



## Original article

# Postoperative D-dimer predicts venous thromboembolism in patients undergoing urologic tumor surgery

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## Abstract

**Purpose:** We examined the incidence of pulmonary thromboembolism (PE) and deep venous thromboembolism (DVT) in patients who underwent urologic tumor surgery. The aim of this study was to investigate the postoperative D-dimer for prediction of venous thromboembolism events (VTE), as well as to identify other risk factors associated with the occurrence of thromboembolisms.

**Patients and methods:** This was a prospective observational cohort study, which included 1,269 patients who underwent major urologic tumor surgery, from August 2015 to February 2017, at our center. Data comprising age, sex, body mass index, Charlson comorbidity index, type of surgery, Caprini score, postoperative D-dimer levels, and other laboratory tests were collected for analyses. Lower limb venous ultrasound was performed before surgery and the day before hospital discharge to measure DVT. Computerized tomography or ventilation/perfusion lung scan was applied to detect PE.

**Results:** The overall incidence of VTE was 2.4% (31 cases) in 1,269 patients, consisting of 23 PE events and 9 DVT events. Patients undergoing radical cystectomy were most likely to suffer VTE (4.3%). The optimal cutoff value for postoperative D-dimer was 0.98  $\mu\text{g/ml}$ , according to the receiver operating characteristic curve analysis, with a sensitivity of 83.9%, and a specificity of 80.0%. On multivariate analysis, hypertension (odds ratio, OR = 2.5, 95% CI: 1.1–5.7;  $P = 0.026$ ), Charlson comorbidity index  $\geq 2$  (OR = 5.6, 95% CI: 2.2–14.6;  $P < 0.001$ ), and D-dimer level  $\geq 1 \mu\text{g/ml}$  on postoperative day 1 (OR = 12.52, 95% CI: 4.6–35.2;  $P < 0.001$ ) were independently associated with VTE after urologic tumor surgery.

**Conclusions:** The overall incidence of urologic-tumor-surgery-associated VTE in an Asian population is similar to those reported in European and North American series. Elevated D-dimer early after operation is an independent predictor of VTE in patients undergoing urologic tumor surgery. In addition, hypertension and the Charlson comorbidity index are both important clinical risk factors. The Caprini score recommended by the guideline is inadequate in this study population. The postoperative D-dimer plasma level is a more reliable marker for identifying patients at high-risk of developing venous thromboembolisms. © 2018 Published by Elsevier Inc.

**Keywords:** Venous thromboembolism; Urologic tumor surgery; Risk factors; D-dimer

## 1. Introduction

Venous thromboembolism events (VTE) are common and serious complications after urologic surgery. The risk of

death in patients diagnosed with VTE is 13.5 times higher than that of those without VTE [1]. Therefore, VTE prediction and prevention deserve special consideration.

Use of the Caprini risk assessment is recommended for patients undergoing surgery [2]. However, the validity of this model has to be questioned since a high proportion of patients would be classified as high-risk after the urologic surgery. Different cancer types and surgical procedures have a major influence on the overall VTE risk [3]. High plasma D-dimer level was associated with hypercoagulable status, and is an important predictor of VTE in cancer patients who are not receiving any therapy [4]. Measurements of D-dimer and fibrinogen degradation

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product (FDP) have been proven useful for evaluating the risk of VTE in patients with major orthopedic surgery [5]. At present, research on the clinical relevance of D-dimer and FDPs for the prediction of urologic-surgery-associated VTE is lacking. In our study, we hypothesized that surgery would elevate D-dimer levels in a predictable and systematic way in the absence of VTE, and thrombosis events would further increase D-dimer levels beyond this range. Consequently, we attempted to define a feasible threshold for the identification of VTE.

Due to differences in thromboprophylaxis and the demographic characteristics of patients in previous studies, the reported incidence of VTE varies from 0.7% to 4.7% after radical prostatectomy [1,6,7], 0.54% to 8% after radical cystectomy [1,8], and 0.14% to 1.67% after upper tract surgery [1,9]. Additionally, some studies showed that the incidence of VTE in Asia is relatively lower when compared to that in Western countries [10,11]. However, these findings are dependent on the aging population, dietary pattern changes and lifestyle differences. Although current guidelines provide optimal thromboprophylaxis strategies, data on Asian patients are limited.

Therefore, we designed a prospective observational analysis to identify the incidence and risk factors of VTE in Asian patients undergoing urologic tumor surgery. Furthermore, we investigated the predictive value of coagulation markers, specifically D-dimers and FDPs, and attempted to determine a suitable threshold for the postoperative assessment of urologic tumor patients.

## 2. Methods

### 2.1. Patients

This study was approved by the Institutional Review Board of Renji Hospital affiliated to Shanghai Jiaotong University, Medical school. The study was initiated in August 2015, and we prospectively collected the data of all patients who underwent urological tumor surgery at Renji hospital affiliated to Shanghai Jiao tong University

School of Medicine, until February 2017 ( $n = 1,269$  patients). Patients taking any dose of antiplatelet or anticoagulant drugs at the time of hospital admission, and those with incomplete clinical data were excluded from this study. A total of 72 patients were excluded because of taking antiplatelet drug or anticoagulants. Of them, 64 patients were excluded due to incomplete clinical data, consisted of 25 cases didn't get ultrasound, 16 cases didn't get D-dimer tests, and 27 cases didn't get other laboratory tests. All preoperative, intraoperative and postoperative clinical variables were recorded, including patient age, sex, body mass index (BMI), Charlson comorbidity index [12], type of surgery, Caprini score, predictive biomarkers, and operation time. All biomarker values were obtained from the same laboratory affiliated to the hospital.

### 2.2. Surgical methods and VTE prophylaxis

All surgeries were performed by experienced surgeons, according to a standardized protocol. Pelvic lymphadenectomy, including obturator field nodes, and external and internal iliac nodes up to the common iliac artery, was performed in patients undergoing radical cystectomy. Early ambulation was encouraged, and mechanical thromboprophylaxis with graduated compression stockings was used in all patients. Heparin prophylaxis was not administrated in our center, due to the controversial use of anticoagulant prophylaxis according to Chinese guidelines.

### 2.3. Laboratory assays

Laboratory tests, including complete blood count, conventional coagulation test (prothrombin time, activated partial thromboplastin time, etc.), renal function, D-dimer, FDPs, and serum total cholesterol, were performed the day before surgery and on postoperative day 1 (POD 1). The detection of D-dimer was measured by the latex-enhanced immunoturbidimetry (CA-7000; Sysmex, Kobe, Japan). Based on receiver operating characteristic (ROC) curve analysis, the best cutoff point for D-dimer level on the

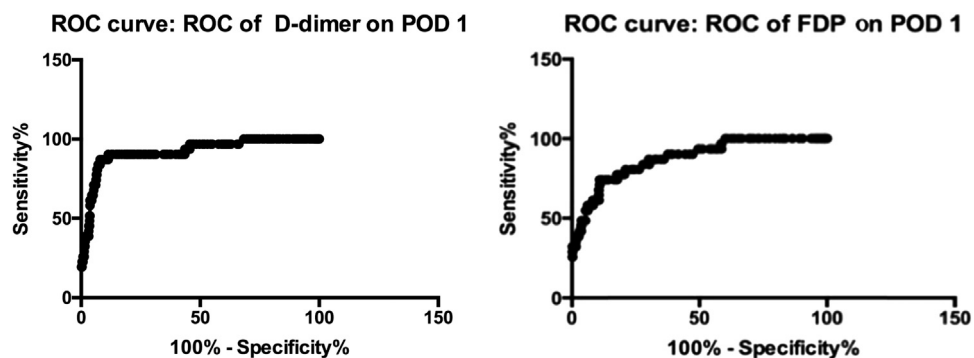


Fig. 1. Receiver operating characteristic curve for D-dimer and FDPs on the POD1.

\*FDP = fibrinogen degradation product; POD = postoperative day.

AUC (ROC of D-dimer):0.918; AUC (ROC of FDP):0.850.

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