

Original article

NLR is predictive of upstaging at the time of radical cystectomy for patients with urothelial carcinoma of the bladder

Aaron Potretzke, M.D.^{a,*}, Luke Hillman, B.S.^b, Kelvin Wong, M.D.^a, Fangfang Shi, M.S.^a, Ryan Brower, M.S.^b, Stephanie Mai, B.S.^b, Jeremy P. Cetnar, M.D.^c, Edwin Jason Abel, M.D.^{a,c}, Tracy M. Downs, M.D.^{a,c}

^a Department of Urology, University of Wisconsin, Madison, WI

^b University of Wisconsin School of Medicine and Public Health, Madison, WI

^c University of Wisconsin Carbone Cancer Center, Madison, WI

Received 12 September 2013; received in revised form 30 November 2013; accepted 23 December 2013

Abstract

Objective: To evaluate the ability of preoperative neutrophil-lymphocyte ratio (NLR) to predict pathologic upstaging and nonorgan-confined (NOC) (\geq pT3) disease.

Methods and materials: After institutional review board approval, the records of consecutive patients undergoing radical cystectomy (RC) for urothelial carcinoma from 2002 to 2012 at the University of Wisconsin Hospital were reviewed. A total of 102 patients with NLR within 100 days of surgery were eligible for analysis. The primary outcome was difference in stage from preoperative assessment to time of RC. Differences in preoperative NLR between groups were evaluated with an unequal variance *t* test. A univariate analysis assessed whether NLR, preoperative stage, grade, associated lymphovascular invasion, preoperative hydronephrosis, gender, previous pelvic radiotherapy, previous intravesical bladder cancer treatments, or nodal stage were related to upstaging. Multivariate analyses were performed to evaluate the relationship of NLR to upstaging and relative organ-confined (\leq pT2) and NOC disease.

Results: Of 390 consecutive patients undergoing RC, 102 patients met study criteria. Overall, 55 (53.9%) patients were upstaged, 25 (25.5%) were unchanged, and 21 (20.6%) were downstaged. Fifty-one patients (50%) were upstaged to more advanced disease (\geq pT3). NLR and preoperative hydronephrosis were significantly related to pathologic tumor staging. NLR, preoperative hydronephrosis, and preoperative tumor stage were significantly related to upstaging to NOC disease. Patients who were upstaged to \geq pT3 demonstrated statistically significant greater NLRs (4.33 ± 0.87) compared with patients who remained at \leq pT2 stage (2.66 ± 0.29) ($P < 0.001$).

Conclusions: Preoperative NLR is a simple measurement that can be used to identify high-risk patients who may be upstaged at the time of RC and may benefit from neoadjuvant chemotherapy. © 2014 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Upstaging; Neutrophil; Lymphocyte; Neoadjuvant chemotherapy

1. Introduction

Bladder cancer represents a significant health problem, as it is often a lethal disease. In the United States, there will be an estimated 72,570 new cases of and 15,210 deaths from bladder cancer in 2013 [1]. Prognosis and effective management of bladder cancer depend on preoperative staging with transurethral resection of bladder tumor (TURBT). Bladder cancer is clinically understaged in ~50% cases; upstaging from organ-confined (OC) (\leq T2)

to nonorgan-confined (NOC) (\geq T3) cancer occurs in 32% to 43% of patients at time of radical cystectomy (RC) [2–5]. Importantly, patients who are upstaged at the time of RC have significantly higher recurrence rates and bladder cancer-specific death when compared with those who are correctly staged [4,5]. This relationship is most pronounced in patients upstaged from preoperative T2 cancer compared with those who are not—46% vs. 16% 10-year disease-specific mortality [3].

Currently, reliable predictors of extravesical upstaging at the time of RC do not exist. Some authors have suggested correlations of T2 staging, hydronephrosis, carcinoma in situ, high-grade disease, lymphovascular invasion (LVI),

* Corresponding author. Tel.: +1-952-2-128-644; fax: +1-608-2-626-453.
E-mail address: apotretzke@uwhealth.org (A. Potretzke).

and female gender with pathologic upstaging [3,6]. Evidence of systemic inflammation, as marked by leukocytosis or elevated C-reactive protein, is a known poor prognostic factor in cancers. Such markers portend worse prognosis and response to therapy. Similarly, neutrophil-lymphocyte ratio (NLR) has tumor and stage independent associations with poorer survival and response to therapy (including surgery) in the following cancers: gastric, pancreatic, colorectal, lung, ovarian, and cholangiocarcinoma [7].

Evidence exists demonstrating a survival benefit of neoadjuvant chemotherapy in patients with NOC bladder cancer [8]. However, neoadjuvant therapy is minimally utilized owing to concern for overtreating patients with lower-stage disease, and thereby delaying time to RC. If those patients likely to have NOC disease could be accurately identified before RC, they could be offered neoadjuvant therapy. The purpose of our study was to evaluate the NLR as a predictor of upstaging at the time of cystectomy with a secondary outcome assessment of NOC disease after RC.

2. Patients and methods

2.1. Patients

Institutional internal review board approval was obtained. We retrospectively reviewed the records of 390 patients who underwent RC at the University of Wisconsin Hospital and Clinics between 2002 and 2012. A routine complete blood count (CBC) test is included as part of the standard preoperative blood work. Before 2011, the differential was not included as part of the routine CBC test ordered in preparation for surgery. The NLR was obtained from the differential of the CBC test. If there was more than one CBC before surgery, the CBC closest to the date of surgery was chosen for our analysis. The median number of days the NLR was obtained before RC was 11 days (interquartile range 0–26 days). Clinical and pathologic staging was based on the American Joint Committee on Cancer TNM 2010. Study criteria included NLR within 100 days of RC, clinical T stage \leq T2, urothelial cell cancer of the bladder, mixed histologies urothelial cell cancer with squamous or glandular differentiation but no sarcomatous features, no extreme leukocytosis (white blood cells $>$ 20,000), and no prior chemotherapy or radiation therapy. The interval of 100 days was used as it is near the established, recommended time from diagnosis to cystectomy of 90 days. Compared with their clinical stage determined at TURBT, patients were categorized as being upstaged, no change in stage, or downstaged following RC.

2.2. Statistical analysis

Differences in preoperative NLR were evaluated with an unequal variance *t* test. A univariate analysis was performed to assess whether NLR, preoperative stage, grade,

associated LVI, preoperative hydronephrosis, gender, previous pelvic radiotherapy, previous intravesical bladder treatments (i.e., Bacillus Calmette–Guérin or mitomycin C or both), or nodal stage were related to upstaging and relative OC or NOC disease status. Multivariate analysis by logistic regression was performed to assess the relationship of NLR, preoperative hydronephrosis, and preoperative stage in relation to OC and NOC disease. Clinical stages Tis, Ta, and T1 were grouped owing to the relatively small numbers of such patients, and compared with T2 in the multivariate analysis. Similarly, logistic regression analysis was performed to assess the relationship of NLR and preoperative hydronephrosis to upstaging. Receiver operating characteristic curve was constructed comparing NLR with a published bladder cancer nomogram [9]. NLR values are expressed as mean with 95% confidence interval. Preoperative NLR relationship to nodal status was also evaluated with an analysis of variance.

3. Results

A total of 102 patients met criteria for the study; Table 1 shows their clinical characteristics. Table 2 compares the clinical stages of patients before RC and their final pathologic stages. Of patients with cT2 lesions, 22.1% had pT2 lesions, 19.5% were downstaged (7.8% pT0, 2.6% pTis, 3.9% pTa, and 5.2% pT1), and 58.4% were upstaged (49.4% pT3 and 9.1% pT4). Overall, 55 (53.9%) patients were upstaged, 26 (25.5%) were unchanged, and 21 (20.6%) were downstaged (Table 3). Fifty-one patients (50%) were upstaged to \geq pT3 (Table 4). Seventy-seven (75.5%) patients had node negative lesions, 8 (7.8%) had N1 lesions, 9 (8.8%) had N2 lesions, and 8 (7.8%) did not undergo a lymph node dissection because of prior radiation therapy, recent vascular surgery, or prior lymph node dissection.

The primary end point of the current study is upstaging at RC. In univariate analysis, NLR and preoperative hydronephrosis were the only factors significantly associated with upstaging ($P = 0.001$ and $P < 0.0001$, respectively) (Table 1). Multivariate analysis showed that both NLR and preoperative hydronephrosis predicted upstaging ($P = 0.04$ and $P = 0.002$, respectively). The secondary outcome was NOC disease after RC. Univariate analysis was conducted and demonstrated NLR, preoperative hydronephrosis, and preoperative stage were associated with NOC disease ($P = 0.0007$, $P = 0.0003$, and $P = 0.01$, respectively). A multivariate logistic regression analysis of these variables found a significant relationship between NLR, preoperative hydronephrosis, and preoperative stage and NOC disease ($P = 0.02$, $P = 0.009$, and $P = 0.006$, respectively). NLR ratio was significantly greater in patients who were upstaged (4.19 ± 0.82) compared with patients who remained the same stage (2.78 ± 0.42 ; $P = 0.004$), or were downstaged (2.55 ± 0.44 ; $P < 0.001$) (Table 3). Patients who were upstaged to NOC disease demonstrated

Download English Version:

<https://daneshyari.com/en/article/6194338>

Download Persian Version:

<https://daneshyari.com/article/6194338>

[Daneshyari.com](https://daneshyari.com)