Stockholm
17-21 March 2009

Fact sheet 4 – Important studies on renal cell cancer

Studies are being conducted in several areas related to renal cell cancer. For example, the exact role of partial nephrectomy and its oncological outcome is being investigated. A relevant study in this respect is 'The indications for partial nephrectomy in the treatment of renal cell carcinoma' by Joniau S, Vander Eeckt K and Van Poppel H in Nature Clinical Practice Urology 3 (4): 198-205, Apr 2006.
Abstract: Partial nephrectomy is performed more frequently for small, incidentally discovered, low-stage renal tumors. Importantly, one should distinguish the imperative indications for such surgery from the relative and elective indications, while taking contraindications to nephron-sparing surgery into account. The main advantage of partial nephrectomy over radical nephrectomy is the avoidance of renal insufficiency; the major disadvantages include the possibility of local recurrence and perioperative complications. In this article, the literature on nephron-sparing surgery was reviewed in order to put the management of renal cancer into a modern perspective.

Targeted therapy for renal cell cancer is an area of interest as well. 'Renal cell carcinoma 2005: new frontiers in staging, prognostication and targeted molecular therapy' by J.S. Lam, O. Shvarts, J.T. Leppert, R.A. Figlin and A.S. Belldegrun in The Journal of Urology, Vol. 173, 1853–1862, June 2005 is a major study in this respect.
Abstract: Purpose: Renal cell carcinoma (RCC) has traditionally been staged using a purely anatomical staging system. Although current staging systems provide good prognostic information, data published in the last few years has led to significant controversies as to whether further revisions are needed and whether improvements can be made with the introduction of new, more accurate and predictive prognostic factors not currently included in traditional staging systems. This review highlights such controversies and provides an update on current staging modalities, prognostic factors and targeted molecular therapy for RCC.
Materials and Methods: A comprehensive review of the peer reviewed literature was performed on the topic of current staging modalities, validated prognostic factors, predictive nomograms, molecular markers and targeted molecular therapy for RCC.
Results: A staging system for malignant disease such as RCC uses various characteristics of tumors to stratify patients into clinically meaningful categories, which can be used to provide patients with counseling regarding prognosis, select treatment modalities and determine eligibility for clinical trials. The TNM staging system is currently the most extensively used one. However, it has undergone recent systematic revision due to rapidly emerging data from longer patient followup. The identification of various histological and symptomatic factors has led groups at many centers to develop more comprehensive staging systems that integrate these factors and include patients with metastatic and local disease. While integrated staging systems have improved RCC staging, the recent discovery of molecular tumor markers is expected to revolutionize RCC staging in the future and lead to the development of new therapies based on molecular targeting.
Conclusions: Staging systems for RCC serve as a valuable prognostic tool. Several new patient and tumor characteristics have been reported to be important prognostic factors and they have been integrated into current staging systems. In addition, the field of RCC is rapidly undergoing a revolution led by molecular markers and targeted therapies. With this information urologists will be updated with the most current and comprehensive staging strategies, and be provided with a glimpse of the molecular and patient specific staging and treatment paradigms that will in our opinion transform the future management of this malignancy.

In the field of carbonic anhydrase in the treatment of renal cell carcinoma, 'Carbonic Anhydrase IX Expression Predicts Outcome of Interleukin 2 Therapy for Renal Cancer' by M. Atkins et al gives a good overview.
Abstract: Purpose: Renal cancer response to interleukin 2 (IL-2) therapy and patient survival has been correlated with tumor histology and carbonic anhydrase IX (CAIX) expression. In an effort to confirm and expand these observations, we examined CAIX expression in pathology specimens from renal cancer patients who had previously received IL-2 therapy.
Experimental Design: Paraffin-embedded tissue sections of renal cancer were immunostained with the MN-75 monoclonal antibody to CAIX and expression levels were correlated with histologic

findings and clinical outcome.
Results: Tissue specimens were obtained from 66 patients; 27 of whom (41%) had responded to IL-2^ based therapy. Fifty-eight specimens were assessed as clear cell, with 56, 33, and 4 having alveolar, granular, and papillary features, respectively. Twenty-four (36%), 31 (47%), and 11 (17%) were classified into good, intermediate, and poor prognosis groups according to the Upton pathology model. Forty-one specimens (62%) had high CAIX expression. Twenty-one of 27 (78%) responding patients had high CAIX expressing tumors compared with 20 of 39 (51%) nonresponders (odds ratio, 3.3; P = 0.04).Median survival was prolonged (P = 0.04) and survival >5 years was only seen in high CAIX expressers. In patients with intermediate pathologic prognosis, all nine responders had high CAIX expression versus 11of 22 nonresponders. A resultant group with good pathologic prognosis alone or with intermediate pathologic prognosis and high CAIX contained 26 of 27 (96%) responders comparedwith18 of 39 (46%) nonresponders (odds ratio, 30; P < 0.01) and exhibited longer median survival (P < 0.01).
Conclusions: CAIX expression seems to be an important predictor of outcome in renal cell carcinoma patients receiving IL-2^ based therapy and may enhance prognostic information obtained from pathology specimens.

In The Journal of Urology, Vol. 169, 821–827, March 2003, the article 'Prognostic factors of renal cell carcinoma' by A. Méjean, S. Oudard and N. Thiounn was published.
Abstract: Purpose: Determination of prognostic factors is essential for the management of renal cell carcinoma. Stage, histological grade and type, and performance status are now well known and commonly used. During the last decade numerous predictors of patient outcome were tested. This review summarizes the most important studies, explores and compares the results, and tries to respond to the question, "Today, what do we expect of clinical, molecular and genetic factors concerning survival of patients with renal cell carcinoma?"
Materials and Methods: Based on MEDLINE literature searches we comprehensively reviewed the literature on the prognostic factors associated with the tumor, the patient and the treatment.
Results: During the last decades numerous factors have been studied but few of them maintained independent significance in terms of overall survival as assessed by multivariate analysis.
Results are more often controversial from one series to another. No known molecular or cytogenetic tumor marker has been identified to help diagnose, manage or confirm renal cell carcinoma remission, progression or relapse.
Conclusions: The classical prognostic factors remain histological grade, histological type, performance status, patient age, number and location(s) of metastatic sites, time to appearance of metastases and prior nephrectomy. The only striking advancement during the last few years has been the proven contribution of radical nephrectomy for metastatic disease in patients with good performance status.

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