI (median 9 years female vs. 7.4 years in male) (Figures 1 and 2).

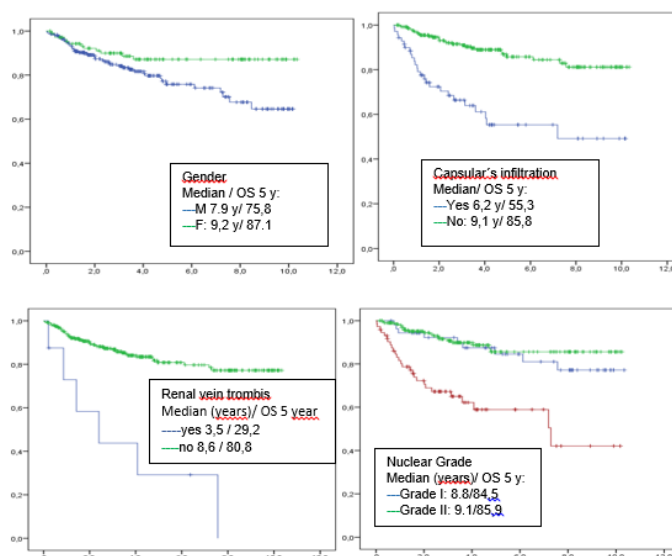


Figure 1: Overall Survival (OS) estimation (years) according to risk factors identified in patients with renal cell carcinoma.

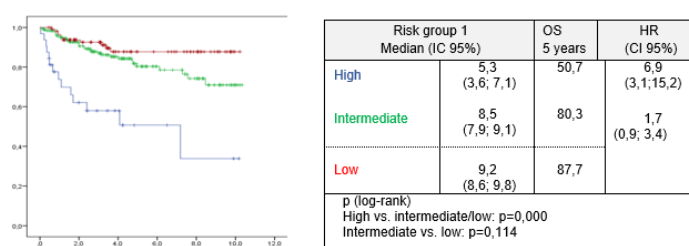
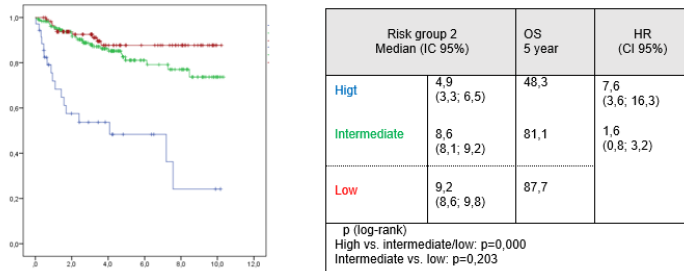


Figure 2: Overall Survival (Kaplan-Meier) according to correlational Risk Group I.

The most frequent comorbidities were Arterial Hypertension (59.2%) and Diabetes Mellitus (36.0%), 14.9% of the patients

(n=50) did not report any comorbidity. Only five patients were able to document Chronic Renal Failure associated with the diagnosis. Most of the patients were diagnosed without referred symptoms (64%), in correspondence to general average check-up or by alteration of some laboratory parameter. The symptoms and signs present had a similar distribution in hematuria (12.2%), low back pain (13.1%) and palpable tumor mass (10.7%) without significant predominance of one or the other and with a low frequency in the sample. Majority of the histological samples analyzed corresponded to classical RCC (72.9%), and 11.9% to the papillary variant type I. Only in six samples was the sarcomatoid and mixed or tubular pattern identified, chromophobic pattern was confirmed in 23 biopsy samples. Majority corresponded to nuclear Grade II (59.5%), Grade III (21.7%), according to the ISUP Classification (International Society of Urological Pathology) (Figure 3).



**Figure 3:** Overall Survival (Kaplan-Meier) according to correlational Risk Group 2.

The tumors characterized by less than 7 cm of diameter (79.2%), vascular permeation in 14.6%, capsular infiltration in 20.8% and the presence of thrombi in the renal vein only in 2.4% of them. Clinical Stage I was represented by the 70.2%, whereas only 3% turned into Stage IV. There was a similar frequency of patients classified as Stage II and III (49 and 41 respectively). Clinical stage was one of the significant variables to survival analyze with p=0.000 between I and II stage vs. III (84,5-85,9 years vs. 58,9 years) and tumour size showed statistical difference (p=0,008 per ≤ 7 vs. 7-10 cm of diameter and p=0,018 per ≤ 7 vs. > 10 cm of diameter). Regarding the laboratory parameters evaluated during the diagnosis, the average velocity erythrocyte sedimentation rate (ESR) was 68 mm/h (30-190); by categorizing this variable into intermediate (20.1-50 mm/h) and very high (> 50 mm/h) values, which represented 76.5% of the case subjects. The median haemoglobin value was 11 mg/dL (81% of patients were diagnosed with anaemia). Lactate dehydrogenase (LDH) values patients debuted with values above the normal upper limit (140 to 570 mg/dL). In most cases, surgery could be performed (96.4%). In the small remaining group, only incisional renal biopsy was performed; 60.8% were nephrectomy (radical and partial) and in the remaining 38.3% only lumpectomy. The nephrectomy

performed had a distribution of between the radical and partial nephrectomies (50.9 vs. 9, 8% respectively). Only 3% of cases received systemic treatment with adjuvant (with recombinant interferon α 2r). A global survival analysis of the patients performed according to clinical and pathological variables, laboratory testing and treatment received. Death events occurred for 56 (16.7%). The overall survival of the 336 cases was between 8 and 9 years (95% CI: 8.1 - 8.9). The 5-year overall survival rate was 79.9%. To study the influence of baseline variables, both clinical and histological, a Cox model was adjusted, where a statistically significant dependence for survival was confirmed according to the presence of capsular infiltration and renal vein thrombi in addition to the nuclear grade. The risk of dying in those with capsular infiltration is 2.6 times higher; as well as in those who have thrombi in the renal vein (3.7 times higher), nuclear grade I and II it is significantly lower (half and a third) than those who have grade III and males present a one year lower survival than females. Although, from the multivariate review no other significant associations regarding survival were detected, some cases to collinearity among vascular permeation, capsule infiltration and presence of thrombi. Statistically significant influences in gender, tumour size, clinical stage, vascular permeation, anaemia, LDH greater than 400 mg/dL were detected. Two individual risk scenarios were estimated based on the following variables:

**Risk 1:** Presence of Anaemia, high DHL values (≥ 400 mg / dL) and ESR (intermediate or high range)

**Risk 2:** Presence of Anaemia, elevated DHL values (≥ 400 mg/) and ESR (intermediate or high range) plus presence of thrombi in renal vein

## Discussion

Overall, a maximum incidence of presentation between 60 and 70 years old was described. A study with 112 patients with RCC with a similar frequency (33.9%) in the 50-59 age group. Also, although they did not sub classify the sample in the same age range, reported a similar frequency of individuals (38.6%) between the ages of 50 and 64 [8,9].

In the Cuban context, a higher frequency of the male gender has been reported, for a male: female ratio of 1.8: 1. These results are very close to those found in this work where male sex prevailed in a 2: 1 ratio and totally coincident. However, a slightly higher ratio in favour of men (2,5:1) [8-10]. The absence of symptoms are in correspondence with the evolution of imaging techniques (incidentally in about 40-50% of cases). Due to the wide availability of imaging techniques such as ultrasound, computed tomography and nuclear magnetic resonance, the number of incidentally diagnosed renal tumors has increased in early organ-confined stages, (I and II), which allows more conservative treatments and with good survival results [11]. On the other hand,

the absence of symptoms may also be influenced by the fact that most tumors measured less than 7 cm of diameter, which corresponds to a lower clinical stage of the disease. Local

invasion of the tumor with infiltration of the renal capsule occurs in 20% of patients according to several studies, as in the present study [13] (Tables 1-3).

**Table 1: Demographic characteristics of patients.**

Basal Characteristic		Frequency	%
N		336	100
Gender	Masculine	228	67,9
	Female	108	32,1
Skin color	White	259	77,1
	Black	32	9,5
	Mixed	45	13,4
Age	Median ± DS	57,8 ± 10,6	
	Mean (minim; maxim)	58,0 (20; 79)	
	• ≤39	13	3,9
	• 40-49	59	17,6
	• 50-59	110	32,7
	• 60-69	109	32,4
	• 70-79	45	13,4

**Table 2: Pathological tumors characteristics.**

Anatomy-pathological characterizations		Frequency	%
N		336	100,0
Tumor size	≤ 7 cm	266	79,2
	7 - 10 cm	47	14,0
	> 10 cm	23	6,8
Vascular-lymphatic Permeation	yes	49	14,6
	No	279	83,0
	No specific	8	2,4
Capsular Infiltration	yes	70	20,8
	No	257	76,5
	No specific	9	2,7
Renal vein thrombus	Si	8	2,4
	No	319	94,9
	No specific	9	2,7
Clinical stage <sup>i</sup>	I	236	70,2
	II	49	14,6
	III	41	12,2
	IV	10	3,0

<sup>i</sup> TNM classifications. Renal Cell Carcinoma. American Joint Cancer Committee (AJCC) (7maed., 2010)

The low frequency of thrombi in renal vein observed may be due to the low frequency of Stage IV patients with metastases which has been reported on between 4% and 10% of cases; this effect is more frequently (up to 25%) in patients with metastatic renal carcinoma (13,14). A quarter of the patients presented

preoperative anaemia, totally contrary to what was observed in this investigation, where more than three quarters of the sample presented anaemia (haemoglobin <10mg/dl) even when they did not refer related symptoms such as paleness or bleeding at that same frequency. Surgery that prevailed in the case series

coincides with what was notified by other authors and with the current recommendation for this entity (IA). In the study 81.2% of the patients underwent radical nephrectomy, although this the frequency was slightly higher than that observed in the present

work. Because most patients are diagnosed when the tumor is still relatively localized and is susceptible to surgery, approximately 73% of all patients with RCC survive for 5 years [11].

**Table 3: Laboratory test baseline values.**

Baselines values		Descriptive	
N		=336	
Erythrocyte sedimentations rate, ESR, (mm/h)	Median ± DS	68,9 ± 20,2	
	Mean ± RI	68,0 ± 27,0	
	(minim; maxim)	(30; 190)	
	20,1- 50	79	23,5%
	> 50	257	76,5%
Hemoglobin (mg/dL)	Median ± DS	10,3 ± 1,9	
	Mean ± RI	11,0 ± 3,0	
	(Minim; maxim)	(6; 14)	
Anemia (Hb < 10,0 mg/dL)	Yes	272	81,0%
	No	64	19,0%
HLD (mg/dL)	Median ± DS	299,7 ± 81,9	
	Mean ± RI	280,0 ± 110,0	
	(Minim; Maxim)	(140; 570)	
	<=400	302	89,9%
	>400	34	10,1%

In this series of patients, the 5-year overall survival rate was higher too. Rodríguez (2008) identified the factors with the greatest prognostic, such as clinical stage and nuclear grade. Nuclear grade and tumor size are currently important prognostic factors for survival in renal cell carcinoma [12-14]. The study collects the characteristics of the patients with CRC treated in a national reference institution but has limitations such as the non-representation of national cases despite being a population of an island of 11 million people.

### Conclusion

The precise determination of prognostic factors is an essential to evaluate patients with RCC, for the determination of adjuvant treatments and prediction of the evolution of the disease. In the present study, a direct influence of the male sex, tumor size > 7cm of diameter), clinical Stage III-IV, vascular and/or lymphatic permeation, anaemia and DHL > 400 mg / dL was observed in the outcome of the patients (lower survival). The risk of individual stratification established from laboratory tests is an independent and significant predictor of overall survival.

### Declaration of Interest

The authors declare the non-existence of a conflict of interest, and strict compliance with the confidentiality of the data collected.

### References

1. Parkin DM, Ferlay J, Jemal A, Borok M, Manraj SS, N'da GG, et al. Cancer in sub-saharan africa. Lyon: international agency for research on cancer. IARC scientific publication. 2018; 167.
2. Anuario estadístico de salud 2019. Statistical yearbook of health 2019. MINSAP, Havana.
3. DeVita VT, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's cancer: principles and practice of oncology: Tenth edition. Wolters Kluwer Health Adis. 2015; 2231-2280.
4. Guide to clinical diagnostic practice and treatment of renal cancer in adults. Ministry Health. 2013.
5. Escudier B, Porta C, Schmidinger M, Leclercq NR, Bex A, Khoo V, et al. Renal cell carcinoma: ESMO clinical practice guidelines. Ann Oncol. 2019; 30: 706-720.
6. Clinical practices guidelines in oncology (NCCN guidelines) kidney cancer. 2020.
7. Delahuunt B, Cheville J, Martignoni G, Humprey G, Gallusi CM, McKenney J, et al. The international society of urological pathology (ISUP) grading system for renal carcinoma and others prognostic parameters. Am J Surg Path. 2013; 37: 1490-1504.



8. Peerez AN, Lopez GA, Gonzalez AP. Characterization of renal cancer, relationship of tumor size and nuclear grade with survival. *Rev cmehavana*. 2014; 20.
9. Garcia A, Roman FBG, Morales IG. Simple enucleation in the treatment of renal tumors. *Rev Cub Urol*. 2017; 6.
10. Choi Y, Park B, Kim K, Jeong BC, Seo SI, Jeon SS, et al. Erythrocyte sedimentation rate and anaemia are independent predictors of survival in patients with clear cell renal cell carcinoma. *British J Cancer*. 2013; 108: 387-394.
11. Kidney and renal pelvis cancer SEER stat fact sheets. National Cancer Institute. 2017.
12. Rodriguez H, Serrano E, Maldonado E. Prognostic factors in localized and locally advanced renal cancer. *Actas Urol Esp*. 2008; 32: 320-324
13. Huang H, Pan XW, Huang Y. Micro vascular invasion as a prognostic indicator in renal cell carcinoma: a systematic review and meta-analysis. *Int J Clin Exp Med*. 2015; 8: 10779-10792.
14. Leibovich BC, Zisman A, Figlin RA. Current staging of renal cell carcinoma. *Urol Clin North Am*. 2003; 30: 481-497.