Morbidity and Mortality of Radical Nephrectomy for Patients With Disseminated Cancer: An Analysis of the National Surgical Quality Improvement Program Database

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OBJECTIVE To determine the effect of disseminated cancer on perioperative outcomes following radical nephrectomy.

METHODS We conducted a retrospective cohort study of patients undergoing radical nephrectomy for kidney cancer from 2005 to 2014 using the American College of Surgeons National Surgical Quality Improvement Program, a multi-institutional prospective registry that captures perioperative surgical complications. Patients were stratified according to the presence (n = 657) or absence (n = 7143) of disseminated cancer at the time of surgery. We examined major complications (death, reoperation, cardiac event, or neurologic event) within 30 days of surgery. Secondary outcomes included pulmonary, infectious, venous thromboembolic, and bleeding complications; prolonged length of stay; and concomitant procedures (bowel, liver, spleen, pancreas, and vascular procedures). Adjusted odds ratio (aOR) and 95% confidence interval (95% CI) were calculated using multivariate logical regression models.

RESULTS Patients with disseminated cancer were older and more likely to be male, have greater comorbidities, and have undergone open surgery. Major complications were more common among patients with disseminated cancer (7.8%) than those without disseminated cancer (3.2%; aOR 2.01, 95% CI 1.46-2.86). Mortality was significantly higher in patients with disseminated cancer (3.2%) than those without disseminated cancer (0.5%; $P < .0001$). Pulmonary (aOR 1.68, 95% CI 1.09-2.59), thromboembolic (aOR 1.72, 95% CI 1.01-2.96), and bleeding complications (aOR 2.12, 95% CI 1.73-2.60) were more common among patients with disseminated cancer as was prolonged length of stay (aOR 1.27, 95% CI 1.06-1.53).

CONCLUSION Nephrectomy in patients with disseminated cancer is a morbid operation with significant perioperative mortality. These data may be used for preoperative counseling of patients undergoing cytoreductive nephrectomy. UROLOGY 95: 95–102, 2016. © 2016 Elsevier Inc.

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MeSH: carcinoma, renal cell; cytoreduction surgical; nephrectomy; quality improvement; registries; postoperative complications.

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Cytoreductive nephrectomy (CN) for patients with metastatic renal cell carcinoma (mRCC) has been adopted on the basis of 2 randomized controlled trials that demonstrated a survival advantage for patients treated with CN and interferon as compared to interferon alone.[1] Since that time, therapies targeting pathways in mRCC pathogenesis have been introduced and have significantly changed the landscape of mRCC management. Although these therapies have improved survival,[2,3] there is only observational evidence to support CN with contemporary targeted therapy.[4,5] The utilization of CN is declining[6] and appears most suitable for patients with favorable or intermediate-risk disease[4,5] with low tumor burden[7] and clear cell histology.[8]

There is a need to characterize contemporary perioperative morbidity of CN to further inform optimal

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patient selection for surgery and balance oncological benefit with perioperative risk. Analyses of cases from a high-volume, single center indicate that complications for CN were not only common (57% of patients), but also a significant proportion of complications were severe (Clavien ≥3, 30%).[9] Although a number of groups have recently reported on perioperative outcomes following cytoreductive nephrectomy,[10-15] these studies lacked a comparator group to allow for an assessment of the incremental effect of disseminated disease on perioperative outcomes. Using administrative data (Florida inpatient database), Abdollah et al showed that patients undergoing nephrectomy for mRCC had significantly higher rates of in-hospital mortality, complications, and transfusions than those treated for nonmetastatic cancer.[16]

In contrast to these data sources, the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database is a multi-institutional, multinational registry focused on perioperative outcomes within 30 days of surgery.[17] It has excellent data quality, owing to data abstraction directly from medical records by trained personnel,[18] and more reliably identifies complications when compared to administrative databases or institutional series.[19,20] NSQIP captures data on disseminated cancer (American Joint Committee on cancer Stage IV) status at the time of surgery. Thus, we sought to utilize NSQIP to characterize complication rates in patients undergoing nephrectomy in the setting of disseminated cancer and compare these to patients without disseminated cancer.

METHODS

The Sunnybrook Health Sciences Centre Research Ethics Board granted approval for this study. The study was conducted and reported according to the recommendations of the RECORD statement.

Study Design and Population

We conducted a retrospective cohort study of patients undergoing radical nephrectomy between January 1, 2005 and December 31, 2014 using the participant use files of the American College of Surgeons NSQIP. We used Common Procedural Terminology (CPT) codes to identify patients undergoing radical nephrectomy (CPT 50220, 50225, 50230, 50545, and 50546) as the primary procedure (n = 14,111). We excluded 2 patients who were under the age of 18 and other patients due to missing data (n = 118): on American Society of Anesthesiology (ASA) class (n = 16), weight (n = 47), height (n = 99), or length of stay (n = 3). We then restricted our cohort to those with a postoperative diagnosis of International Classification of Diseases-9 189 or 189.0 (malignant neoplasm of kidney), excluding nonspecific diagnoses such as renal mass (total excluded n = 6191).

Outcomes

The primary outcome was major complications (mortality, reoperation, cardiac event, or neurologic event). Secondary outcomes included pulmonary complications (reintubation or prolonged ventilation), infectious complications (surgical site infections (SSIs), pneumonia, urinary tract infection (UTI), or sepsis), venous thromboembolism (deep vein thrombosis or pulmonary embolism), bleeding requiring transfusion, and prolonged length of stay, comprising hospital stays greater than the median in this cohort (4 days from the date of surgery).

To characterize the operative complexity of nephrectomy performed in the setting of disseminated cancer, we captured the type and frequency of concomitant procedures (Supplementary Table S1). We did not capture procedures performed at the time of surgery that were likely to be unrelated to the complexity of nephrectomy (ie, hernia repair). Concomitant procedures included bowel-related procedures (including repair, resection, or diversion), pancreatectomy, splenectomy, hepatectomy, and major vascular repair.

Exposure

Our exposure of interest was the presence of disseminated cancer at the time of nephrectomy. Disseminated cancer is defined by NSQIP as the presence of a primary cancer that has metastasized to a major organ (American Joint Committee on Cancer Stage IV), but not exclusive metastasis to lymphatic tissue. A probabilistic matching algorithm to link colorectal cancer patients to the National Cancer Database has shown that the disseminated cancer variable has fair-good agreement[21] with metastatic stage (Cohen kappa coefficient, 0.454).[22] Previous research from NSQIP has shown that patients with disseminated cancer have worse outcomes, including mortality.[22]

Covariates

Standard demographic and clinical information including age, race, body mass index (BMI), ASA physical status class, history of cardiac disease, history of neurologic disease, history of chronic obstructive pulmonary disease (COPD), history of diabetes (requiring oral agent or insulin), end-stage renal disease requiring dialysis, current smoking status (active smoker within 1 year), chronic steroid use, and functional status prior to surgery (independent, partially dependent, totally dependent, or unknown) were abstracted for all patients. Glomerular filtration rates were calculated using the Modification of Diet in Renal Disease equation[23] and categorized according to the National Kidney Foundation classification. BMI was categorized in keeping with the World Health Organization stratification (<18.5, 18.5-25, 25-30, >30 [kg/m^2]). Using CPT codes, we identified the use of minimally invasive surgical (MIS) techniques from the primary procedure code (MIS: 50545, 50546 vs open: 50220, 50225, 50230).

Statistical Analysis

We examined the proportion of cases performed on patients with disseminated cancer over time and examined temporal trends using the Cochrane-Armitage test for trend.[24] Descriptive statistics were used to compare baseline demographic factors: frequencies and proportions were calculated for categorical variables and medians and

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