1. Introduction

Worldwide over 200,000 new cases of kidney cancer are diagnosed and approximately 100,000 deaths occur from this disease each year. The highest incidence is found in North America, Europe, and Australia [1]. Surgery of early detected RCC can be curable, but 20–30% of the patients present with metastases on time of first diagnosis. In addition, 20–40% of patients with primary localised disease develop metastasis [2]. The survival of these patients is very poor with 5-yr survival rates < 10%. Treatment with immunotherapy using interferon-α and/or interleukin-2 leads to response rates of 10–20%, some of which are durable. Recently multigated tyrosine-kinase inhibitors sorafenib and sunitinib, and temsirolimus, an inhibitor of mammalian target of rapamycin, became available for treatment of RCC; these medications showed stabilisation or some response in up to 80% of patients. However, present treatment options for RCC remain palliation of disease.

The variable natural history of RCC highlights the need for prognostic factors used to predict outcome for an individual patient. The development of a reliable prognostic model can help in specific treatment strategies and follow-up strategies, and can provide patient with valuable information.

2. Current system: TNM staging system

Although the TNM staging system [3] provides good prognostic information, there has been much debate about the accuracy of this system.
2.1. Tumour size

Primary tumour size is a key component of the TNM staging system and remains one of the most important prognostic factors for RCC. The most recent revision (2002) of the TNM staging system introduced the subdivision of T1 into T1a and T1b, using a 4-cm threshold. On the basis of actual studies, this tumour breakpoint for localised RCC is under discussion [4]. Classification of locally advanced RCC is at present controversial. For example, in T3 cases, some studies identified subgroups with different prognosis, which is controversial to the actual TNM staging system [4].

2.2. Regional lymph node involvement

Terrone et al [5] reported that lymph node density correlated better with prognosis than the current N classification of the TNM system.

3. Pathological prognostic factors not included in the TNM staging system

RCC is mostly predicted by anatomical parameters. Numerous histological as well clinical criteria have been shown to impact prognosis in patients with RCC: nuclear grade, histological subtype, sarcomatoid features, tumour necrosis, collecting system invasion, microvascular invasion, performance status, paraneoplastic symptoms, thrombocytosis, and inflammatory response [6]. On the basis of these and other parameters, a number of useful nomograms and scoring systems have been developed.

4. Molecular biomarkers

Current staging systems are based on pathological and clinical criteria. Molecular biomarkers may be more effective for predicting outcome than traditional parameters. The development of techniques that screen for the expression of thousands of genes have identified a large number of potential prognostic biomarkers: carbonic anhydrase IX, hypoxia-inducible factor, vascular endothelial growth factor ligands and receptors, p53, phosphatase and tensin homologue deleted from chromosome 10 (PTEN), CD44, matrix metalloproteinases, and so on [6]. Biomarkers can be integrated into a multimarker prognostic system. Despite encouraging results, all biomarkers need further validation.

5. Conclusion

The prognostic accuracy in the management of patients with RCC was improved by the existing staging and prognostic models. Improved understanding of the molecular mechanism of RCC provides a tool of potential biomarkers. In the future, integrating prognostic systems with both clinical and molecular markers will enhance the ability to predict the tumour behaviour of an individual patient.

Conflicts of interest

Drs Heinzer, Eichelberg, and Heuer are study investigators for Bayer, Pfizer, Wyeth, Wilex, and Roche.

References