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Original Research Article

Incidence of renal cell carcinoma in Santiago de Cuba

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ABSTRACT

Introduction: renal parenchymal tumors account for approximately 2-3% of tumors in adults' patients and in turn the 85% of primary kidney tumors. An increased incidence of renal parenchymal tumors has been observed around the world and in Cuba in the last years. It is the most deadly cancer in the urinary tract worldwide. Objective: to identify incidence and the clinical- epidemiological and histopathological features of renal cell carcinoma in the province of Santiago de Cuba. Method: a descriptive and cross-sectional study was conducted concerning renal adenocarcinoma in 88 patients from Santiago de Cuba. Period of study was from January 1, 2012 throughout January 1, 2017. The diagnosis was based on histopathological studies from patients who underwent surgery and died due to this disease. Variables studies were as follow: incidence, age, sex, risk factors, symptoms and signs, histologic type and cancer staging. Results: it was more frequent between the fifth and sixth decades of life and in males. Smoking was the main risk factor. More than 50% of cases were diagnosed incidentally and asymptomatically, although symptoms such as flank pain, hematuria, general symptoms and palpable abdominal mass appeared. Clear cell tumor was the histologic variety most affected. They were diagnosed mainly in stage T3a. Conclusions: family physicians, clinicians, urologists and radiologists are involved in the diagnosis of renal carcinoma, so it is important to be aware of this illness since it can present in the most unsuspected way.

Keywords: adenocarcinoma; kidney; renal cell carcinoma; incidence; diagnosis

1. Introduction

Renal cell carcinoma (RCC) or renal cancer is also called alveolar carcinoma, clear cell adenocarcinoma, dark cell adenocarcinoma, granular cell carcinoma, hypernephroid carcinoma, renal adenocarcinoma, Grawitz tumor, hypernephroma or internist's

tumor. This includes many distinct subtypes originating in the various parts of the nephron, each with a particular genetic basis and tumor biology.[1]

Renal parenchymal tumors account for approximately 2-3% of adult tumors and 85% of primary kidney tumors.[2] Worldwide, it is considered the most deadly cancer of the urinary tract.[3] About one third of cases present at a locally advanced or metastatic stage at diagnosis. Annually worldwide about 300000 men and women are diagnosed with kidney cancer and 1500000 of them die.[4]

The etiology of this cancer remains unknown. However, several risk factors have been implicated in its occurrence.[5] Renal cancer is among the human neoplasms with the least predictable clinical course and the patient may remain completely asymptomatic, with a bulky tumor, while in other cases, it is from its diagnosis aggressive and destructive.[6] The form of manifestation influences survival to disease, even accounting for higher rates in asymptomatic patients, with fortuitous diagnosis.[7,8]

Renal cell cancer can often be cured if it is diagnosed and treated while it is still localized to the kidney and immediate surrounding tissue. The likelihood of cure is directly related to the stage or extent of tumor spread. Because most patients are diagnosed when the tumor is still relatively localized and amenable to surgical removal, approximately 40% of all renal cell cancer patients survive for 5 years. Occasionally, some patients with locally advanced or metastatic disease may have an indolent course for several years. Late tumor recurrence also occurs many years after initial treatment. Surgical resection is the mainstay of treatment for this disease. Even in patients with disseminated tumor, locoregional therapies can play an important role in alleviating symptoms of the primary tumor or ectopic hormone production. Systemic treatment has shown to have only limited efficacy.[1,3]

In recent years there has been an increase in the number of cases diagnosed in early stages but also in advanced stages of the disease, without knowing the true incidence in our territory. Its diagnosis is usually incidental and on other occasions with the least suspected symptomatology and in late stages, presenting a worse prognosis. Family physicians, clinicians, urologists, including radiologists are involved to a greater or lesser extent in its diagnosis, so determining the incidence and clinical-epidemiological and histopathological characteristics of renal cell carcinoma in the province of Santiago de Cuba, would allow everyone a better reinterpretation of its risk factors, clinical picture, evolution and treatment and, therefore, offer better quality of life to patients.

2. Method

A descriptive, cross-sectional study of the incidence of renal cell carcinoma in the province of Santiago de Cuba was carried out from January 2012 to January 1, 2017, covering five years.

The study included all hospital centers with Urology surgical services in the province. The participation in the study of the different centers was voluntary and carried out by specific invitation in order to obtain a representative and real sample of the population of Santiago de Cuba. A total of five centers participated: Hospital Provincial Clínico Quirúrgico Docente "Saturnino Lora Torres", Hospital General Docente "Orlando Pantoja Tamayo", Hospital General Docente "Dr. Juan Bruno Zayas Alfonso", Hospital Militar "Dr. Joaquín Castillo Duany" and Hospital Oncológico Provincial Docente "Conrado Benítez García", with an overall assigned population of 1053966 inhabitants for the year 2016.

All patients over 18 years of age diagnosed with CRC who presented histopathological studies and underwent nephrectomy for this tumor or during necropsy findings were taken. The universe consisted of 88 patients, of whom 86 were treated surgically and this condition could be determined histologically, and to obtain the real data we included another 2 who died without having been treated for this cause, but in necrological studies renal cancer was confirmed by histology.

To carry out the research, authorization was re-

quested from the departments of Pathological Anatomy and Medical Records of the hospitals with Urology surgical services in the province of Santiago de Cuba, where the clinical histories related to this study were reviewed during the planned period of time, as well as the biopsy reports. The study was approved by the Scientific Committee and the Ethics Committee of the Hospital.

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

Incidence: it was tabulated according to the total number of affected cases of renal cell tumor in the aforementioned period presented in tables with number of cases and percentages, and the incidence rate was determined according to the total population of inhabitants of the province of Santiago de Cuba with data obtained from the Demographic Yearbook of Santiago de Cuba 2016[9].

Age: was collected naturally and then grouped into 10 years each, starting with 30 years. No patients younger than 30 years were found. Percentages, measures of central tendency and dispersion (median and standard deviation) were estimated.

Sex: tabulated dichotomously in male and female, a table was presented with the number of each group, percentages and male: female ratio.

Risk factors: smoking (smoking habit), advanced age (age above 60 years), systemic arterial hypertension (chronic elevation of blood pressure values above 120/80 mmHg), chronic renal lithiasis (lithiasis of long evolution), obesity (abnormal or excessive accumulation of fat that can be detrimental to health), diabetes mellitus (set of metabolic disorders characterized by an increase in blood glucose levels), renal cysts (abnormal pockets in the renal parenchyma containing fluid), previous renal cell carcinoma (for a case who 10 years earlier had partial nephrectomy for renal tumor, not being able to determine whether the latter was primary or a consequence of the former), with no risk factors.

Symptoms and signs present at diagnosis: incidental (asymptomatic patients who were ultrasonographically diagnosed with renal tumor), flank pain (constant dull pain of variable intensity in the affected flank), hematuria (emission of blood with urination), palpable abdominal mass (palpable tumor in the affected flank), constitutional syndrome (refers to the loss of the patient's general condition whose manifestations are: asthenia, anorexia, weight loss (5% or more in 6 to 12 months), anemia, nausea, varicocele, fever, night sweats, bone pain, lower limb edema, tumor necrosis.

Histological type and sarcomatoid differentiation: tabulated according to the histological classification of renal cell tumors[10] of the WHO 2016 and according to the diagnoses found in the pathology report, based on the WHO classification, in addition, of a secondary tumor: non-Hodking's lymphoma, high grade diffuse intermediate cell and large cell that was included in others. Those of sarcomatoid pattern were found in the histological type of clear cell except for one of the cases, which was found in the type of mixed clear cell and chromophobe carcinoma.

TNM staging:[11] T1a, T1b, T2a, T2b, T3a, T3b, T4, N0, N1, N2, M0, M1.

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 five years, related to renal cancer, in accordance with the subject of the study and the proposed objectives in Spanish and English.

To obtain population demographic data, the Demographic Yearbook[12] was accessed at the Provincial Statistics Department, as well as the Department of Statistics and the Department of Pathological Anatomy of all the hospitals with Urology surgical

services in the province to obtain data on patients with reported kidney cancer in the period covered.

An electronic database was designed using the Microsoft Excel 2010 statistical system for the collection of basic epidemiological, clinical and histological data. For statistical calculations, the percentage (%) was used as a summary measure.

The statistical management of the data was carried out with the SPSSv21 package. The crude annual incidence rate was calculated as the number of cases of CRC in the period in question, 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 presented in tables and illustrated with graphs, offering the tabulation of the data and information at the different stages of the research.

3. Results

A total of 88 valid CRC cases were registered in the five participating centers. For a total population of 1053966 inhabitants for the year 2016, the crude incidence rate was 1.66 cases/100000 inhabitants/year. Higher incidence was observed in the years 2014 and 2015, with 22.7% and 29.5%, respectively (Figure 1).

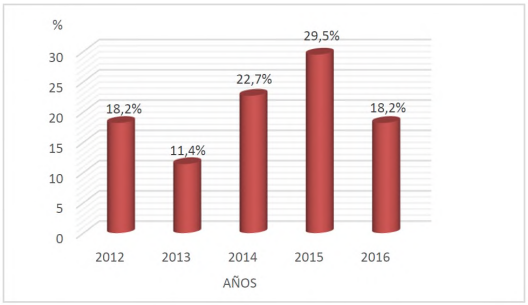

Figure 1. Incidence of renal carcinoma in the province of Santiago de Cuba, 2012-2016.

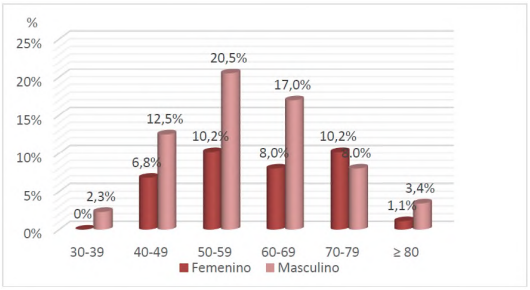

Figure 2. Renal carcinoma according to age group and sex.

Renal cell cancer was rare in patients younger than 39 years of age (2.3%) (Figure 2). Most patients were found in the 50-59 age group (30.7%), with a mean age at diagnosis of 59.8 years. Males predominated (63.7%) over females (36.3%), resulting in a male-to-female ratio of approximately 2:1.

Among the associated risk factors, smoking was identified as the most frequent (54.5%), followed by advanced age (47.7%). (Figure 3).

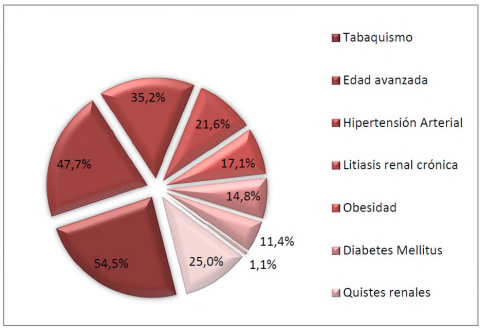

Figure 3. Risk factors associated with renal carcinoma.

The main symptom that motivated the diagnosis was flank pain for 22.7%, despite the fact that in 58% of all patients the diagnosis was incidental (Figure 4). In addition, in others, constitutional syndrome (17%) and hematuria (12.5%) were motivating factors.

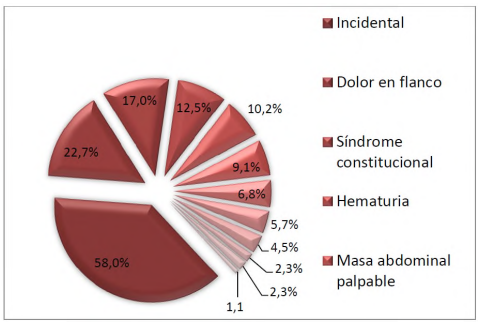

Figure 4. Symptoms and signs of renal carcinoma present at diagnosis.

Table 1. Histopathological diagnosis and presence of necrosis.

Histopathological diagnosis	Presence of necrosis		
	Yes	No	Total

	No.	%	No.	%	No.	%
Clear cell carcinoma	19	21,6	37	42,0	56	63,6
Papillary carcinoma	7	8,0	3	3,4	10	11,4
Clear cell carcinoma granular variety	1	1,1	2	2,3	3	3,4
Clear cell carcinoma tubular arrangement	3	3,4	5	5,7	8	9,1
Renal cystic multilocular cystic carcinoma	-	-	2	2,3	2	2,3
Chromophobe carcinoma	1	1,1	1	1,1	2	2,3
Tubulocystic carcinoma	1	1,1	-	-	1	1,1
Mixed clear cell and chromophobe carcinoma	2	2,3	2	2,3	4	4,6
Mixed clear cell, papillary and chromophobe carcinom	1	1,1	-	-	1	1,1
Others	-	-	1	1,1	1	1,1
Total	35	39,8	53	60,2	88	100,0
Sarcomatoid differentiation	5	5,6	1	1,1	6	6,8

Source: medical records.

Clear cell carcinoma was predominant in the series of patients (63.6%), followed by papillary carcinoma (11.4%). Tumor necrosis was absent in 60.2%, 6.8% of the total showed sarcomatoid differentiation, of which 5.6% showed necrosis (Table 1).

The results of the variables that showed statistical significance are presented in bold.

In our study, it was observed that the pT3a stage prevailed, representing 25%, followed by pT1b in 20.5%, with the majority of these in the N0 M0 stage for 20.5% and 19.4% respectively, and it was also observed that 88.8% of the cases did not present local or distant metastatic invasion.

Table 2. TNM staging

pT	**N0 M0**		**N0 M1**		**N1 M0**		**N1 M1**		**N2 M0**		**N2 M1**		**Total**	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
15	17,1	-	-	1	1,1	-	-	-	-	-	-	16	18,2	15
17	19,4	-	-	1	1,1	-	-	-	-	-	-	18	20,5	17
10	11,4	-	-	-	-	-	-	-	-	-	-	10	11,4	10
5	5,7	-	-	-	-	-	-	-	-	-	-	5	5,7	5
18	20,5	-	-	3	3,4	-	-	1	1,1	-	-	22	25,0	18
7	7,9	-	-	-	-	-	-	-	-	-	-	7	7,9	7
3	3,4	-	-	-	-	-	-	-	-	-	-	3	3,4	3
3	3,4	-	-	1	1,1	1	1,1	-	-	2	2,3	7	7,9	3
78	88,8	-	-	6	6,7	1	1,1	1	1,1	2	2,3	88	100,0	78

Primary tumor (T). Regional lymph nodes (N). Distant metastases (M)

T1a: Tumor 4 cm or less T1b: Tumor > 4 cm but < or = 7 cm T2a: Tumor >7 but < or = 10 cm T2b: Tumor > 10 cm.

T3a: Macroscopic extension of the tumor to the renal vein or its segmental branches or invasion of the perirenal fat and/or renal sinus (peripelic).

T3b: Macroscopic extension of the tumor to the cava below the diaphragm.

T3c: Macro extension to the cava above the diaphragm or invades the wall of the vena cava.

T4: Invasion beyond Gerota's fascia (including contiguous extension to the adrenal gland).

N0: No regional lymph node metastasis.

N1 Metastasis in a single regional lymph node.

N2 Metastasis in more than one regional lymph node.

M0: No distant metastasis.

M1: There are distant metastases.

4. Discussion

So far, the present study on the actual incidence of renal cell carcinoma is the only one based on a population-based registry in the territory. The presentation of cases of renal cancer, according to the data collected, has not followed a linear trajectory, despite the increase over time, a slight decrease in incidence was noted in the last year studied, which could be due to the silent course of some of them that does not allow suspicion.

The incidence rate for the five years studied was estimated at 1.66 per 100,000 inhabitants. Globally, kidney cancer according to Globocan data in 2012, the incidence of kidney cancer represented 4.4 cases/100000 inhabitants/year. This varies according to the areas of the world and the type of population studied, and it is observed that it increases in areas of greater development and industrialization. In Cuba, an incidence of 517 new cases was estimated in 2012[(12)].

The data presented reflect a relatively lower real incidence in our environment than that reported so far in other countries and the world, a fact that undoubtedly has to do with the design of the study and the representativeness of the sample.

With respect to the characteristics of the patients and the lesions found, there were no major differences in relation to other currently available data. The analysis of the age distribution shows that the mean age in our casuistry was 59.8 years, this age corresponds to that published in the literature where a mean age between 58 and 65 years is mentioned. The sex ratio was 2:1 male/female, which coincides with that published in the literature, where there is a clear preponderance of the male sex in all the series 2-3/1.

Its cause remains unknown according to Darias[13], however, numerous risk factors have been implicated in its appearance.[1,3,6,13] García, et al[14] report, as in this study, that among the toxic habits smoking is the most frequent, a criterion shared by other authors[15,16].

Regarding symptoms and signs at diagnosis, our series coincides with the literature where a marked incidence of asymptomatic tumors is published. There are no precise symptoms and it is not uncommon to discover CRC accidentally during studies performed for other causes.[1,3,6,17]

Arteche[17] reports that the most frequent reasons for admission in his series were low back pain and hematuria, respectively. Hematuria is an essential sign, but late. Inamura[18] points out urinary manifestations and general symptoms as other causes of admission.

Garcia, et al[14] in their study report that the most frequent histological type is clear cell carcinoma and with less frequency papillary carcinoma is detected. On the other hand, Lorente, et al[19] observed the absence of tumor necrosis in the highest percentage of the tumor masses studied, which suggested a better prognosis for these patients than for those who did present it. The sarcomatoid variety represents in the world approximately 4-5% of all renal cell carcinomas, coinciding with the present study, where it could also be appreciated that the tumors with sarcomatoid differentiation almost entirely presented tumor necrosis, which denotes greater aggressiveness and worse prognosis than the rest of the histological varieties[20,21,22].

The pT values found in the literature, where the highest percentage has been found in stage pT1b followed by pT3a coincide with this study, as described by García[14] and Prokopowicz, et al[23], which may be largely due to an increase in the detection of incidental tumors due to the profusion of abdominal imaging diagnostic tests for the first stage and for the most advanced stage due to the late appearance of symptoms and the low specificity of the same on many occasions.

At the time of the study, some of the statistics departments did not have digitalized information that would facilitate the proper identification of patients with kidney cancer. An underreporting in the statistical report of renal cancer was found when it was evidenced through medical records and pathology reports that several of these patients did not suffer from this disease and had other urological pathologies (tumors at another level or lithiasis), in addition, some of the medical records were not complete, so it was not possible to include other useful variables to expand the research, being these limitations for the study.

5. Conclusions

There has been a modest but significant increase in the incidence of renal carcinoma in the province of Santiago de Cuba in recent years. It appears more frequently between the fifth and sixth decades of life and in the male sex. Smoking is the main risk factor. More than half of the cases are diagnosed incidentally and asymptomatically, but symptoms such as flank pain, hematuria, general symptoms and palpable abdominal mass are motivating for its diagnosis. Clear cell tumor is the histologic variety most commonly affected. Currently, renal tumors are diagnosed in early stages, but the tendency towards late diagnosis is even more pronounced. Family physicians, clinicians, urologists and radiologists are involved in its diagnosis, so it is important to be aware of this entity since it can present in the most unsuspected way.

References

1. Campbell Steven C, Lane Brian R. Malignant renal tumors. In: Wein Alan J, et al. Campbell-Walsh Urology. 10maed [Internet]. Mexico: DF; 2015. [cited 16 May 2021]; v.2. p:1431-1509. Available from: https://booksmedicos.org/campbell-walsh-urology-10a-edition/.
2. Calvo Vazquez I, Santander Flores SA, Gonzales Villegas P, Bravo López GM, Yañes Sosa AL, Reyna Blanco I. Radical nephrectomy: incidence of morbidity and mortality in a tertiary level hospital. Rev Mex Uro l [Internet]. 2017 Nov-Dec [cited 16 May 2021]; 77(6):446-452. Available from:

https://docplayer.es/137750357- Nefrectomy-radical-radical-incidence-of-morbidity-and-mortality-in-a-third-level-hospital.html.
3. Mahdavifar N, Mohammadian M, Ghonchen M, Salehiniya H. Incidence, Mortality and risk factors of Kidney cancer in the world. World Cancer Res J [Internet]. 2018 [cited 16 May 2021]; 5(1):1-9. Available from: https://www.wcrj.net/wp- content/uploads/sites/5/2018/03/e1013- Incidence-Mortality-and-Risk-Factors-of- Kidney-Cancer-in-the-World.pdf.
4. Ljungberg B, Albiges L, Abu-Ghanem Y, Bensalah K, Dabestani S, Fernández-Pello S, et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update Eur Urol [Internet]. 2019 [cited 16 May 2021]; 75:799-810. DOI: https://doi.org/10.1016/j.eururo.2019.02.01 1
5. Campbell S, Uzzo R, Allaf M, Bass E, Cadeddu J, Chang A, et al. Renal mass and Localized renal cancer: AUA Guideline. Am Urol Assoc Educ Res [Internet]. 2017 [cited 16 Apr 2021]; 1-50. Available from: https://www.ncbi.nlm.nih.gov/pubmed/284 79239.
6. Sánchez-Lorenzo IM, Torres-Reyes JE, Espinosa-Rondón L, Alvares-Sánchez IM, Peña-Rodríguez H. Characterization of clinical and therapeutic variables in patients with clear renal cell adenocarcinoma. Rev Electron Dr. Zoilo E. Marinello Vidaurreta [Internet]. 2018 [cited 16 May 2021]; 43(4). Available from: http://www.revzoilomarinello.sld.cu/index.p hp/zmv/article/view/1459.
7. Uscanga-Yépez J, Martnez-González A, Segovia-Sandoval K, Barrera-Juárez E, González-Oyervides R. Clinical manifestations and oncologic outcomes of renal cancer in a hospital in northern Mexico. Rev Mex Urol [Internet]. 2018 May-Jun [cited 16 May 2021]; 78(3):176-182. DOI: https://doi.org/10.24245/revmexurol.v78i3. 1929
8. Cancer of the Kidney and Renal Pelvis - SEER Stat Fact Sheets [Internet]. 2020 Oct [cited16May2021].Availablefrom:http://seer.cancer.gov/statfacts/html/kidrp. html.
9. ONEI. Statistical Yearbook of Santiago de Cuba 2016 [Internet]. Santiago de Cuba: National Office of Statistics and Information; 2017. [cited 16 May 2021]. Available from: http://www.onei.gob.cu/sites/default/files/ anuario_est_provincial/00_santiago_de_cub a.pdf.
10. Montironi R, Cheng L, Scarpelli M, Lopez- Beltran A. Pathology and Genetics: The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, Penile, and Testicular Tumours. Eur Uro [Internet]. 2016 Jul [cited 16 May 2021]; 70(1):93-105. Available from: https://www.clinicalkey.es/service/content/ pdf/watermarked/1-s2.0- S0302283816002062.pdf?locale=en_US&sear chIndex=
11. Motzer RJ, Bolger GB, Boston B, Carducci MA, Fishman M, Hancock SL, et al. Clinical Practice Guidelines in Oncology Kidney Cancer. J Natl Compr Canc Netw [Internet]. 2006 Nov [cited 16 May 2021]; 4(10):1072-81. Available from:https://pubmed.ncbi.nlm.nih.gov/19555584/
12. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Cancer Incidence and Mortality Worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer [Internet]. 2015 Mar [cited 16 May 2021]; 136(5):E359-86. DOI: https://doi.org/10.1002/ijc.29210
13. Darias Martín JL, Rodríguez Collar TL. Influence of initial tumor stage on survival in patients with renal adenocarcinoma Rev Cubana Med Mil [Internet]. 2018 [cited 16 May 2021]; 47(1):33-42. Available from: http://www.revmedmilitar.sld.cu/index.php/mil/article/view/101
14. García García A, Guerra Román F B, García Morales I. Simple enucleation in the treatment of renal tumors Rev Cubana Urol [Internet]. 2017 [cited 16 May 2021]; 6(1). Available from: http://www.revurologia.sld.cu
15. Velis J, et al. Risk models for patients with localized renal cell carcinoma. Actas Urol Esp [Internet]. 2017 [cited 16 May 2021]; 41(9):564-570. DOI: https://doi.org/10.1016/j.acuroe.2017.08.00 7
16. Gelfond J, et al. Modifiable risk factors to reduce renal cell carcinoma incidence: Insight from the PLCO trial. Urol Oncol [Internet]. Jul 2018 [cited 16 May 2021]; 36(7):340.e1-340.e6.DOI: https://doi.org/10.1016/j.urolonc.2018.04.0 11
17. Arteche AH. Descriptive epidemiology and survival analysis of kidney cancer in public hospitals of the Autonomous Community of Madrid Doctoral Thesis. Madrid: Universidad Complutense de Madrid, Facultad de Medicina; 2017 [cited 16May2021].Available-from:https://eprints.ucm.es/id/eprint/47126/1/T39799.pdf
18. Inamura K. Renal Cell Tumors: Understanding Their Molecular Pathological Epidemiology and the 2016 WHO Classification. Int J Mol Sci [Internet]. 2017 [cited 16 May 2021]; 18(10). DOI:https://dx.doi.org/10.3390%2Fijms1810219 5
19. Lorente D, Trilla E, Meseguer A, Planas J, Placer J, et al. Systematic review of prognostic factors in renal carcinoma. Actas Urol Esp [Internet]. 2017 [cited 16 May 2021]; 41(4):215-225. DOI:http://dx.doi.org/10.1016/j.acuro.2016.08.0 03
20. Lorente ED, Trilla A, Meseguer J, Arévalo S, et al. Value of STAT3c protein as a prognostic factor in clear cell renal carcinoma. Systematic review. Actas Urol Esp [Internet]. 2019 [cited 16 May 2021];43(3):118-123. DOI: https://doi.org/10.1016/j.acuro.2018.08.003
21. Clemmensen T, et al. Pathologic and clinical characteristics of early onset renal cell carcinoma. Human Pathology [Internet].2018[citado16May2021];74:25-

31.DOI:https://doi.org/10.1016/j.humpath.2017.11.005
22. Alevizakos M, Gaitanidis A, Nasioudis D, Msaouel P, Appleman LJ. Sarcomatoid renal cell carcinoma: population-based study of 879 patients. Clin Genitourin Cancer [Internet]. 2019 [cited 16 May 2021]; 17:e447-e453. DOI: https://doi.org/10.1016/j.clgc.2019.01.005
23. Prokopowicz G, Kowski M, Nowakowski K, Bogacki R, Bryniarski P, Paradysz A. Basic Parameters of Blood Count as Prognostic Factors for Renal Cell Carcinoma. Bio Med Res Int [Internet]. 2016 [cited 30 Nov 2021]:8687575.Available-from:https://www.hindawi.com/journals/bmri/2016/8687575/