SUMMARY

Renal cell carcinoma (RCC) is one of the most lethal of the urologic malignancies with 40% of patients dying of cancer progression. Its incidence has increased in the last years due to a greater number of patients diagnosed with localized disease. Its specific mortality rate has also increased, and it seems that in a subpopulation of these patients the tumor will progress despite the surgical treatment. Because of the resistance to conventional chemotherapy and a low response to immunotherapy, the prognosis of metastatic RCC remains poor.

Therefore, the identification of high-risk patients is an important issue in the management of the disease. As the classical prognostic parameters, such as stage, nuclear grade and vascular invasion are not sufficient to predict its clinical outcome, the detection of some new, more sensitive and specific prognostic markers of tumor behavior is of upmost importance.

OBJECTIVES

The aim of this study is:

I. To evaluate both the immunohistochemical expression of the proliferation marker Ki67 and its impact on disease progression on patient survival after surgical treatment for RCC.
II. To analyze the immunohistochemical expression of biomarkers related to apoptosis such as p53, MDM-2, Bcl-2 and survivin and its impact on disease progression and on patient survival after surgical treatment for RCC.
III. To determine the prognostic value of the histopathological tumor profile according to the classical parameters.
IV. To study the presence and extension of some additional histological parameters such as coagulative necrosis and mononuclear cell infiltrate in localized RCC, and its prognostic value following surgical treatment.

METHODOLOGY

148 patients with localized CCR who underwent radical or partial nephrectomy between 1993 and 2006 were selected on the basis of the adequacy of the pathological sample, and the availability of clinical follow-up-date at the Urology and Pathology Departments of the "Principe de Asturias" University Hospital.

The clinical diagnosis was initially established using imaging tests, ultrasonography or intravenous urography, and confirmed by computed tomography (CT). The tumor extension was determined by CT and a plan x-ray chest.

The histopathological examination and classification was performed according to TNM staging of RCC (2002), Fuhrman grade-classification and the WHO histological classification of RCC.

Immunohistochemical evaluation was performed on 4 tissue microarray blocks including to samples per patient.

CONCLUSIONS

1. Tumor stage (pT) behaves like an independent prognostic factor for predicting disease-specific survival and disease-free survival in RRC.
2. Ganglionar stage (pN) pN2 is an independent prognostic factor for predicting disease-specific survival and disease-free survival in RCC. Nevertheless, considering the clear cell subtype alone, it is not a prognostic factor.
3. Histological type appeared not to be an independent prognostic factor for predicting disease-specific survival and disease-free survival in RRC.
4. Fuhrman's nuclear grade is associated to a worse disease-specific survival and disease-free survival, but it doesn't behave like an independent prognostic marker in multivariate model in RCC.

5. The presence of coagulative tumor necrosis appeared to be an independent prognostic factor for predicting disease-specific survival and disease-free survival in RCC. In the clear cell type alone it doesn't behave like a prognostic marker.
6. The presence of mononuclear cell infiltration is an independent prognostic marker for predicting disease-specific survival and disease-free survival in RCC.
7. The elevated immunoexpression of Ki67 behaves like a prognostic factor for predicting disease specific survival in the clear cell subtype of RCC. In the whole series of RCC it is associated with a poor prognosis but without statistic significance. It doesn't behave like a prognostic factor for predicting disease-free survival.
8. Elevated expression of p53, MDM-2, Bcl-2 and Survivin can not be considered an independent prognostic factor for predicting disease-specific survival or disease-free survival in RCC: