ELSEVIER

CrossMark

Urologic Oncology: Seminars and Original Investigations 32 (2014) 625–630

UROLOGIC ONCOLOGY

Original article

Effect of ABO blood type on mortality in patients with urothelial carcinoma of the bladder treated with radical cystectomy

Tobias Klatte, M.D.[a], Evanguelos Xylinas, M.D.[b,c], Malte Rieken, M.D.[b,d], Morgan Rouprêt, M.D.[e], Harun Fajkovic, M.D.[a], Christian Seitz, M.D.[a], Pierre I. Karakiewicz, M.D.[f], Yair Lotan, M.D.[g], Marko Babjuk, M.D.[h], Michela de Martino, Ph.D.[a], Shahrokh F. Shariat, M.D.[a,b,*]

[a] *Department of Urology, Medical University of Vienna, Vienna General Hospital, Vienna, Austria*
[b] *Department of Urology, Weill Cornell Medical College, Presbyterian Hospital, New York, NY*
[c] *Department of Urology, Cochin Hospital, APHP, Paris Descartes University, Paris, France*
[d] *Department of Urology, University Hospital Basel, Basel, Switzerland*
[e] *Department of Urology, Groupe Hospitalier Pitié—Salpêtrière, Assistance Publique Hopitaux de Paris, Faculty of Medicine Pierre et Marie Curie, Institut Universitaire de Cancérologie GRC5, University Paris 6, Paris, France*
[f] *Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Centre, Montreal, Quebec, Canada*
[g] *Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX*
[h] *Department of Urology, Hospital Motol, Second Faculty of Medicine, Prague, Czech Republic*

Received 17 October 2013; received in revised form 20 November 2013; accepted 20 November 2013

Abstract

Objective: ABO blood type is an inherited characteristic that has been associated with the prognosis of several malignancies, but there is little evidence in urothelial carcinoma of the bladder (UCB). The purpose of this study was to evaluate the effect of ABO blood type on mortality in patients with UCB treated with radical cystectomy (RC).

Methods: Multi-institutional data from 7,906 patients with UCB treated with RC between 1979 and 2012 were retrospectively analyzed. The effect of ABO blood type on UCB-related mortality was evaluated with univariable and multivariable competing-risks regression models.

Results: ABO blood type was O in 3,728 (47%), A in 2,748 (35%), B in 888 (11%), and AB in 532 (7%) patients. Blood type B was associated with a greater likelihood of lymphovascular invasion ($P = 0.010$) and positive soft tissue margins ($P = 0.008$). The median follow-up was 41 months. The 5-year cumulative UCB-related mortality rates for blood type O, A, B, and AB were 29.5%, 30.5%, 33.2%, and 25.8%, respectively. In univariable competing-risks regression, patients with blood type B had worse UCB-related mortality than those with blood type O ($P = 0.026$) and AB ($P = 0.020$). In multivariable analysis, however, blood type lost its statistical significance.

Conclusions: Among patients treated with RC, ABO blood type is associated with a statistically significant but clinically insignificant difference in UCB-related mortality. This association was not present in multivariable analysis. Our data therefore suggest no relevant association of ABO blood type with UCB-related prognosis.

Keywords: ABO; Blood group; Blood type; Prognosis; Cystectomy; Biomarker

1. Introduction

Urothelial carcinoma of the bladder (UCB) is the leading malignant tumor of the urinary system, with more than 70,000 newly diagnosed cases in the United States annually [1]. At initial diagnosis, approximately three-fourths of patients have non–muscle-invasive UCB, and approximately one-fourth present with muscle-invasive disease. For high-risk and recurrent non–muscle-invasive as well as muscle-invasive UCB, radical cystectomy (RC) and pelvic lymphadenectomy are the treatment of choice [2]. Despite aggressive treatment, mortality rates are high, with approximately 50% of patients succumbing in the first 5 years after the operation [2]. Established prognostic factors for UCB treated with RC include pathological T classification, lymph node involvement, grade,

* Corresponding author. Tel.: +43-140-400-2615; fax: +43-140-400-2332.
E-mail address: sfshariat@gmail.com (S.F. Shariat).

1078-1439/$ – see front matter
http://dx.doi.org/10.1016/j.urolonc.2013.11.010

lymphovascular invasion (LVI), and soft tissue surgical margin (STSM) status [3–8].

The ABO blood type is available for every patient who undergoes elective surgery and represents a potential prognostic biomarker. In North America and Europe, 37% to 44% of the population are blood type O, approximately 42% are A, 10% to 14% are B, and 4% to 6.5% are AB [9]. The corresponding ABO gene is located on chromosome 9q34.1-34.2, an area that is frequently affected in UCB [10,11]. Studies show that ABO blood group antigen expression within the UCB decreases with grade [12] and may be linked with outcomes [13,14]. In terms of patients' blood type status, studies conducted several decades ago suggested that blood type O and B are associated with a more unfavorable pathology and possibly worse prognosis, although the differences were clinically small or statistically insignificant [15,16]. In contrast, data from other malignancies indicate that ABO blood type is significantly associated with stage and survival [17–19].

We hypothesized that ABO blood type is a prognostic factor in UCB and tested this hypothesis in an international cohort of more than 7,000 patients treated with RC.

2. Patients and methods

2.1. Study population

For this retrospective study, all participating sites obtained institutional review board approval and provided the necessary institutional data sharing agreements before study initiation. In all, 11 international academic urology centers from North America and Europe provided data. The initial study cohort consisted of 8,141 patients who underwent RC with bilateral pelvic lymphadenectomy for UCB between 1979 and 2012. The indications for RC were tumor invasion in the muscularis propria or prostatic stroma, or non–muscle-invasive UCB refractory to transurethral resection with intravesical chemotherapy or immunotherapy or both. No patient had distant metastases at the time of RC. Patients who received neoadjuvant chemotherapy or radiotherapy were excluded ($n = 235$), leaving 7,906 patients for final analysis.

2.2. Study variables

Data collection and coding was described previously [3,4,20]. The collected variables were abstracted from patient charts and included ABO blood type, age, gender, T classification, N classification, lymph tumor grade, concomitant carcinoma in situ, STSM status, administration of adjuvant chemotherapy, follow-up interval, date of death, and cause of death. A computerized database was generated at each center. After the data sets were merged, reports were created for each variable and inconsistencies, and data integrity problems were resolved before analysis. The database was frozen on September 10, 2013, and the final data set was produced for the current analysis.

Information on ABO blood types was gathered from the blood type identity cards. For pathological staging, surgical specimens were processed according to standard procedures. The cystectomy specimen was inked, and multiple sections were obtained from the tumor, the bladder wall, and the mucosa adjacent to and distant from the tumor in addition to the ureters and regional lymph nodes. In men, tissue sections were obtained from the seminal vesicles and the prostate. In women, sections were obtained from uterus, vagina, and ovaries. Pelvic lymph nodes were examined grossly, and all lymphoid tissue was submitted for histological examination.

Tumors were staged according to the 2009 TNM classification [21], and tumor grade was assigned according to the WHO/International Society of Urological Pathology consensus classification. LVI was defined as the presence of nests of tumor cells within an endothelium-lined space [4]. STSM was defined as tumor at inked areas of soft tissue on the RC specimen [3].

Adjuvant chemotherapy was administered in 1,687 patients (21.3%) at the discretion of the treating physician based on pathological stage, performance status, renal function, and patient preference.

Postoperative follow-up and imaging was institution and physician dependent [3]. In general, patients were followed up at least every 3 to 4 months in year 1, every 6 months in year 2, and annually thereafter. Follow-up visits consisted of physical examination and serum chemistry evaluation. Diagnostic imaging was performed at the discretion of the treating physician. In case of death, cause of death was determined by the treating physician through chart review, death certificate, or the clinical history.

2.3. Statistical analysis

Categorical variables are presented as numbers and percentages, and continuous variables as median and interquartile range. Associations of ABO blood type with categorical variables and continuous variables were assessed with chi-square tests and Kruskal-Wallis tests, respectively.

Because patients are at a significant risk of dying from non–UCB-related causes, Fine and Gray's competing-risks regression was used to determine UCB-related mortality. We defined the event of interest as death from UCB, and the competing event as non–UCB-related death. Univariable and multivariable estimates were obtained as subhazard ratios (SHR) and 95% CI. Cumulative incidence curves were generated with the postestimation function after fitting the regression model. All analyses were conducted with the cmprsk package in R 2.15.2 (The R Foundation for Statistical Computing, Vienna, Austria). Statistical testing was 2-sided, and a $P < 0.05$ was considered statistically significant.