ELSEVIER

Urologic Oncology: Seminars and Original Investigations ▮ (2016) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

The prognostic role of preoperative serum albumin/globulin ratio in patients with bladder urothelial carcinoma undergoing radical cystectomy

Jianye Liu, M.D.[a,b], Yingbo Dai, M.D.[a,b], Fangjian Zhou, M.D.[c,e], Zhi Long, M.D.[a,b], Yonghong Li, M.D.[c,e], Bin Liu, M.D.[a,b], Dan Xie, Ph.D.[d,e], Jin Tang, M.D.[a,b], Jing Tan, M.D.[a,b], Kun Yao, M.D.[a,b], Yichuan Zhang, M.D.[a,b], Yuxin Tang, M.D.[a,b], Leye He, M.D.[a,b,*]

[a] *Department of Urology, The Third Xiangya Hospital of Central South University, Changsha, China*
[b] *Institute of Prostate Disease of Central South University, Changsha, China*
[c] *Department of Urology, Sun Yat-sen University Cancer Center, Guangzhou, China*
[d] *Department of Pathology, Sun Yat-sen University Cancer Center, Guangzhou, China*
[e] *State Key Laboratory of Oncology in South China, Guangzhou, China*

Received 31 January 2016; received in revised form 17 May 2016; accepted 20 May 2016

Abstract

Objective: To date, only a few studies have demonstrated the prognostic value of pretreatment serum albumin in bladder urothelial carcinoma (BUC). The aim of this study was to evaluate the association between the pretreatment albumin/globulin ratio (AGR) and the survival of patients with BUC treated with radical cystectomy (RC).

Materials and methods: Data from 296 patients with BUC who underwent RC between June 2000 and June 2013 were analyzed. The AGR was calculated as follows: albumin/(total protein − albumin). The AGR was divided into 2 groups for receiver operating characteristics curve analysis. Survival was estimated using Kaplan-Meier analysis and compared using the log rank test. Cox proportional hazards models were used for univariate and multivariate survival analyses.

Results: Patients in the high AGR group (AGR $\geq$ 1.60) had a lower 5-year recurrence-free mortality rate compared with those in the low AGR group (AGR $<$ 1.60) (87.0% vs. 48.0%, $P < 0.001$). The median cancer-specific survival (CSS) time was 71.1 months for low AGR patients and 156.0 months for the high AGR patients ($P < 0.001$). After adjusting for confounding variables, the AGR remained an independent predictor of recurrence-free survival (RFS) (hazard rate = 0.356; 95% CI: 0.170–0.748; $P = 0.006$) and CSS (hazard rate = 0.280; 95% CI: 0.115–0.683; $P = 0.005$). Moreover, in the subset of 167 patients with normal serum albumin (albumin of $\geq$ 40.0 g/l), serum AGR continues to be an independent predictor of RFS ($P = 0.012$) and CSS ($P = 0.008$).

Conclusions: High AGR is a strong independent predictor of long-term RFS and CSS in patients with BUC undergoing RC. Additionally, among patients with normal albumin ($\geq$40 g/l) levels, patients with higher globulin, but lower AGR have worse survival. The pretreatment AGR is an easily accessible and cheap to use for predicting mortality in patients with BUC treated by RC.

Keywords: Bladder urothelial carcinoma; Albumin/globulin ratio; Survival; Prognosis

Introduction

Bladder urothelial carcinoma (BUC) is the fourth most common malignant disease in men in the United States of America [1]. Moreover, it is the most common genitourinary tract malignancy and one of the leading causes of cancer-related death in China [2]. Radical cystectomy (RC) is the standard treatment for muscle-invasive bladder cancer (MIBC) and also has a role in treating non-MIBC [3]. To date, assessing the prognosis of patients with MIBC is mainly based on tumor-related factors. Extravesical tumor stage (pT3–4), lymph node metastasis, and nonurothelial variant histology have been established as poor prognostic factors for patients treated with RC [4–8]. However, each separate tumor stage shows a wide individual range regarding

* Corresponding author. Tel.: +86-731-8861-8129; fax: 86-731-8861-8129.
E-mail address: heleye_csu@163.com (L. He).

http://dx.doi.org/10.1016/j.urolonc.2016.05.024
1078-1439/

survival after RC, therapeutic decision-making after RC for BUC remains a major challenge [9,10]. Therefore, identifying new biological markers for determining the risk of poor prognosis is important for designing treatment strategies for patients with BUC.

Recently, several new predictors of oncological outcome were studied [11]. However, some factors have limitations in clinical application because of their tissue-specific expression and high cost of testing, warranting improvement of the efficiency and accuracy of the existing factors. There is still a need for a promising predictive factor that is simple to detect and that is closely linked to survival in patients with BUC who have undergone RC.

Albumin (ALB) and globulin (GLB) are the 2 major components of human serum proteins. Serum ALB is generally applied to assess nutritional status and the severity of disease. Moreover, prior studies have demonstrated that low serum ALB can be used to evaluate progression and poor prognosis in various cancers as well as in BUC [12–15]. GLB functions as a carrier of the sex hormones and play a major role in immunity and inflammation. The ALB to GLB ratio (AGR = ALB/(total serum protein − ALB) is the ratio of serum ALB to non-ALB proteins (i.e., GLB and other protein particles). A decreased ALB level and increased GLB level reflect chronic inflammation [16–18]. As systemic inflammation causes an increase in the levels of various proinflammatory cytokines, which subsequently promote tumor progression because of changes in the cancer microenvironment [19,20], a decreased AGR is thought to correlate with tumor progression. Recently, the AGR was reported to be a prognostic marker in patients with colorectal cancer, lung cancer, breast cancer, and

Table 1
Clinical and pathological characteristics stratified by AGR level in 296 patients

Variables	Total patients (%)	Low AGR group (n = 154) AGR < 1.6	High AGR group (n = 142) AGR ≥ 1.6	P value
Median follow-up, months (IQR)	72.0 (49.0, 121.0)	74.0 (47.75, 129.50)	72.0 (49.75, 115.50)	0.437
Age, y	61.71 ± 11.08	63.39 ± 10.50	59.88 ± 10.41	**0.007**
BMI, kg/m²	23.12 ± 3.58	22.96 ± 4.12	23.42 ± 3.05	**0.023**
Sex				0.325
Male	250 (84.5)	127 (50.8)	123 (49.2)	
Female	46 (15.5)	27 (58.7)	19 (41.3)	
Smoking status				0.385
Never smoked	162 (54.7)	88 (54.3)	74 (45.7)	
Smoked in past	134 (45.3)	66 (49.3)	68 (50.7)	
Recurrent tumor				0.219
No	200 (67.6)	109 (54.5)	91 (45.5)	
Yes	96 (32.4)	45 (46.9)	51 (53.1)	
Diversion type				**0.034**
Conduit	97 (32.8)	59 (60.8)	38 (39.2)	
Neobladder	199 (67.2)	95 (47.7)	104 (52.3)	
Tumor multiplicity				0.437
Unifocal	110 (37.2)	54 (49.1)	56 (50.9)	
Multifocal	186 (62.8)	100 (53.8)	86 (46.2)	
Grade				0.282
Low	75 (25.3)	35 (46.7)	40 (53.3)	
High	221 (74.7)	119 (53.8)	102 (46.2)	
Pathological T stage				**0.001**
T0,Ta, Tis, T1	95 (32.1)	44 (46.3)	51 (53.7)	
T2	99 (33.4)	41 (41.4)	58 (58.6)	
T3	73 (24.7)	52 (71.2)	21 (28.8)	
T4	29 (9.8)	17 (58.6)	12 (41.4)	
Pathological N stage				**<0.001**
N−	233 (78.7)	105 (45.1)	128 (54.9)	
N+	63 (21.3)	49 (77.8)	14 (22.2)	
Adjuvant chemotherapy				**0.003**
No	221 (74.7)	104 (47.1)	117 (52.9)	
Yes	75 (25.3)	50 (66.7)	25 (33.3)	
Laboratory				
Albumin, g/l)	40.23 ± 4.37	38.85 ± 3.89	42.54 ± 3.81	**<0.001**
Hemoglobin, g/dl)	129.37 ± 21.63	127.65 ± 20.03	138.23 ± 17.20	**<0.001**
White blood cell count, k/cc)	7.55 ± 2.43	9.20 ± 2.78	7.12 ± 1.96	**<0.001**
Neutrophil count, k/cc)	4.73 ± 2.06	6.59 ± 2.47	4.06 ± 1.11	**<0.001**
Platelet count, k/cc)	230.15 ± 79.72	286.62 ± 92.32	216.44 ± 61.20	**<0.001**

Bold values indicate that P-value ≤ 0.05, and considered statistically significant.
IQR = interquartile range.