Effect of Preoperative Nutritional Deficiency on Mortality After Radical Cystectomy for Bladder Cancer

Justin R. Gregg, Michael S. Cookson,* Sharon Phillips, Shady Salem, Sam S. Chang,† Peter E. Clark,‡ Rodney Davis, C. J. Stimson, Jr., Monty Aghazadeh, Joseph A. Smith, Jr. and Daniel A. Barocas§,‖

From the Department of Urologic Surgery (JRG, MSC, SS, SSC, PEC, RD, CJS, MA, JAS, DAB), Department of Biostatistics (SP), and Center for Surgical Quality and Outcomes Research (DAB), Vanderbilt University Medical Center, Nashville, Tennessee

Abbreviations and Acronyms

ASA = American Society of Anesthesiologists

AA CCI = age adjusted Charlson comorbidity index

BMI = body mass index

CCI = Charlson comorbidity index

ND = nutritional deficiency

NRS = Nutritional Risk Score

RC = radical cystectomy

VUMC = Vanderbilt University Medical Center

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‡ Financial interest and/or other relationship with Tengion.

§ Correspondence: Department of Urologic Surgery, Vanderbilt University Medical Center, 2525 West End Ave., Suite 600, Nashville, Tennessee 37203 (e-mail: Dan.barocas@vanderbilt.edu).

‖ Financial interest and/or other relationship with Ferring.

Purpose: Poor preoperative nutritional status is a risk factor for adverse outcomes after major surgery. We evaluated the effect of preoperative nutritional deficiency on perioperative mortality and overall survival in patients undergoing radical cystectomy for bladder cancer.

Materials and Methods: A total of 538 patients underwent radical cystectomy for urothelial carcinoma between January 2000 and June 2008, and had nutritional parameters documented. Patients with preoperative albumin less than 3.5 gm/dl, body mass index less than 18.5 kg/m^2 or preoperative weight loss greater than 5% of body weight were considered to have nutritional deficiency. Primary outcomes were 90-day mortality and overall survival. Survival was estimated using Kaplan-Meier analysis and compared using the log rank test. Cox proportional hazards models were used for multivariate survival analysis.

Results: Of 538 patients 103 (19%) met the criteria for nutritional deficiency. The 90-day mortality rate was 7.3% overall (39 deaths), with 16.5% in patients with nutritional deficiency and 5.1% in the others ($p < 0.01$). Nutritional deficiency was a strong predictor of death within 90 days on multivariate analysis (HR 2.91; 95% CI 1.36, 6.23; $p < 0.01$). Overall survival at 3 years was 44.5% (33.5, 54.9) for nutritionally deficient patients and 67.6% (62.4, 72.2) for those who were nutritionally normal ($p < 0.01$). On multivariate analysis nutritional deficiency cases had a significantly higher risk of all cause mortality (HR 1.82; 95% CI 1.25, 2.65; $p < 0.01$).

Conclusions: Nutritional deficiency, as measured by preoperative weight loss, body mass index and serum albumin, is a strong predictor of 90-day mortality and poor overall survival. Prospective studies are needed to demonstrate the best indices of preoperative nutritional status and whether nutritional intervention can alter the poor prognosis for patients treated with radical cystectomy who have nutritional deficiencies.

Key Words: urinary bladder neoplasms, cystectomy, nutritional status, albumins, treatment outcome

THERE are approximately 70,980 new cases of bladder cancer annually in the United States, about 25% of which involve muscle invasive disease.[1] Radical cystectomy remains the standard treatment for muscle invasive bladder cancer and also has a role in treating nonmuscle invasive bladder cancer.[2] RC is associated with excellent 5-year recurrence-free survival in lymph node negative (78%) and even lymph node positive (35%) cases.[3] However, as

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many as two-thirds of patients experience 1 or more complications within 90 days of surgery.[4,5] The 30-day perioperative mortality in patients who underwent RC is estimated at between 1% and 3%, but it may be as high as 7% within 90 days of surgery.[4,6,7] Known risk factors for perioperative death and other severe complications include age, estimated blood loss, prior abdominal/pelvic surgery and ASA score greater than 2.[4] Risks for overall mortality include preoperative stage, tumor size, margin status, extravesical involvement, margin status and older age.[3,8]

In general surgical cases nutritional deficiency is a well-known risk factor for complications such as infection and poor wound healing, and may influence perioperative mortality and overall survival.[9] However, the role of nutritional deficiency in the outcomes of patients with bladder cancer undergoing RC has been incompletely explored. To our knowledge no standardized method exists to evaluate patients for nutritional risk preoperatively.[10] Serum albumin is often part of a nutritional evaluation and low preoperative serum albumin predicts mortality in various groups of surgical patients including those undergoing RC.[11–13] Preoperative BMI less than 18.5 kg/m^2, the World Health Organization definition of underweight,[14] is associated with increased perioperative mortality in patients who have undergone surgery for intra-abdominal cancers.[15] Weight loss has also been associated with decreased survival in patients with advanced stage cancer.[16]

Studies of patients who underwent RC suggest that postoperative complications and mortality may be associated with each of these nutritional parameters.[13,17,18] Thus, we explored the effect of preoperative nutritional status as measured by preoperative BMI, weight loss and serum albumin, on 90-day mortality and overall survival in a large cohort of patients with bladder cancer undergoing RC.

METHODS

We performed a retrospective cohort study of 905 consecutive patients who underwent RC at VUMC between January 2000 and June 2008. RC was performed and postoperative care administered as previously described by Lowrance et al.[7] Pathological specimens were evaluated by a staff surgical pathologist and staged according to American Joint Committee on Cancer guidelines.[19]

Institutional review board approval was obtained for the creation of a prospective database and for this study in particular. Clinical, pathological and outcome data were collected prospectively, and were supplemented by review of the medical records. We excluded patients from the study who underwent cystectomy for nonurothelial carcinoma such as pure squamous or adenocarcinoma (80), or for salvage therapy after radiation therapy or chemoradiation therapy with curative intent (24). Of this potential cohort of 801 we were able to categorize 538 (67.2%) with respect to nutritional status.

In 335 of 538 patients (62.3%) information related to nutrition status was gathered from a structured dietary evaluation by a registered dietician. In the remaining 203 patients (37.7%) nutritional status information was gathered through review of the electronic medical records. Patients were classified into 2 groups of nutritionally normal and nutritionally deficient. ND was defined as the presence of 1 of more of the factors of preoperative albumin lower than the lower bound of VUMC normal values (3.5 to 5 gm/dl), unintentional preoperative weight loss 5% or greater of body weight, or preoperative BMI less than 18.5 kg/m^2 (table 1).

Covariates including age, gender, race, smoking status, preoperative hematocrit, ASA classification, CCI, neoadjuvant chemotherapy, diversion type, perioperative complications, transfusion rate, pathological stage, pathological cell type and lymph node status were obtained through patient charts. Vital status was ascertained through the VUMC cancer registry, the Social Security Death Index and patient charts. Patients were censored at the date of last followup or date of death up to August 1, 2009.

We investigated and modeled the relationship between ND and survival after radical cystectomy. The primary outcomes measured were mortality within 90 days of surgery, mortality after 90 days and overall survival. Clinical variables including demographic information, procedural details and disease characteristics were investigated as potential confounders of the relationship of interest. These characteristics were compared across groups using Kruskal-Wallis tests and Wilcoxon rank sum tests for continuous variables, and Fisher's exact tests for categorical variables. The 90-day and overall survival were evaluated with Kaplan-Meier curves and log rank tests. Cox proportional hazards models for 90-day, post-90-day and overall survival were constructed. Variables included in these models were AA CCI, transfusion, complications, lymph node density and pathological stage. The additional number

Table 1. *Cohort nutritional status*

	No. (%)
Albumin (gm/dl):	
Less than 3.5	29 (6)
3.5 or Greater	493 (94)
BMI (kg/m^2):	
Less than 18.5	18 (3)
18.5–Less than 25	168 (32)
25–less than 30	200 (38)
30–less than 40	125 (24)
40 or Greater	11 (2)
% Wt loss:	
Greater than 10	33 (6)
5–10	38 (7)
None–less than 5%	467 (87)
Normal nutrition status	435 (81)
Nutritionally deficient	103 (19)