Blood Type, Lymphadenectomy and Blood Transfusion Predict Venous Thromboembolic Events Following Radical Prostatectomy with Pelvic Lymphadenectomy

Matthew K. Tollefson,* R. Jeffrey Karnes, Laureano Rangel, Rachel Carlson and Stephen A. Boorjian

From the Departments of Urology and Health Sciences Research (LR, RC), Mayo Medical School and Mayo Clinic, Rochester, Minnesota

Abbreviations and Acronyms

DVT = deep venous thrombosis

PE = pulmonary embolism

PSA = prostate specific antigen

RP = radical prostatectomy

VTE = venous thromboembolic event

vWF = von Willebrand factor

Accepted for publication October 7, 2013.

Study received institutional review board approval.

* Correspondence and requests for reprints: Department of Urology, Mayo Clinic, 200 First St. Southwest, Rochester, Minnesota 55905 (telephone: 507- 266-6091; FAX: 507-284-4951; e-mail: tollefson.matthew@mayo.edu).

Purpose: Venous thromboembolic events are the most common nonoperative complication after radical prostatectomy and they represent the most common cause of death within 30 days of surgery. While effective mechanical and chemoprophylaxis exists, such prophylaxis may also be associated with increased complications. To identify venous thromboembolic event risk factors and, thereby, facilitate targeted prophylaxis we characterized clinicopathological variables associated with these events in patients undergoing radical prostatectomy.

Materials and Methods: We reviewed the records of 18,472 consecutive patients who underwent radical prostatectomy with pelvic lymphadenectomy for prostate cancer at our institution from 1987 to 2010. Patients were followed postoperatively for complications. Venous thromboembolic events within 30 days of surgery were recorded. Logistic regression models were used to analyze clinicopathological variables associated with venous thromboembolic events.

Results: We identified symptomatic venous thromboembolic events in 271 patients (1.4%). This diagnosis was not associated with preoperative body mass index, prostate specific antigen, Gleason score or cancer recurrence. However, the diagnosis was significantly associated with nonO blood type (OR 1.98, $p = 0.004$), an increasing number of lymph nodes removed (OR 1.05, $p = 0.035$) and blood transfusion (OR 1.30, $p = 0.02$). Patients with venous thromboembolic events were significantly more likely to die within 30 days of surgery (3.0% vs 0%, $p < 0.001$).

Conclusions: Blood type, pelvic lymphadenectomy extent and blood transfusion are significant risk factors for symptomatic venous thromboembolic event before radical prostatectomy plus pelvic lymph node dissection. These data should be used for patient counseling, particularly in regard to obviating lymphadenectomy in patients at low risk and for individualizing prophylaxis for venous thromboembolic event in patients at higher risk.

Key Words: prostate, prostatic neoplasms, prostatectomy, venous thromboembolism, ABO blood-group system

Deep venous thrombosis and PE combine to represent the continuum of VTE. VTE is a serious common complication of pelvic surgery for malignancy, representing the most common cause of mortality in patients who die within 30 days of surgery.[1–5] Accordingly, multiple international medical and surgical societies have made VTE detection

0022-5347/14/1913-0646/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2013.10.062
Vol. 191, 646-651, March 2014
Printed in U.S.A.

and prevention a priority for postoperative patient safety initiatives. Furthermore, DVT and PE are now individually recorded in the National Surgical Quality Improvement Program (NSQIP) as postoperative complications and considered an important quality indicator of surgery.

Patients undergoing RP are at risk for VTE since many identified risk factors for VTE are common in men with prostate cancer. For example, surgery for malignancy is associated with a fivefold to sevenfold increase in the risk of VTE.[6,7] Age is also a known risk factor for VTE with older patients more likely to experience thrombotic complications.[8] As such, in a recent review of NSQIP data prostatectomy was associated with a 2.5-fold increased risk of VTE within 30 days compared to procedures such as breast surgery.[9] In fact, ultrasound revealed that the VTE rate may be as high as 20% after RP.[10] These concerns led the American College of Chest Physicians to recommend thromboprophylaxis in all patients undergoing laparoscopic or open urological procedures, including 1 or more of low dose unfractionated heparin, low molecular weight heparin, intermittent pneumatic compression devices or graduated compressive stockings. This recommendation was graded as 1A evidence, indicating a strong recommendation that the benefits of such prophylaxis outweigh the risks, burdens and costs.[1] Furthermore, the American Urological Association issued a Best Practice Statement for patients undergoing laparoscopic or open urological surgery.[11] The recommendation states that all patients should receive intermittent pneumatic compression and those at high risk may be treated with low molecular weight or unfractionated heparin.

However, while in large population studies the estimated incidence of VTE after RP is between 2.9% and 3.9%,[12] these studies frequently included limited clinical information for identifying individual risk factors. Moreover, a number of published single institutional series show a VTE rate of between 0.0% and 0.5%, which raises questions of generalizability, followup and lack of power to detect significant contributing factors.[13,14] Indeed, limited data exist to identify patients undergoing RP who are at highest risk for VTE and who might most benefit from an aggressive thromboprophylactic strategy.

While effective mechanical and pharmacological prophylaxis for VTE exists, its use may be associated with increased postoperative complications such as bleeding and lymphocele formation.[15,16] As such, VTE prophylaxis remains underused in patients treated with surgery for prostate cancer.[17,18] Therefore, identifying reproducible risk factors for VTE may allow for more discriminative use of anticoagulant approaches to VTE prophylaxis. We report factors associated with VTE in a large series of men undergoing RP with pelvic lymphadenectomy.

METHODS

Patient Cohort

After receiving institutional review board approval we identified 19,798 patients treated with RP at our institution from 1987 to 2010. We eliminated from analysis 1,098 patients with a lack of information on VTE and 228 who refused the release of records. These exclusions led to our final study cohort of 18,472 men.

Multiple physicians performed surgery during the study period using standard techniques. Of the patients in this cohort 16,374 (88.6%) underwent open retropubic RP and 2,098 (11.4%) underwent robot-assisted RP. Pelvic lymphadenectomy was routinely done at our institution throughout this period. VTE prophylaxis during and after the procedure included routine use of graduated compressive stockings and pneumatic compression devices until patients were fully ambulatory and discharged from the hospital. Low molecular weight heparin and unfractionated heparin were given at treating physician discretion but were only rarely used during this period. Postoperatively patients were encouraged to ambulate at least 8 times daily while at home. Patients who traveled from a long distance were encouraged to ambulate frequently during the return trip to decrease the risk of VTE. Distance traveled for surgery was estimated by extrapolating the billing address of the patient and comparing it to the address of the hospital where the procedure was performed.

Postoperative assessments, including physical examination and serum PSA measurement, were done quarterly for the initial 2 years, semiannually for an additional 2 years and annually thereafter. Biochemical recurrence was defined as PSA 0.4 ng/ml or greater. Local recurrence was defined as cancer on biopsy of the prostatic bed or the receipt of salvage radiation therapy to the prostatic bed without evidence of systemic recurrence. Systemic progression was defined as demonstrable metastatic deposits on radionuclide bone scan or on biopsies other than biopsy of the prostatic bed. Cause of death was identified from death certificates or physician correspondence. For patients followed elsewhere the prostatectomy registry at our institution monitors outcomes annually by correspondence.

Statistical Analysis

Clinicopathological features were compared using the chi-square, Fisher exact and Wilcoxon-Mann-Whitney tests as appropriate. Postoperative survival was estimated using the Kaplan-Meier method and compared using the log rank test. Patients were censored at last followup or death if the end point of interest was attained. Univariate and multivariate logistic regression models were used to analyze clinicopathological variables associated with postoperative VTE. All tests were 2-sided with $p \leq 0.05$ considered significant. Statistical analyses were done using SAS®, version 9.2.