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Epidemiology and Factors Related to the Survival of Metastatic Kidney Cancers: Retrospective Study at the Mohamed VI Center for the Cancer Treatment in Casablanca, Morocco

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Abstract:-

- ***Background***

Kidney cancer in adults has a high metastatic potential with poor survival rates. Pronostic factors would improve the choice of a therapeutic method. We decided to revisit epidemiology and evaluate survival factors in kidney metastatic carcinomas in a Moroccan setting.

- ***Method:***

Retrospective data collect from 2017 to 2020 of all adults patients presenting with metastatic kidney carcinomas. Epidemiology and survival rates were analysed using SPSS.

- ***Results*:**

We included 79 patients, predominantly over 60yo and male. Metastases were observed in lungs (73.4%), lymph nodes (39.2%), livers (31.6%), bones (35.4%) and peritoneum (17.8%). Metastases were concurrent to the primitive tumor in 59.5%. Histology was predominantly clear cell renal carcinoma. According to IMDC score, 77% of patients had an intermediate score. Global survival was 29%, better for patients with an intermediate score (p=0.009) as well as progression free survival (p=0.001). In multivariate analysis, only the OMS performance status (p=0.008) and height (0.02) were associated with survival.

- ***Conclusion***

Thé IMDC score is a suitable tool to classify patients with metastatic kidney cancers, in order to guide therapeutic choices.

Keywords:- *Epidemiology, Kidney, Cancer, Metastatic, Survival, Morocco.*

I. INTRODUCTION

Kidney cancer accounts for 3% of malignant tumors in adults. It is the third most common urological cancer after prostate and bladder [1]. According to the Cancer Registry of the greater Casablanca region in its 2022 version, kidney cancer ranks 21st among all cancers with a proportion of 1% [2]. The metastatic potential of renal cancer is significant. We find 10 to 40% who are metastatic from the outset at the time of diagnosis [3] with mediocre survival. More than a third of patients treated by nephrectomy for localized disease will develop metastases during their evolution [1]. Survival has been improved by the advent of targeted therapies and immunotherapy with checkpoint inhibitors. Therapeutic choices remain oriented according to the classification into prognostic groups [4, 5]. Knowing other factors that influence the survival of metastatic kidney cancers despite the prognostic classification would allow a better choice of treatment plan in the era of new therapies. We therefore undertook to study the epidemiology and evaluate the factors related to the survival of metastatic kidney cancers in the Moroccan context.

II. METHOD

We retrospectively collected from 2017 to 2020 all adult patients with metastatic renal cell carcinoma. In addition to collecting epidemiological data, we assessed progression-free survival and overall survival at 6 months, 12 months and 24 months. The evaluation of the patients was clinical every month and radiological every 3 months by a thoraco-abdomino-pelvic scanner. We used as a data collection source the computerized patient registration system of the Mohamed VI center for the treatment of cancers in Casablanca. Data entry and analysis were performed using SPSS software version 21. The proportions were compared using the CHI 2 test in univariate analysis. The ORs adjusted by a multivariate logistic regression model were also presented with their 95% CIs with a significance level of 0.05. We used the Kaplan Meier model for the comparison of survivals.

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III. RESULTS

Our collection covered 79 patients. The average age was 61 years with extremes of 31 years and 91 years. The majority of patients were over 60 years old representing 54.4% of our study population. Only 3.8% were under 40 years old. Patients aged between 40 and 60 years were 33 or 41.8%. Most of the patients were male, i.e. 73.4%. A comorbidity was found in 56% of patients with type of diabetes in 11% of cases and type of hypertension in 14%. Only 3.8% of patients had a history of heart disease. In terms of proven risk factors for kidney cancer, 42% had a history of smoking, no patient was known to be obese. A family history of cancer other than kidney cancer was found in 06 (7, 6%) patients divided into 01 cases of breast cancer, 01 cases of stomach cancer and 04 cases of prostate cancer. The majority of patients had a good general condition at the first consultation with a WHO Performans status (PS) between 0 and 1 in 73.4% of patients. On the circumstances of diagnosis: the discovery of cancer was fortuitous in 06 patients, the cancer was revealed by a metastasis in 11 patients. Low back pain was the major symptom at diagnosis, ie 72.2%, followed by hematuria in 39.2%, then a lumbar mass in 11.4%. Only 04 patients presented the classic triad made up of low back pain, hematuria and a lumbar mass at the time of diagnosis. No patient had a delay between diagnosis and the start of systemic treatment greater than 1 year. The delay in consultation greater than 3 months after the first symptoms was 48.1%. Renal function was impaired in 25% of patients. The left kidney was more involved, ie 51.9%, there was not one case of damage to 02 kidneys simultaneously. The tumor larger than 10 cm was the most represented, i.e. 49.4%. Respectively 29.1%, 20.3% and 1.3% of the tumors had a size between 7 and 10 cm, between 4 and 6 cm and less than 4 cm. The average size of the tumor was 11 cm in the whole population with extremes of 4 cm and 25 cm. The tumor was of upper polar seat in majority, i.e. 46.8%, followed by the mid-renal seat in 19% of cases and the lower polar seat in only 10.1% of cases. The entire kidney was the site of the tumor at the time of diagnosis in 24.1%. The type of tumor development was exophytic in 65.8% of cases. Metastasis sites were lung 73.4%, lymph nodes 39.2%, liver 31.6%, bone 35.4%, peritoneum 17.8%, adrenal 8.9% and brain in only 3.8%. Metastasis was synchronous in 59.5% of cases, revealing in 13.9% and metachronous in 26.6%. The time to onset of metachronous metastases varied between 12 months and 180 months. For the number of metastasis sites at the time of diagnosis: 31.6% had a metastasis in a single organ, of which 01 cases were immediately resectable; 35.4% had metastasis in 2 organs; 20.3% had metastasis in 3 organs and 12.7% had metastasis in more than 3 organs. The tumors were stage cT3a in 29.1% of cases, cT2b in 27.8%; cT2a and cT3b in 11.4%, cT4 in 10.1% of cases, cT1b in 6.3%, cT3c and cT1a respectively in 1.3%. The therapeutic approach applied was systemic treatment alone by targeted anti-angiogenic therapy in the majority of cases, ie 46.8%; cytoreductive nephrectomy plus targeted anti-angiogenic therapy in 30.4% of cases; cytoreductive nephrectomy alone in 7.6% and palliative and supportive care alone in 15.2%. On the therapeutic level, 03 patients benefited from surgery on the metastasis. Palliative radiotherapy was performed in 05 patients including 02 cases of radiotherapy on the entire brain and 03 cases of analgesic radiotherapy on the spine. The most represented histological type was clear cell renal carcinoma (78.5%) followed by papillary carcinoma (8.9%), chromophobe carcinoma (6.3%), collecting tubule carcinoma (3.8%) and medullary carcinoma (2.5%). For the factors of poor histo-pathological prognosis, we found the presence of vascular emboli in 70% of cases, the presence of perineural sheathing in 35%, the presence of a sarcomatoid component in 9%, invasion of the system collectors in 18%, the presence of tumor necrosis in 43%. Fuhrman's grade was 3 in 44%, grade 2 in 42% and grade 4 in 8%, was unspecified in 6%. According to the prognosis classification of the International Metastatic Renal-Cell Carcinoma Database Consortium (IMDC), also known as the Heng score: 77% of patients had an intermediate score while 23% had a poor prognosis score. None of the patients had a good prognosis according to the IMDC score. Overall survival is 29%. The overall survival at 6 months, 12 months and 24 months was 85%, 60% and 34% respectively. Progression-free survival at 6 months, 12 months, and 24 months was 71%, 43%, and 20%, respectively. Median overall survival was 14 months. According to the IMDC score, there was better overall survival in intermediate risk patients (27%) versus low risk patients (1.3%) with $p = 0.009$. The average overall survival time in the intermediate risk group was 29 months with a 95% confidence interval between 23 and 35 months while the average overall survival time in the low risk group was 09 months with a 95% confidence interval between 06 and 12 months ($p = 0.001$). The mean duration of progression-free survival was 24 months with a 95% confidence interval between 17 and 31 months in the group of patients at intermediate risk. On the other hand, this average duration of progression-free survival in the low-risk group according to the IMDC score was 07 months with a confidence interval of 95% between 04 and 10 months. This result was statistically significant with $p = 0.001$. In multivariate analysis, only the WHO performans status and the size of the tumor at the time of diagnosis are associated with survival: patients with a WHO status between 0 and 1 had a better survival ($p = 0.008$), as well as for patients whose tumor was ≤ 6 cm in size ($p = 0.02$). On the other hand, this average duration of progression-free survival in the low-risk group according to the IMDC score was 07 months with a confidence interval of 95% between 04 and 10 months. This result was statistically significant with $p = 0.001$. In multivariate analysis, only the WHO performans status and the size of the tumor at the time of diagnosis are associated with survival: patients with a WHO status between 0 and 1 had a better survival ($p = 0.008$), as well as for patients whose tumor was ≤ 6 cm in size ($p = 0.02$). 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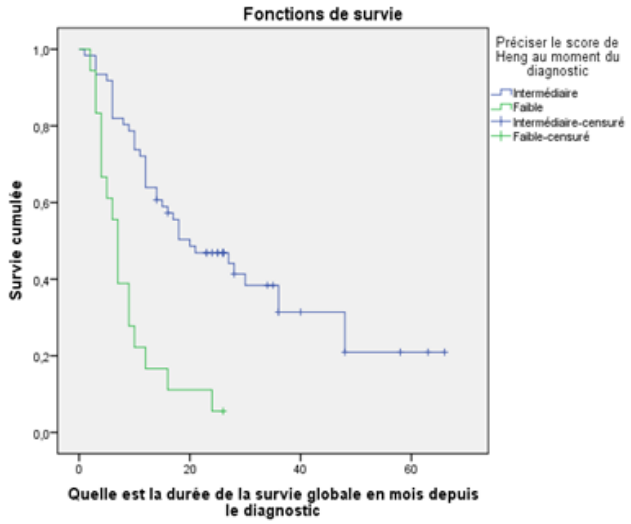

Fig.1. Survie globale selon le score de Heng

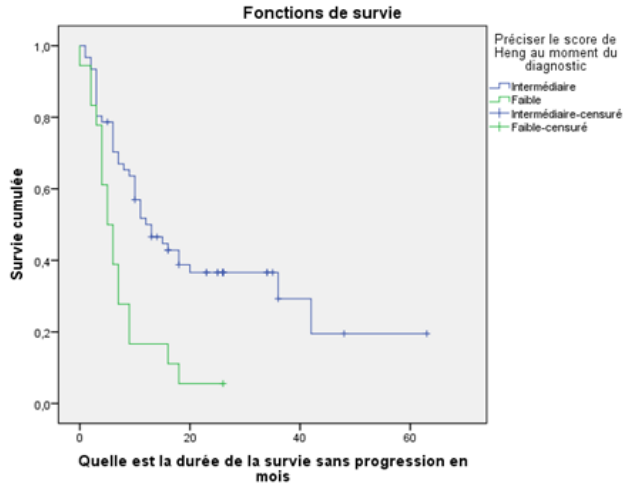

Fig.2. Survie sans progression selon le score de Heng

IV. DISCUSSION

Kidney cancer is a rare localization even if its incidence has increased in recent years with the forms of incidental findings due to medical imaging techniques. In adults, kidney cancer is encountered from the age of 60 [1, 6], in our cohort we have the same average age. The very strong male predominance in the literature [6] is also found in our study with 73.4% male. The risk factors commonly incriminated and found in our patients are smoking, arterial hypertension and diabetes. Very few patients have presented the classic triad of urinary symptoms, which is explained by the fact that the classic triad made up of low back pain, lumbar mass and hematuria is a late sign that most often appears in the very advanced phase. Pulmonary and bone metastatic sites were the most represented, as in the literature [7]. But survival was not correlated with sites of metastasis or number of metastases. The histological type of clear cell renal cell carcinoma is the most frequent entity [8], ie 78.5% in our cohort. For several years, the management of metastatic kidney cancer has been more personalized with the consideration of prognostic groups to better adapt the treatment to the severity of the pathology [9]. Several prognostic group models have been evaluated and used from the past with the use of cytokines until the advent of targeted angiogenic therapies in systemic treatment. The most widely used model is the Memorial Sloan-Kettering Cancer Center (MSKCC) model [10], which contains many of the same factors as the Database Consortium model. Other models have been used, including: the Cleveland Clinic Foundation (CCF) model [11], the French model updated and adapted to the AVOREN trial [12, 13], and the model of the International Working Group on kidney cancer (IKCWG) [14]. Currently, the prognostic model commonly used in clinical practice is the International Metastatic RCC Database Consortium (IMDC) classification, known as the Heng score [4]. It is a score that takes into account the general condition (Karnofsky index < 80%), the time between diagnosis and the start of systemic treatment < 1 year, the hemoglobin level < normal, the rate of neutrophils > to normal, the platelet count > to normal as well as the corrected calcemia > to 10 mg/dl, thus making it possible to define 3 groups: good prognosis without any factor, intermediate prognosis if 1 or 2 factors and poor prognosis beyond 3 factors. This classification remains the current classification standard for metastatic kidney cancer. We found no other clinical or histological factors in our cohort that were significantly associated with survival apart from tumor size, general condition being taken into account in the Heng score. Since the CARMENA [15] and SURTIME [16] clinical trials, the management of metastatic renal cell carcinoma remains dependent on the prognostic classification: there is no interest in survival by performing cytoreductive nephrectomy in the poor and intermediate prognosis but rather systemic treatment with targeted angiogenic therapy of the tyrosine kinase inhibitor type. Cytoreductive nephrectomy can even prove to be deleterious for the patient, rendering him unfit for systemic treatment. In our cohort, 7.6% of patients who immediately underwent cytoreductive nephrectomy were unable to undergo systemic treatment with targeted therapy due to poor general condition after surgery. On the other hand, a first-line systemic treatment could make it possible to operate on the patient later if he responds to the treatment. Admittedly, in our study there were no patients with a favorable prognosis, but we found that survival was better in the intermediate prognosis group compared to the unfavorable prognosis group (p = 0.001). It is judicious to note that the survival factors identified and grouped together in the prognostic classifications, including that of the IMDC, belong to the era of cytokines (interferon alpha and interleukin 2) and anti-VEGFR TKIs. We are currently in the era of immunotherapy by immune checkpoint inhibition: since 2020 with the KEYNOTE 426 [17] and CheckMate 214 [18] trials, but also the CheckMate 9ER [19] and CLEAR [20] studies. , the standard first-line treatment algorithm to date is double immunotherapy or immunotherapy in combination with an anti-VEGFR Tyrosine Kinase Inhibitor [21]. The reassessment of prognostic factors through a clinical trial based on immunotherapy as systemic treatment could be necessary in order to further optimize the management of metastatic renal cell carcinoma.

V. CONCLUSION

The IMDC classification remains the appropriate tool for classifying patients with metastatic kidney cancer in order to guide therapeutic choices. But in the current era of checkpoint inhibitors, the place of surgery in the prognostic model remains to be elucidated. Therapeutic choices remain personalized according to each patient.

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