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Original article

A novel preoperative model to predict 90-day surgical mortality in patients considered for renal cell carcinoma surgery

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Abstract

Introduction: Surgical benefits for renal cell carcinoma must be weighed against competing causes of mortality, especially in the elderly patient population. We used a large cancer registry to evaluate the impact of patient and cancer-specific factors on 90-day mortality (90DM). A nomogram to predict the odds of short-term mortality was created.

Materials and Methods: The National Cancer Database was queried to identify all patients with clinically localized, nonmetastatic disease treated with partial or radical nephrectomy. Using a random sample of 60%, multiple logistic regression with 90DM outcomes were performed to identify preoperative variables associated with mortality. Variables included age, sex, race, co-morbidity score, tumor size, and presence of a thrombus. A nomogram was created and tested on the remaining 40% of patients to predict 90DM.

Results: 183,407 patients met inclusion criteria. Overall 90DM for the cohort was 1.9%. All preoperative variables significantly influenced the risk of 90DM. Patient age was by far the strongest predictor. Nomogram scores ranged from 0 to 12. Compared to patients with 0 to 1 points, those with 2 to 3 (odds ratio [OR] 2.89, 2.42−3.46; $P < 0.001$), 4 to 5 (OR 6.25, 5.26−7.43; $P < 0.001$), and >6 (OR 12.86, 10.83−15.27; $P < 0.001$) were at incrementally significantly higher odds of 90DM. Being >80 years of age alone placed patients into the highest risk of surgical mortality.

Conclusions: Management of localized kidney cancer must consider competing causes of mortality, especially in elderly patients with multiple co-morbidities. We present a preoperative tool to calculate risk of surgical short-term mortality to aid surgeon−patient counseling.

Keywords: Renal cell carcinoma; Perioperative mortality; Risk prediction; Patient counseling; Nomogram

1. Introduction

Kidney cancer is the 8th leading cancer diagnosis in the United States with an estimated 63,990 of new cases resulting in 14,400 deaths based on 2016 data [1]. In contrast to many of the other most commonly diagnosed malignancies, the incidence of kidney cancer has risen over the last few decades in men and women of every racial and ethnic group [2]. The rise in incidence of kidney cancer has coincided with a downward drift stage migration likely secondary to the more frequent diagnosis of small, incidental renal masses on cross-sectional imaging [3−6]. This rise in incidence, however, has not been observed in conjunction with a decrease in mortality despite increases in surgical treatment [5]. In fact, in some studies, mortality from renal cell cancer has risen calling into question current treatment paradigms thus stressing appropriate patient selection for operative procedures [2,5,7].

Surgical resection remains the gold standard therapy for patients with renal cell carcinoma. The survival benefit from surgery for renal cell carcinoma is variable and is dependent upon patient and disease-specific factors. Age and associated medical comorbidities weigh heavily on patient's overall survival and short-term surgical morbidity and mortality [8,9]. Tumor-specific characteristics such as tumor grade, stage and local/metastatic extent confer

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different risks of morbidity and mortality [10]. Previously, various studies have evaluated predictors of short-term surgical morbidity, mortality, and long-term overall-survival [11–13]. These studies have been influential in preoperative patient counseling.

In our current study, we sought to expand on these previous studies to evaluate preoperative patient and tumor-specific variables to evaluate their impact on short-term surgical mortality. We hypothesized that age, tumor size and stage, gender, race and co-morbidity status affect short-term surgical mortality. Using the National Cancer Database (NCDB), we evaluated the impact of these variables on 90-day mortality to develop a nomogram to predict the odds of short-term surgical mortality to help aid in patient counseling.

2. Materials and methods

2.1. Data source

The NCDB is a joint cancer registry that was established in 1989 by the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The database serves as a comprehensive clinical surveillance resource for cancer care in the United States [14,15]. The NCDB captures >70% of all newly diagnosed cancer cases from over >1,500 Commission on Cancer-accredited cancer programs in the United States and Puerto Rico.

2.2. Study population

The NCDB user file for renal cell carcinoma was queried from 2003 to 2011. The American Joint Committee on Cancer staging system was used to identify patients with clinically localized, nonmetastatic renal cell carcinoma (cT1-4, N0, M0). Patient's with clinically suspected or histologically confirmed locally advanced or metastatic lesions (N+: 22,956; ≥M1: 40,580), upper-tract urothelial cell carcinoma ($n = 34{,}279$) and who were not treated surgically were excluded ($n = 23{,}481$). Patients with incomplete Charlson–Deyo co-morbidity data ($n = 68{,}324$), pathologic surgical staging ($n = 67{,}414$), or 90-day mortality data (90DM) were excluded ($n = 35{,}446$). Ultimately, 183,407 met inclusion criteria.

2.3. Co-variables and endpoints

90-day mortality was used as the primary endpoint for analysis. Co-variables used to construct the multivariable model included preoperative patient (age, gender, race, and Charlson–Deyo co-morbidity scores) and tumor-specific variables (size and presence or absence of a thrombus) that were presumedly known to the surgeon prior to the operation. Tumor size was used as a surrogate for tumor stage. Since the NCDB incompletely captures radiographic involvement of the inferior vena cava (IVC) in clinical stage variables, we elected to use pathologic demonstration of an IVC thrombus as a reasonable presumption that its involvement would be known preoperatively in all cases with rare exceptions. Finally, an exploratory analysis excluding patients with pT1 disease was done to identify preoperative predictors of 90DM in patients who would likely not be candidates for active surveillance.

2.4. Statistical analysis

Descriptive analysis of the data was performed using Pearson's chi-squared test for categorical data, Student's *t* test for continuous data, and the Mann–Whitney test in the case of non-normally distributed continuous data. Using a random sample of 60% of the patients in the dataset, multivariable logistic regression with the outcome of 90DM was performed to identify preoperative variables associated with mortality. Variables were determined *a priori* to be included in the model. A nomogram was derived from the odds ratios in the logistic regression model and tested on the remaining 40% of the patients in the dataset for ability to predict 90DM. Area under the curve (AUC) was calculated for the original multivariable logistic regression model and for the tested model to confirm accuracy between the models. All statistical calculations were completed in STATA 12.1 (STATA Corp. LP, College Station, TX).

3. Results

183,407 patients with clinically localized renal cell carcinoma treated with either partial or radical nephrectomy met inclusion criteria. The median age was 62 (IQR: Interquartile Range: 52–70). Most of the patients were male (112,597, 61.4%) and white (155,771, 84.9%). Most patients were classified as Charlson–Deyo co-morbidity index of 0 (70.6%) with few having extensive comorbidities (Charlson–Deyo index 2, 7.3%). The distribution of tumor stage, as defined by TNM staging, was as expected with lower stage tumors being more common (I: 69%; II: 12%; III: 18%, IV: 1%). Most patients had low-grade tumors (I–II: 59.1%). Despite the predominance of stage I and low-grade tumors, only 29.2% of patients underwent partial nephrectomy. Overall, the 30 (30DM) and 90-day mortality rates for the entire cohort were low at 0.9% and 1.9%, respectively. These results and other baseline demographic, tumor specific and short-term mortality data separated by age (decade) of surgery can be visualized in Table 1.

After separating patients into age category by decade, several findings were noted. Overall, 18.6%, 25.4%, 28.6%, 20.6%, and 6.8% of patients were aged ≤49, 50–59, 60–69, 70–79, and ≥80, respectively. Predictably, increasing age was associated with increasing co-morbidity scores. Twenty five percent and 9.3% of the oldest group of patients had Charlson–Deyo index scores of 1 and 2, respectively, compared to only 14% and 3.9% of those