



Original article

Comparative analysis of comorbidity and performance indices for prediction of oncological outcomes in patients with upper tract urothelial carcinoma who were treated with radical nephroureterectomy¹

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Abstract

Objective: Comorbidity and performance indices (CPIs) are useful tools to evaluate patient's risk of comorbidities and thus may guide clinical decision making regarding surgery or multimodal therapy approaches. Hence, the aim of the current study was to assess the predictive capacity of CPIs comprising the American Society of Anaesthesiologists (ASA)-score, the Charlson comorbidity index (CCI), the age-adjusted CCI (ACCI), and the Eastern Cooperative Oncology Group performance status (ECOG-PS) in patients with upper tract urothelial carcinoma (UTUC) who were treated with radical nephroureterectomy (RNU).

Methods and materials: A total of 242 patients with UTUC underwent RNU without neoadjuvant chemotherapy between 1992 and 2012 at 3 German academic centers. Patients were stratified according to the pre-RNU CPIs dichotomized as ASA 1/2 vs. ≥ 3 , CCI 0 to 2 vs. > 2 , ACCI 0 to 5 vs. > 5 , and ECOG-PS 0 to 1 vs. > 1 . We assessed the associations of CPIs with clinicopathologic features, as well as the prognostic effect on recurrence-free survival, cancer-specific survival (CSS), overall survival, and cancer-independent mortality (CIM), using univariable and multivariable Cox regression analyses.

Results: Sixty-two patients (25.6%) had an ASA-score ≥ 3 , 71 patients (29.3%) a CCI > 2 , 50 patients (20.7%) an ACCI > 5 , and 122 (50.4%) patients an ECOG-PS > 1 . The ASA-score ($P = 0.001$), CCI ($P = 0.029$), and the ECOG-PS ($P < 0.001$) were significantly associated with age. In addition, the ECOG-PS was associated with pelvicalyceal tumors ($P = 0.012$), and the CCI with preoperative hydronephrosis ($P = 0.026$). The median follow-up was 30 months. In Kaplan-Meier analyses, ACCI > 5 ($P \leq 0.025$) and ECOG-PS > 1 ($P \leq 0.042$) were associated with recurrence-free survival, CSS, and overall survival, and ASA-score ≥ 3 ($P = 0.011$) and ACCI > 5 ($P = 0.006$) with CIM. In multivariable analysis that adjusted for standard clinicopathologic parameters, an ECOG-PS > 1 was an independent predictor for CSS (hazard ratio = 1.89, $P = 0.019$), and an ASA-score ≥ 3 (hazard ratio = 1.86, $P = 0.026$) was a predictor for CIM.

Conclusion: CPIs are easy assessable predictors for outcome in patients with UTUC who were treated with RNU. CPIs have carefully to be taken into account in patient counseling regarding operative decision making and multimodal treatment. © 2014 Elsevier Inc. All rights reserved.

Keywords: Urothelial carcinoma; Upper urinary tract; Comorbidity; Survival

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1. Introduction

Upper tract urothelial carcinoma (UTUC) is a rare, but potentially lethal disease [1]. Once the malignancy recurs

after radical nephroureterectomy (RNU), most patients succumb to their disease within 2 years [2]. In addition, at time of RNU, a significant number of patients with UTUC present with comorbidities such as hypercholesterolemia [3], diabetes mellitus [4], obesity [5], and risk factors such as cigarette smoking [6] that may have a considerable risk for non-cancer-related survival. Indeed, previous studies have demonstrated that these risk factors also may influence UTUC outcomes [3–6]. Although several clinicopathologic parameters predicting outcomes of patients with UTUC who were treated with RNU were identified in the past decade [7], the effect of comorbidities on UTUC outcomes has only been marginally surveyed.

Comorbidity and performance indices (CPIs) are useful clinical tools to estimate the risk of comorbidities, which may guide decision making regarding operative procedures or multimodal therapy approaches. The American Society of Anesthesiologists (ASA)-score was established to predict perioperative outcomes according to comorbidities [8]. The Charlson comorbidity index (CCI) [9] and age-adjusted CCI (ACCI) [10] were developed to predict the 1-year mortality according to comorbidities. The Eastern Cooperative Oncology Group performance status (ECOG-PS) was established to evaluate the overall well-being and functional status of patients with cancer [11]. In UTUC, the ASA-score [12] and the ECOG-PS [13,14] have been evaluated regarding their effect on UTUC outcomes. However, these data have not been validated yet, and there is still a lack of information regarding the CCI and ACCI in outcome prediction for patients with UTUC who were treated with RNU.

As every CPI focuses on a distinct and individual end point, a combined assessment of different CPIs may help the treating physician obtain a complete insight in comorbidities. In addition, although other investigators previously analyzed the effect of individual risk factors or comorbidities on UTUC outcomes [3–6], we believe that CPIs represent a holistic consideration of factors that need to be taken into account for treatment decision making. Therefore, the aim of this study was to perform a comparative analysis of the predictive capacity of the 4 previously described CPIs on oncological and cancer-independent outcomes in patients with UTUC who were treated with RNU.

2. Patients and methods

2.1. Patient selection

This was an institutional review board approved, retrospective study of 3 German academic centers (Hamburg, Regensburg, and Tübingen). Between 1992 and 2012, 348 patients with UTUC were treated with RNU on curative intent. Patients with a history of radical cystectomy (RC) for treatment of muscle-invasive or high-risk non-muscle-invasive urothelial carcinoma of the bladder (UCB) were excluded

from the study ($n = 11$). In total, 95 patients were excluded from final analysis owing to missing data on clinicopathologic variables or follow-up ($n = 43$), application of neoadjuvant chemotherapy ($n = 1$), and missing information about either one or more CPIs ($n = 51$), resulting in a final study group of 242 patients. Preliminary analyses controlled for variances between excluded and included patients and found no statistically significant differences between these patients (data not shown).

RNU (open: $n = 226$ [93.4%] and laparoscopic: $n = 16$ [6.6%]) was performed according to the standard criteria [15]. Hilar or regional lymphadenectomy was generally performed in patients with suspicious lymph nodes on preoperative imaging or with suspicious intraoperative findings [16]. Tumor multifocality was defined as the synchronous presence of 2 or more pathologically confirmed tumors in any location (renal pelvicalyceal system, ureter, or both) [17]. No patient received preoperative systemic chemotherapy or perioperative radiotherapy. Adjuvant chemotherapy (89% platinum based) was administered in 47 patients (16.7%) at the investigator's discretion based on evidence of advanced disease stage, performance status, renal function, and patients' desire.

2.2. Comorbidity and performance indices

We included 4 indices in this study: ASA, CCI, ACCI, and ECOG-PS. Preoperative assessment of the CPIs was performed by the treating anesthesiologist and urologist at time of hospitalization. Both the CCI and the ACCI were calculated according to Charlson et al. [9] and Koppie et al. [10]. Each patient's comorbidity was registered based on the patient's record. The sum of the comorbidities without taking urothelial cancer into account finally defined the patient's CCI and ACCI.

The cutoffs for CPI stratification were identified through preliminary analyses and adopted to previous analysis in UCB [18]. For analyses, the CPIs were dichotomized as follows: ASA 1/2 vs. ≥ 3 ; CCI 0 to 2 vs. > 2 ; ACCI 0 to 5 vs. > 5 , and ECOG-PS 0 to 1 vs. > 1 .

2.3. Pathologic evaluation

Tumors were staged according to the 2010 American Joint Committee on Cancer TNM classification [19]. Tumor grading was assessed according to the 1998 World Health Organization/International Society of Urological Pathology consensus classification [20]. Histopathologic assessment comprised concomitant carcinoma in situ, tumor architecture (papillary or sessile based on the predominant feature of the index lesion [21]), tumor necrosis (defined as the presence of microscopic coagulative necrosis in more than 10% of the tumor [22]), and lymphovascular invasion (defined as the presence of tumor cells within an endothelium-lined space without underlying muscular walls [23]).

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