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Original article

Results of a comparative study analyzing octogenarians with renal cell carcinoma in a competing risk analysis with patients in the seventh decade of life

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Abstract

Objectives: To analyze clinicopathological features and survival of surgically treated patients with renal cell carcinoma (RCC) ≥80 years of age in comparison with patients between the ages of 60 and 70 years.

Materials and methods: The data for 2,516 patients with a median follow-up of 57 months were retrieved from a multinational database (Collaborative Research on Renal Neoplasms Association [CORONA]), including data for 6,234 consecutive patients with RCC after radical or partial nephrectomy. Comparative analysis of clinicopathological features of 241 octogenarians (3.9% of the database) and 2,275 reference patients between the ages of 60 and 70 years (36.5%) was performed. Multivariable regression analysis adjusted for competing risks was applied to identify the effect of advanced age on cancer-specific mortality (CSM) and

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other-cause mortality (OCM). Furthermore, instrumental variable analysis was employed to reduce residual confounding by unmeasured parameters.

Results: Significantly more women were present (50% vs. 40%, $P = 0.004$), and significantly less often nephron-sparing surgery was performed in octogenarians compared with the reference group (11% vs. 20%, $P < 0.001$). Although median tumor size and stages did not significantly defer, older patients less often had advanced or metastatic disease (N+/M1) (4.6% vs. 9.6%, $P = 0.009$). On multivariable analysis, higher CSM (hazard ratio = 1.48, $P = 0.042$) and OCM rates (hazard ratio = 4.32, $P < 0.001$) were detectable in octogenarians (*c*-indices = 0.85 and 0.72, respectively). Integration of the variable age group in multivariable models significantly increased the predictive accuracy regarding OCM (6%, $P < 0.001$), but not for CSM. Limitations are based on the retrospective study design.

Conclusions: Octogenarian patients with RCC significantly differ in clinical features and display significantly higher CSM and OCM rates in comparison with their younger counterparts.

Keywords: Renal cell carcinoma; Octogenarians; Nephrectomy; Cancer-specific mortality; Competing risks regression analysis; Instrumental variable

1. Introduction

Renal cell carcinoma (RCC) represents the most lethal common genitourinary malignancy. Based on registry data from European countries, lifetime risk for developing RCC is 1.8% for men and 1.1% for women [1]. The conventional peak of disease onset is located within the seventh life decade, and also most studies evaluating prognostic parameters in surgically treated patients with RCC largely refer to this age group [2–4]. However, due to increasing life expectancy and broader application of imaging studies, the incidence of RCC also in patients older than 80 years has increased. Although surgical treatment is considered the therapeutic mainstay for localized RCC, one has to acknowledge that current guidelines and standard treatment protocols were developed predominantly for patients at the typical age of disease onset with a longer remaining life expectancy [2]. In addition, the significance of prognostic parameters for postsurgical cancer-specific mortality (CSM) (TNM stage, grade, and tumor size) has not been validated specifically for older patients, who usually present with enhanced comorbidity likely decreasing life expectancy [2]. On the contrary, one also has to consider that life expectancy in old to very old patients has considerably increased. For example, based on data from the German Statistical Federal Office, 80-year-old women and men have median remaining life expectancy of 9.1 and 7.8 years, respectively. Hence, simultaneous to growing tumor detection rates, also the need for patient counseling regarding optimal treatment in this age group is increasing [5]. Also considering a potentially different tumor biology in older patients, different risk profiles in application of traditional prognostic markers in these patients might be the consequence [6,7]. Moreover, the real benefits of surgery for elderly patients with RCC have not reliably been validated and should be reconsidered.

Few studies have addressed this issue and results are neither concordant nor conclusive [7–10]. Mostly, it was suggested that patients with RCC ≥ 80 years of age are rarely treated with nephron-sparing surgery (NSS) and show higher CSM than younger patients [8,9]. However, until now no study has compared the individual prognostic outcome of this patient group with a matched group of patients in the seventh life decade as the typical age of primary diagnosis. Furthermore, previous studies focused on CSM only and neglected other-cause mortality (OCM), which might vary widely between different age groups. This would consequently reduce the pool of individuals at risk for CSM in patients at higher risk for OCM and, hence, also lead to misinterpretation of the effect of age on CSM.

Thus, to identify the independent effect of age on CSM adjusted for OCM, we compared patients with RCC ≥80 years of age with patients between the ages of 60 and 70 years with regard to clinical presentation, histopathological findings, and postsurgical outcome based on competing risks regression analysis.

2. Materials and methods

2.1. Patient selection, data collection, and features of pathologic evaluation

After obtaining local ethics committee approval, clinicopathological data of 6,234 patients with unilateral surgically treated RCC from 11 centers of the Collaborative Research on Renal Neoplasms Association (CORONA) project were pooled. All patients were consecutively included and underwent radical nephrectomy or NSS (1992–2010).

The final study group included 2,516 participants representing 2 different age groups: the first group comprised 241 patients ≥80 years of age (3.9% of the entire database) and the reference group included 2,275 patients between the ages of 60 and 70 years (36.5%). Abdominal computed tomography, chest imaging (chest x-ray/computed tomography), and a comprehensive serum metabolic panel were used for clinical staging. When indicated by symptoms, bone scan and brain imaging were performed. None of the patients received (neo) adjuvant therapy. Information on patient features was obtained from institutional databases. All surgical specimens were processed according to standard pathologic procedures and analyzed by experienced genitourinary pathologists at each institution. Pathologic stage was reassigned according to the