European Journal of Cancer (2014) 50, 2583–2591

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original research

Prognostic relevance of postoperative platelet count in upper tract urothelial carcinoma after radical nephroureterectomy

Georgios Gakis [a,*], Hans-Martin Fritsche [b], Fahmy Hassan [a], Luis Kluth [c], Florian Miller [a], Armin Soave [c], Wolfgang Otto [b], Christian Schwentner [a], Tilman Todenhöfer [a], Roland Dahlem [c], Maximillian Burger [b], Margit Fisch [c], Arnulf Stenzl [a], Atiqullah Aziz [b], Michael Rink [c]

[a] *Department of Urology, University Hospital Tübingen, Tübingen, Germany*
[b] *Department of Urology, University Hospital Regensburg, Regensburg, Germany*
[c] *Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

Received 3 June 2014; received in revised form 30 June 2014; accepted 2 July 2014
Available online 31 July 2014

KEYWORDS
Outcome
Platelet
Radical nephroureterectomy
Recurrence-free survival
Thrombocytosis
Upper tract urothelial carcinoma

Abstract ***Aim of the study:*** To assess the impact of perioperative platelet count (PLT) kinetics on recurrence-free survival (RFS) after radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC).

Methods: From three prospectively maintained databases of three tertiary care centres a total of 269 patients undergoing RNU without perioperative treatment between 1996 and 2011 were considered for this analysis. Pre- and postoperatively elevated PLT count was defined as $>400 \times 10^9$/L. PLT levels were measured 1–3 days preoperatively and 7–10 days postoperatively. The median follow-up was 24 months (Interquartile range (IQR): 10–52). A new weighted scoring model was developed to predict recurrence after RNU based on significant parameters of multivariable analysis.

Results: The 5-year RFS in patients with preoperatively normal and elevated PLT count was 58.3% and 29.3%, respectively ($p < 0.001$). The 5-year-RFS was 57.6% in patients with normal postoperative PLT count and 29.7% in those with elevated PLT levels ($p < 0.001$). In multivariable analysis, pT-stage, lymphovascular invasion, ureteral margin status and postoperative thrombocytosis remained independent predictors for RFS. The 5-year RFS in patients with

* *Corresponding author:* Address: Department of Urology, Eberhard-Karls University, University Hospital Tübingen, Hoppe-Seyler Strasse 3, D-72076 Tuebingen, Germany. Tel.: +49 7071 2985092; fax: +49 7071 295092.
E-mail address: georgios.gakis@googlemail.com (G. Gakis).

http://dx.doi.org/10.1016/j.ejca.2014.07.003

a score of 0 (low-risk), 1 (intermediate-risk) and 2–4 (high-risk) was 77.7%, 47.5% and 12.3%, respectively ($p < 0.001$). Consideration of the variable postoperative thrombocytosis in the final model increased its predictive accuracy by 1.9% with a concordance index of 0.758 ($p = 0.015$).

Conclusion: PLT kinetics is significantly associated with RFS after RNU for UTUC. We constructed a simple, PLT-based prognostic model for recurrence after RNU.

1. Introduction

Radical nephroureterectomy (RNU) represents the mainstay of treatment for invasive upper tract urothelial carcinoma (UTUC) or non-invasive UTUC not amenable to kidney-sparing treatment [1]. Despite this, recurrence occurs in up to 50% of the patients undergoing RNU for UTUC [2]). By contrast to muscle-invasive bladder cancer, in which neoadjuvant chemotherapy has shown to improve overall survival [3,4], the adoption of perioperative chemotherapy in UTUC is hampered by staging inaccuracies and lack of predictive factors associated with advanced disease. Furthermore, as outcomes in UTUC may vary considerably inter-individually within a given prognostic group [5], it is essential to individualise treatment based on patient-centred risk factors associated with poor survival in order to selectively advocate neoadjuvant and adjuvant modalities [6].

Haematologic and inflammatory changes have been identified as prognostic factors in solid urological malignancies [7,8]. Elevated platelet count (PLT) is frequently observed in patients with cancer [9] and has been reported as a prognostic factor in several urological malignancies [10,11]. In contrast to bladder cancer, in which thrombocytosis has been shown to be associated with poor survival [12,13], the role of platelets in UTUC has not been investigated thus far. Therefore, this study aims to evaluate the prognostic significance of platelet count kinetics in patients undergoing RNU for UTUC.

2. Patients and methods

In this Institutional-Review Board approved observational multicenter analysis we reviewed the clinical and pathologic records of 269 consecutive patients obtained from three prospectively maintained databases who underwent RNU for UTUC at three tertiary academic centres between 1996 and 2011. Patients undergoing neoadjuvant or adjuvant treatment were excluded from analysis. The composition of the present cohort, modality of combining the different databases and modality of surgical treatment has been outlined elsewhere [14]. In brief, RNU was performed either open or laparoscopically with bladder cuff excision managed either trans- or extravesically. Lymph node dissection was performed at the discretion of the treating surgeon based on suspect findings of preoperative cross-sectional imaging.

Pre- and postoperatively elevated PLT count was defined as $>400 \times 10^9$/L. The following clinical and pathologic parameters were assessed: age at RC, gender, clinical and pathologic tumour stage, pathologic lymph node tumour involvement, ureteral margins, soft-tissue surgical margins (STSMs), lymphovascular invasion, tumour grade (according to 1973 World Health Organisation [WHO] classification), tumour location (pyelocalyceal versus ureteral versus both), tumour multifocality, modality of RNU (open versus laparoscopic) and presence of preoperative hydronephrosis. In general, preoperative PLT count was measured 1–3 days prior nephroureterectomy while postoperative PLT count was measured at the 7th–10th postoperative day after removal of the bladder catheter prior to discharge.

2.1. Histologic assessment

The histologic assessment was performed at the centre-specific pathology department and was based on the 1973 WHO grading system and 2002 Tumour-Node-Metastasis (TNM) classification as approved by the American Joint Committee on Cancer (AJCC) [15]. The pathologic macro- and microscopic evaluation of cystectomy specimens included cross-sectioning of the entire specimen with immunohistochemical staining to identify the presence of urothelial carcinoma [16]. Positive ureteral margins were defined as the microscopic presence of malignant cells at the distal ureteral margin. Lymphovascular invasion was defined as the microscopic presence of malignant cells within an endothelial cell line [17].

2.2. Follow-up

Electronic hospital charts and physician records were reviewed to determine clinical outcomes. Patients generally were seen postoperatively at least every 3–4 months for the first year, semiannually for the second and third years, and annually thereafter. Follow-up examinations included radiologic imaging with cross-sectional imaging. In addition to physical examination with laboratory testing, intravenous pyelography, cystoscopy, urine cytology, urethral washings and bone scintigraphy were carried out if indicated. Disease recurrence was defined