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Research Article

Epidemiological, Clinical and Morphological Characteristics of Renal Cell Carcinoma in Santiago de Cuba

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Abstract

Background: Renal cancer constitutes a health problem in the world. Despite the increase in its incidence in recent decades, it is curable when diagnosed and treated at a localised stage.

Objective: To describe the epidemiological, clinical and morphological characteristics of renal cell carcinoma.

Methods: Descriptive and cross-sectional study in a series of 88 patients with renal cancer histology from 2012 to 2016. Variables such as incidence, time elapsed from symptom onset to diagnosis, type of diagnosis, histological classification and tumor extension were studied.

Results: The incidence of renal cancer was higher in urban areas. Localised disease was found in 55,6% of patients, with the highest percentage presenting within 90 days. Incidentally, 57,9% of cases were diagnosed. The incidental tumors, limited to the kidney, occurred mainly with a tumor diameter of 7 cm or less. Infiltration of lymphatic vessels was the most common tumor extension with 10,2% of all patients. Clear cell renal carcinoma was present in 58%, being the largest of this histological variety.

Conclusions: The incidence of renal carcinomas is higher in patients from urban areas. Patients who present earlier for consultation have a greater chance of the tumor still being localised, and therefore have a better prognosis. Larger tumors are more likely to have locally advanced or metastatic disease.

Keywords: Renal Cell Carcinoma; Incidental; Diagnosis; Staging; Topography

Introduction

A new growth in the renal parenchyma is considered a tumor. It can be benign or malignant, solid or cystic, primitive or secondary, intrinsic or extrinsic. Renal adenocarcinoma is also known as renal cell carcinoma (RCC), alveolar carcinoma, clear cell adenocarcinoma, dark cell adenocarcinoma, granular cell carcinoma, hypernephroid carcinoma, Grawitz's tumor, hypernephroma, or internist's tumor. The RCC was first reported by Konig in 1826. The modern era brought the concept that renal cell carcinoma includes many distinct subtypes originating in various parts of the nephron, each with a particular genetic basis and tumor biology [1].

Kidney cancer ranks 14th worldwide, with a ratio of 1,7 men per woman, and its mortality is 16th. Its incidence rate varies between 4,4-11,1 cases per 100 000 inhabitants/year worldwide. The highest incidences, between 10,9 and 9,7 per 100 000 inhabitants,

are observed in North America and European countries. Renal cell carcinoma is a less suspicious neoplasm. Clinically, it manifests completely asymptomatic, with the appearance of paraneoplastic symptoms, or it presents with the appearance of a bulky tumor in some very aggressive cases from the time of diagnosis. It may metastasise before or after diagnosis of the primary tumor [2].

Treatment of hypernephroma does not respond to radiotherapy or chemotherapy. Its immunological connection is not yet established and its hormone dependence is still under study. The only curative treatment for localised carcinomas is based on radical nephrectomy, while in case of metastatic stage there is no treatment that eliminates the disease [1-3].

In multivariate studies, tumor size is often shown to be an independent prognostic variable. Most patients with large tumors have a very poor prognosis with reduced survival except for very selected cases [3].

Renal cancer is a global health problem. Despite its increasing incidence in recent decades, it is curable when diagnosed and treated at a localised stage, even in the kidney and immediate surrounding tissue. The likelihood of cure is directly related to the stage or extent of tumor spread [1]. The aim of this study is to characterise epidemiological factors and clinical and morphological features of renal cell carcinoma.

Methods

A descriptive, cross-sectional study of renal cell carcinoma in the province of Santiago de Cuba was carried out from 1 January 2012 to 31 December 2016. The study included all hospital centres with Urology Surgical Services in the province. A total of 5 centres participated: Hospital Provincial Saturnino Lora, Hospital General Orlando Pantoja Tamayo, Hospital Clínico Quirúrgico Quirúrgico Juan Bruno Zayas Alfonso, Hospital Militar Joaquín Castillo Duany and Hospital Oncológico Conrado Benítez García. The participation in the study of the different centres was voluntary and carried out by specific invitation in order to obtain the real incidence of renal cell carcinoma in Santiago de Cuba.

The universe consisted of 88 patients, over 18 years old, who received medical care in the period indicated for the study. There were 56 men and 32 woman. For this purpose, the medical records of all patients who died and underwent surgery with an anatomopathological diagnosis of renal cell carcinoma were reviewed. Patients with renal cavity tumors or inoperable tumors were excluded.

In order to carry out the research, authorisation was requested from the Departments of Pathological Anatomy and Medical Records of the hospitals with Urology Surgical Services in Santiago de Cuba Province, where the medical records related to this study were reviewed during the planned period of time, as well as the biopsy reports. The study was approved by the Ethics Committee and Scientific Committee of the Hospital.

The analysis of the data collected was done by means of tables, percentages and measures of central tendency for better analysis of the data obtained and their better correlation. The following variables were analysed for the study and the following statistical treatment was performed:

- **Incidence:** It was tabulated according to the total of 88 new cases of renal cell carcinoma in the 5 years of the selected period, and the incidence rate was determined according to the total population of inhabitants of the province of Santiago de Cuba by municipality, with data obtained from the Demographic Yearbook Santiago de Cuba 2016 [4].
- **Time elapsed from onset of symptoms to diagnosis:** Time it took the patient to visit the doctor from the onset of symptoms.
- **Type of diagnosis:** How the patient was diagnosed according to whether or not symptoms appeared. It was tabulated as incidental and symptomatic.
- **Histological type and sarcomatoid differentiation:** Tabulated according to the World Health Organization 2016 Histological Classification of Renal Cell Tumors [5], and according to the diagnoses found in the pathology report, based on the WHO classification. It was presented in tables with number of cases and percentages.
- **Tumor extension:** The renal tumor can be localised, locally advanced when it extends to the venous system, adrenal gland or perirenal tissue, or metastatic when it extends beyond the Gerota fascia or perirenal fat. It was distributed according to the data found in the anatomopathological reports.

A national and international bibliographic search was carried out of various scientific articles in indexed and peer-reviewed journals, obtained from the Pubmed, Medscape and Google Scholar databases, published during the last 5 years, related to renal cancer, in accordance with the subject matter of the study and the proposed objectives in Spanish and English. To obtain population demographic data, access was gained to the Demographic Yearbook [4], in the Provincial Statistics Department.

Statistical analysis

An electronic database was designed using the Microsoft Excel 2010 statistical system to collect basic epidemiological, clinical and histological data. For statistical calculations, the percentage was used as a summary measure. Statistical handling of the data was performed with the SPSSv21 package. The crude annual incidence rate was calculated as the number of CRC cases in the period, relative to the assigned population. Quantitative variables were represented by median and interquartile range (IQR) and qualitative variables by absolute frequencies and percentages. The Chi-square test was used to contrast qualitative variables. The results were tabulated in tables and illustrated with graphs, providing the tabulation of the data and information at the different stages of the research.

Results

A total of 88 malignant kidney tumors were diagnosed in the period analysed, with an incidence rate for the province of Santiago de Cuba of 1,66 per 100 000 inhabitants, with the municipality of the same name having the highest incidence with 1,39 per 100 000 inhabitants (Figure 1).

Figure 1: Distribution of renal cell cancer incidence by municipality in Santiago de Cuba. Period 2012-2016.

A total of 55,6% presented with localised disease at the time of diagnosis, of which 25% and 30,7% attended for consultation at 30 days or less and up to 90 days respectively, while the remainder presented with locally advanced or metastatic disease for 36,4% and 8% respectively, who attended for consultation later (Figure 2).

Figure 2: Tumor extension according to time from symptom onset to diagnosis.

In 57,9% of cases, tumors were diagnosed as incidental or asymptomatic findings with tumor diameter most frequently between 0 and 7 cm, while the remaining 42,1% were diagnosed in the presence of symptoms with tumor diameter most frequently between 7,1 and 10 cm (Figure 3).

Figure 3: Type of diagnosis of Renal Cell Carcinoma and tumor size.

With regard to tumor extension (Table 1), of the tumors confined to the kidney, 17,2% and 26,3% occurred in tumors of 0-4 cm and 4,1-7 cm respectively. Lymphatic vessel infiltration was observed in 9,1% distributed almost equally for all sizes. Infiltration of lymphatic vessels and regional lymph nodes occurred consecutively in 9.1% and 7.8%. The rest of the tumor extensions did not present statistical significance.

Tumor Extension	0-4 cm	4,1-7 cm	7,1-10 cm	> 10 cm	Total	P-value
Limited to the kidney	17, 2%	26,3%	5,7%	1,1%	50,3%	0,006**
Infiltrates blood vessels	0,0%	1,1%	0,0%	0,0%	1,1%	0,25
Infiltrates lymphatic vessels	1,1%	4,5%	2,3%	1,1%	9,1%	0,035*
Infiltrates blood and lymphatic vessels	1,1%	3,4%	2,3%	0,0%	6,8%	0,077
Infiltrates renal capsule	0,0%	2,3%	1,1%	0,0%	3,4%	0,077
Extension to perirrenal fat	0,0%	2,3%	1,1%	0,0%	3,4%	0,077
Infiltrates blood and lymphatic vessels, renal vein, renal capsule and renal pelvis	0,0%	1,1%	1,1%	0,0%	2,3%	0,102
Infiltrates blood and lymphatic vessels, renal capsule, perirrenal fat and renal pelvis	0,0%	1,1%	0,0%	3,4%	4,5%	0,062
Infiltrates cava vein	0,0%	0,0%	2,3%	1,1%	3,4%	0,077
Infiltrates regional lymphatic nodes	1,1%	1,1%	2,3%	3,4%	7,8%	0,039*
Extension by contiguity to adrenal gland	0,0%	0,0%	0,0%	1,1%	1,1%	0,25
Distant metastasis	1,1%	2,3%	1,1%	2,3%	6,8%	0,077
Total	21,6%	45,5%	19,3%	13,6%	100%	0,003**

Table 1: Tumor extent and size in patients with renal cell carcinoma.

Source: Data collection form.

p-value >0,05: Non significant (NS).

p-value <0,05: Significant (S).*

p-value <0,01: Highly significant (HS).**

Clear cell carcinoma was present in 58% of the patient series followed by papillary carcinoma 11,4%. Tumors of 0-7 cm, taking into account the representativeness of the sample, were present in all tumor types and tumors larger than 7 cm were more frequent in the clear cell type. The sarcomatoid pattern was present where the clear cell type was present either in its simple form or mixed with other typologies, and was also associated with larger tumors (Table 2).

Renal Cel Carcinoma (RCC)	0-4 cm	4,1-7 cm	7,1-10 cm	> 10 cm	Total	P-value
Clear cell RCC (conventional)	13,6%	28,4%	12,6%	3,4%	58%	0,005**
Granular clear cell RCC	0%	0%	2,3%	1,1%	3,4%	0,077
Sarcomatoid clear cell RCC	0%	0%	1,1%	4,6%	5,7%	0,052*
Papillary RCC	2,3%	6,9%	1,1%	1,1%	11,4%	0,026*
Tubulopapillary clear cell RCC	4,6%	2,3%	1,1%	1,1%	9,1%	0,035*
Multilocular clear cell RCC	1,1%	1,1%	0%	0%	2,3%	0,147
Chromophobe RCC	0%	2,3%	1,1%	0%	3,4%	0,077
Tubulocystic RCC	0%	1,1%	0%	0%	1,1%	0,25
Mixed clear cell and Chromophobe RCC	0%	2,3%	1,1%	0%	3,4%	0,077
Mixed clear cell and chromophobe RCC whith sarcomatoid pattern	0%	0%	0%	1,1%	1,1%	0,25

Mixed clear cell, papillary and chromophobe RCC	0%	1,1%	0%	0%	1,1%	0,25
Total	21,6%	45,5%	19,3%	13,6%	100%	0.003**

Table 2: Histological Type of Renal Cell Carcinoma and Tumor Size.

Source: Data collection form.

p-value >0,05: Non significant (NS).

p-value <0,05: Significant (S).*

p-value <0,01: Highly significant (HS).**

Discussion

In the present study, the incidence rate of renal carcinoma is higher in urban than in rural patients, Which is in agreement with the literature [6,7]. The municipality of Santiago de Cuba presented the highest incidence rate, which may be related to risk factors for renal cancer such as the demographic factor since when comparing the urban and rural areas of the municipality of Santiago de Cuba, the urban areas are significantly higher in relation to the other municipalities where 90% live in these areas according to the 2016 statistical yearbook of Santiago de Cuba [4], with these areas presenting greater development and industrialization.

Worldwide, the incidence of kidney cancer varies more than 10 times between different populations and geographical areas, which is populations and geographic areas, suggesting that lifestyle-related factors play a role, lifestyle factors play an important role. Kidney cancer rates are higher in industrialised countries than in developing countries such as Africa and Asian developing countries, suggesting that it may be related to smoke from cigarettes, cars in some industries or chemicals used by these industries [8-11].

The Tumor-Nodule-Metastasis (TNM) classification classifies renal carcinomas as pT3 or locally advanced disease, when the tumor extends to the venous system, adrenal gland or perirenal tissue, provided it does not extend beyond the fascia of Gerota [12]. Time is an undeniably important variable in the diagnosis and treatment of cancer. Although there is great heterogeneity among the different types of cancer, shortening the time to diagnosis as much as possible is beneficial for all of them [13]. In the series studied by Uscanga [14], the time from onset of symptoms to diagnosis of renal tumor was: 21% in less than 30 days, 23% from 30 to 90 days and 30% more than 90 days, coinciding with this study.

The vast majority of patients diagnosed with renal carcinoma present with localised disease, others with locally advanced disease, while a minority present with metastatic onset. Epidemiological data in the United States describe an increase in the incidence of localised tumors, but at the same time note an increase in the incidence of metastatic tumors, as seen in this series [8]. Twenty to 25% of patients have metastatic disease, mainly to the lungs, liver, bone and central nervous system once diagnosed [15].

Between 25-40% of renal tumors are diagnosed as incidental masses on abdominal ultrasound for other conditions, which is why the incidence rate has also increased over the last 30 years. Many authors suggest a direct relationship between the increase in incidental diagnosis and the growth in the use of complementary radiological methods such as computed tomography and ultrasound. Most patients with renal cancer remain asymptomatic as long as the disease has not spread. If symptoms appear they are due to tumor growth, metastatic disease, paraneoplastic syndrome (20%) or haemorrhage [1,7,12,13,15]. In the present series incidental diagnosis was present in 55,6% of cases being somewhat higher than described in the literature.

Traditionally, renal tumors larger than 7 cm in diameter (T2) have been considered bulky, however, the volume that these neoplasms can reach during the natural course of the disease can be considerably larger. Tumor size has been related to survival in patients with renal cáncer [15].

An increase in the number of incidentally diagnosed, asymptomatic RCC has been observed. These tumors are more frequently smaller in size [1-3,9]. Some studies have observed that small tumors are generally organ confined [7,8,10,11]. However, Diaz [8], observed in his review of the literature that smaller

tumors (<3 cm) showed a high prevalence of tumors with tumor extension beyond the renal capsule, without finding differences in comparison with larger tumors according to other authors, which may be due to the association of other variables and not to this one independently. Darias [16], reported a clinical stage T1 at diagnosis of between 50% and 70%, i.e. no tumor extension with an average tumor size of less than 5 cm. The results obtained in the present series coincide with those reported by both national and international authors.

Locally, RCC can invade the rest of the renal parenchyma, the fibrous capsule, the perirenal fat, the venous and lymphatic system. It spreads by direct lymphatic extension and distantly by haematogenous or lymphohaematogenous spread. Haematogenous and lymphatic spread in renal cancer are equally frequent and most patients with positive lymph nodes may eventually have haematogenous spread at the same time. Moreover, most patients with distant metastases do not have positive nodes on dissection. The incidence of positive nodes increases with pT stage, and is associated with distant metastases and venous involvement [1,17].

Nieblas [17], in a series of four groups found capsule invasion in 19,8%, perirenal adipose tissue invasion in 17,95%, pedicle vascular invasion in 10,91%, lymphatic invasion in 6,16%, adrenal invasion in 1,23%. In this study, these occurred in reverse order of frequency, which may be due to the higher number of cases diagnosed confined to the kidney. Lymphatic invasion occurred most frequently at 12,6% followed by joint infiltration of lymphatic and blood vessels at 9,0%.

It has been shown that the largest renal tumors are usually clear cell tumors, which account for more than 80% of tumors larger than 7 cm, in agreement with this study [1,3,9,12,16].

Apart from tumor extension, malignancy has been related to cell type [7]. The morphological classification of CRCs has been based on cytogenetic, genetic and histological studies. There are currently 10 histological subtypes according to the World Health Organisation classification. Clear cell, papillary and chromophobe carcinoma are the most frequent RCC, accounting for 70-80%, 14-17% and 4-8% respectively. Papillary clear cell or tubulopapillary renal carcinoma is a separate entity from papillary and clear cell RCC, with a distinct genetic profile [7,17]. The study demonstrated a clear predominance of clear cell RCC, as reported in the world literature, and a minority of the other histological subtypes.

Clear cell carcinoma, as the name suggests, derives from the presence of a majority of cells with clear cytoplasm. The growth pattern is tubular, in acinar or solid nests. Sometimes cells with eosinophilic cytoplasm with abundant mitochondria, called granular cells, can be observed among the clear cells and may be exclusive in high-grade tumors, resulting in the loss of the typical acinar growth pattern. In 5% of cases these cells degenerate into sarcomatoid changes [8,17,18].

Sarcomatoid changes can occur in all types of carcinoma. There is no evidence that it appears de novo, so it is not classified as a type per se but as a cellular phenotype, but it is considered as a high-grade manifestation of the type from which it originates; it can even sometimes obliterate the previous carcinoma, and should be categorised as an unclassifiable tumor. Histologically it is characterised by spindle cells with an infiltrative growth pattern, leading to aggressive local and metastatic behaviour and poor prognosis. It is more commonly associated with clear cell and chromophobe variants [8,18].

At the time of the study, some of the statistical departments did not have digitised information to facilitate proper identification of kidney cancer patients. An under-recording was found in the statistical reporting of renal cancer, as it was evident from the medical records and pathology reports that several of these patients did not suffer from this disease but had other urological pathologies (tumors at another level or lithiasis). In addition, some of the medical records were not complete, so other useful variables could not be included to extend the research, and these were limiting factors for the study.

Conclusions

The incidence of renal carcinomas is higher in urban patients. Patients who present earlier for consultation have a greater chance of the tumor still being localised, and therefore have a better prognosis. Larger tumors are more likely to have locally advanced or metastatic disease. The clear cell variety is most responsible for large and sarcomatoid tumors. The present investigation provides evidence that, in addition to constituting an exploratory approach as a basis for future analytical studies, to a certain extent, alerts health professionals to the need for a detailed physical examination and the necessary complementary studies for all patients who come for consultation, in order to identify in time the presence of this tumor that may present in the least suspected way.

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Conflict of Interest

No conflicts of interest are declared to exist.

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