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Epidemiology, Aetiology, and Pathogenesis of Renal Cell Carcinoma

Chris Protzel, Matthias Maruschke, Oliver W. Hakenberg *

Department of Urology, Rostock University, Germany

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Abstract

Significant advances in molecular medicine have made renal cell carcinoma (RCC) the prototype solid organ malignancy for targeted medical cancer treatment. Theseis new options have made it possible to prolong the life of patients with metastatic disease. However, we are far away from thoroughly understanding the molecular processes of RCC development let alone from being able to cure advanced renal cancer. RCC is the most common renal neoplasia and it remains a very aggressive and often fatal disease.

There are several known histologic subtypes of this heterogeneous tumor entity with associated distinct molecular alterations and different clinical outcomes [1–4]. The clear cell renal cell carcinoma (ccRCC) is the most common and apparently most aggressive RCC subtype with the highest rates of local invasion, metastasis and mortality. It constitutes 70–80% of all renal cancers [1,5]. It is estimated that more than 30% of patients with RCC have metastatic disease at the time of diagnosis and 30% of organ-confined RCCs will develop metastatic disease after local treatment [6]. Thus, RCC remains a very major challenge.
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* Corresponding author.
E-mail address: oliver.hakenberg@med.uni-rostock.de (O.W. Hakenberg).

1. Introduction

Significant advances in molecular medicine have made renal cell carcinoma (RCC) the prototype solid organ malignancy for targeted medical cancer treatment. These new options have made it possible to prolong the life of patients with metastatic disease. However, we are far from thoroughly understanding the molecular processes of RCC development, let alone being able to cure advanced renal cancer. RCC is the most common renal neoplasia, and it remains a very aggressive and often fatal disease.

There are several known histologic subtypes of this heterogeneous tumour entity with associated distinct molecular alterations and different clinical outcomes [1–4]. Clear cell renal cell carcinoma (ccRCC) is the most common and apparently the most aggressive RCC subtype with the highest rates of local invasion, metastasis, and mortality. It constitutes 70–80% of all renal cancers [1,5]. It is estimated that >30% of patients with RCC have metastatic disease at the time of diagnosis, and 30% of patients with organ-confined RCCs develop metastatic disease after local treatment [6]. Thus RCC remains a very major challenge.

2. Frequency

RCC overall accounts for 2% of all adult malignancies [7]. Worldwide, based on probably incomplete figures, about 270 000 new cases are diagnosed per year, and about 116 000 patients die per year [8]. In the United States alone, 58 000 new RCC cases were diagnosed in 2010, and approximately 13 000 patients died of RCC in the same year [7,9]. This corresponds to 65 000 new RCC cases per year in the European Union with >25 000 RCC deaths every year [10].

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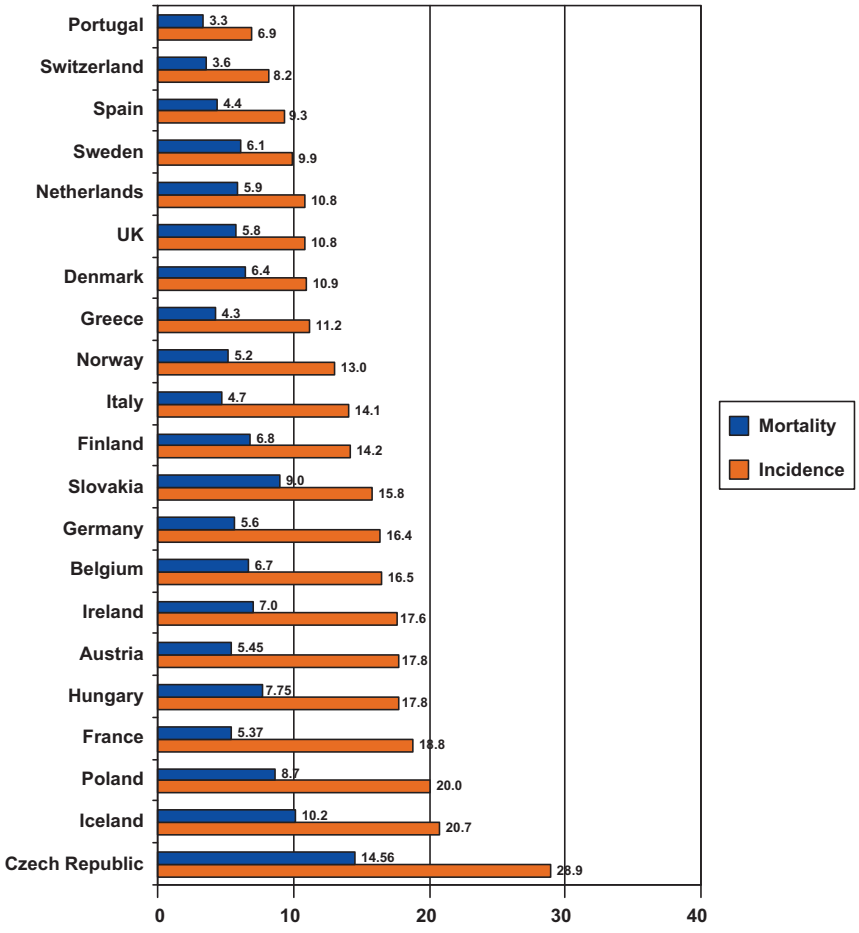

Fig. 1 – Incidence and mortality rates in European countries (modified from Lungberg et al. [10]).

Thus at least 20–40% of patients diagnosed with RCC die of the disease.

Overall, there are some geographic, racial, and gender differences in the incidence of RCC. RCC occurs more than twice as often in men as in women. In Europe, the highest incidence is seen in the eastern parts of Europe; Portugal and Spain report the lowest incidence (Fig. 1). The reasons for this distribution are unclear. The overall incidence rate for Europe is estimated at 14.5 per 100 000 for men and 6.9 per 100 000 for women [10].

There are some indications that a recent increase in incidence together with a stage shift to more organ-confined stages can be observed [11,12]. An apparent stage shift is mainly attributed to a more widespread use of imaging for early detection.

3. Mortality

The mortality from RCC has continually decreased over the last decades. A recent analysis showed a decline in mortality rates (death from RCC per unit of the population) from 4.8 per 100 000 in the period 1990–1994 to 4.1 per 100 000 in 2000–2004 in men [10]. This decline in RCC mortality is also attributed to earlier and the often incidental diagnosis of small RCCs by imaging.

The mortality rates vary, however, among different European countries (Fig. 1). There is no clear explanation for this other than perhaps differences in the use of imaging techniques. As a consequence of the decrease in mortality rates, the 5-yr survival after RCC treatment has increased [13–15].

4. Aetiology

It is poorly understood why people develop RCC. Only a few aetiologic factors have been clinically identified as risk factors for RCC. In contrast, the understanding of some important molecular and genetic factors of RCC development has increased considerably.

4.1. Demographic factors

Age, sex, and race are important factors in RCC development. The incidence of RCC correlates with age, and the highest incidence is found in the sixth and seventh decades. About 80% of all RCC patients are between 40 and 69 yr of age [16]. Due to the increasing life expectancy in many countries and increased early diagnosis, the peak age of RCC diagnosis might shift still further into the seventh and eighth decades of life.

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