

Original article

Is preoperative anemia a risk factor for upper tract urothelial carcinoma following radical nephroureterectomy?

Hsin-Chih Yeh, M.D., M.S.^{a,b,c,d,1}, Tsu-Ming Chien, M.D., M.S.^{c,1},
Wen-Jeng Wu, M.D., Ph.D.^{a,b,c,d,e}, Ching-Chia Li, M.D.^{a,b,c,d}, Wei-Ming Li, M.D., M.S.^{b,c,d,f},
Hung-Lung Ke, M.D., M.S.^{b,c,d}, Yii-Her Chou, M.D., Ph.D.^{b,c}, Chii-Jye Wang, M.D., Ph.D.^{b,c},
Shu-Pin Huang, M.D., Ph.D.^{b,c}, Chien-Feng Li, M.D., Ph.D.^{g,h,i}, Peir-In Liang, M.D.^j,
Chun-Nung Huang, M.D., Ph.D.^{b,c,*}

^a Department of Urology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

^b Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

^c Department of Urology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

^d Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

^e Center for Infectious Disease and Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan

^f Department of Urology, Ministry of Health and Welfare Pingtung Hospital, Pingtung, Taiwan

^g Department of Pathology, Chi Mei Medical Center, Tainan, Taiwan

^h Department of Biotechnology, Southern Taiwan University of Science and Technology, Tainan, Taiwan

ⁱ National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan

^j Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

Received 15 December 2015; received in revised form 9 March 2016; accepted 28 March 2016

Abstract

Purpose: We aimed to identify the effect of preoperative anemia on oncologic outcomes in patients with upper tract urothelial carcinoma (UTUC) who had different levels of renal function.

Methods: Between 2000 and 2013, we enrolled 370 patients who underwent radical nephroureterectomy for nonmetastatic UTUC. Preoperative anemia was defined as hemoglobin <130 g/l in men and <120 g/l in women based on the World Health Organization classification. Kaplan-Meier method was applied to estimate the effect anemia on survival, and hazard ratios (HR) of anemia and other clinicopathological parameters were evaluated by Cox regression model. The analyses were also performed in patients with different chronic kidney disease (CKD) stages.

Results: In all, 242 (65.4%) patients were anemic before surgery. Those with preoperative anemia had worse CKD stage ($P < 0.001$) and higher pathological tumor stage ($P = 0.023$). In univariate analysis, metastasis-free and cancer-specific survival rates were not significantly associated with preoperative anemia (HR = 1.51, 95% CI: 0.93–2.44, $P = 0.093$ and HR = 1.59, 95% CI: 0.93–2.72, $PP = 0.094$, respectively). However, in patients without stage 5 CKD, those with preoperative anemia had apparently inferior metastasis-free and cancer-specific survival than those without (HR = 1.88, 95% CI: 1.14–3.01, $P = 0.014$ and HR = 2.03, 95% CI: 1.16–3.56, $P = 0.010$, respectively). A multivariate Cox proportional hazards model indicated that preoperative anemia was an independent predictor for both metastasis-free (HR = 2.17, 95% CI: 1.21–3.90, $P = 0.010$) and cancer-specific survival (HR = 2.21, 95% CI: 1.15–4.21, $P = 0.017$).

Conclusions: Among patients without stage 5 CKD, preoperative anemia was a significant prognostic factor to predict metastatic progression and cancer-specific death in UTUC following radical nephroureterectomy. It was important to be aware of patients' renal function while evaluating the effect of anemia on outcome of UTUC. © 2016 Elsevier Inc. All rights reserved.

Keywords: Anemia; Metastasis; Prognosis; Upper tract urothelial carcinoma

This study was supported by Grants from Kaohsiung Medical University "Aim for the Top Universities" (KMU-TP104E31, KMU-TP104G00, KMU-TP104G01, KMU-TP104G04), the health and welfare surcharge of tobacco products, Ministry of Health and Welfare (MOHW105-TDU-B-212-13 4007), and Kaohsiung Medical University Hospital (KMUH102-2M42).

¹Hsin-Chih Yeh and Tsu-Ming Chien contributed equally to this article, and both should be considered first author.

* Corresponding author. Tel.: +886-7-320-8212; fax: +886-7-321-1033.

E-mail address: slaochain@gmail.com (C.-N. Huang).

1. Introduction

Upper tract urothelial carcinomas (UTUC) are tumors derived from urothelium along the pyelocaliceal cavities and ureter, accounting for 5% to 10% of urinary tract carcinomas [1,2]. The male-to-female ratio of UTUC is about 2:1 and the incidence of pyelocaliceal tumors is

approximately 2 to 3 times as common as ureteral tumors [1,2]. However, in Taiwan, the incidence of UTUC is as high as 30% of urothelial carcinomas with a slightly female predominance, and ureteral tumors accounts for more than half of all UTUC [3,4]. Renal function impairment is not an infrequent finding in patients with UTUC, and the prevalence of chronic kidney disease (CKD) and end stage renal disease (ESRD) among them could be up to 47% and 28%, respectively [5].

Radical nephroureterectomy (RNU) with bladder cuff excision is the gold standard treatment for adequate local tumor control and better long-term survival. Despite the optimal surgical treatment, the 5-year cancer-specific mortality rates remain relatively high ranging from 20% to 30% among different studies [6,7]. The risk of disease recurrence and progression is even higher in advanced UTUC, with an estimate 5-year survival less than 30% and 10% in cases of regional nodal metastases and distant metastases, respectively [8]. Traditional prognostic factors for UTUC after RNU, such as pathological tumor stage and grade, are inadequate for detailed risk stratification and difficult to be defined before treatment [4]. A better understanding of biomolecular predictors for UTUC is certainly needed to improve planning on neoadjuvant/adjuvant therapy and offer proper follow-up strategies.

Several preoperative blood or biochemical parameters, including low hemoglobin level [6,9–11], impaired renal function [4,5,10], and elevated C-reactive protein [12], were investigated as potential prognostic factors for UTUC. Anemia has been demonstrated as an independent predictor of recurrence and cancer-specific death for UTUC [9]. Preoperative anemia was also reported to be significantly associated with advanced tumor stage, high tumor grade, and lymph node metastasis [11]. Hemoglobin level is routinely tested before surgery and therefore readily applicable in clinical practice. However, the role of preoperative anemia in UTUC has not been fully established because many confounding conditions may exist.

Anemia can result from a variety of causes, including under production of red blood cells, blood loss, renal insufficiency, hemolysis, bone marrow disorders, and hypothyroidism [13]. Anemia is likely to occur in patients with CKD even in an early stage. The mechanisms of anemia in patients with CKD are multifactorial, including erythropoietin deficiency, uremic-induced inhibitors of erythropoiesis, shortened erythrocyte survival, and disordered iron homeostasis [13–15]. Most patients with the fifth stage of CKD have anemia [14]. To our knowledge, anemia has never been analyzed based on different CKD stages to evaluate the outcome of UTUC. In this study, we aimed to investigate the effect of preoperative anemia on prognosis of patients who underwent RNU for UTUC according to their renal function.

2. Materials and methods

2.1. Patient selection and data collection

Between 2000 and 2013, we enrolled 370 Asian patients who underwent either open or laparoscopic RNU with bladder cuff excision for nonmetastatic UTUC at Kaohsiung Medical University Hospital. Patients with enlarged nodes on preoperative imaging or intraoperative examination received lymph node dissection. The present study was approved by the review board of our institution (KMUH-IRB-20120138). Clinical parameters including demographic characteristics, pathological features, oncologic follow-up, and the cause leading to mortality were retrospectively collected by chart review and death diagnosis. Patients with neoadjuvant chemotherapy or radiotherapy, concurrent muscle-invasive bladder tumor, blood disorders, bone marrow diseases, and incomplete clinical information were excluded. Tumor stage was evaluated according to the 2002 American Joint Committee Cancer TNM system. All cases were reviewed by 2 pathologists and re-classified as low or high grade using the 2004 World Health Organization (WHO) grading system. CKD stage was determined by estimated glomerular filtration rate, which was calculated by the Modification of Diet in Renal Disease equation [16].

2.2. Postoperative follow-up

After the operation, outpatient clinics were arranged every 3 months in the first 2 years and every 6 months in the next 2 years. Since the fifth year, annual follow-ups were arranged in patients with no evidence of disease. Detailed history taking, physical examination, urine cytology, cystoscopy, and serial imaging survey were performed following the surveillance guidelines. Metastatic progression was defined as tumor recurrence at the operation site, regional lymph nodes, and distant organ. Tumors occurring in the bladder or contralateral upper urinary tract were thought to be metachronous and not categorized as disease progression. Patients who had deeply invasive tumors, nodal involvement, or metastatic progression were candidates for adjuvant chemotherapy. After taking patients' performance status, renal function, and willingness into consideration, 71 cases received systemic chemotherapy.

2.3. Statistical analysis

Patients were categorized as non-anemia and anemia according to the WHO classification. Anemia was defined as hemoglobin less than 130 g/l and 120 g/l in men and women, respectively [17]. Differences between categorical parameters were assessed using a χ^2 or Fisher's exact test. The Kaplan-Meier analysis was used to estimate the effect of preoperative anemia on metastasis-free survival

Download English Version:

<https://daneshyari.com/en/article/3999404>

Download Persian Version:

<https://daneshyari.com/article/3999404>

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