Editorial

Ongoing efforts to reduce perioperative morbidity of radical cystectomy: towards widespread adoption of extended-duration thromboprophylaxis

Vignesh T. Packiam[1], Joseph J. Pariser[2]

[1]Section of Urology, Department of Surgery, University of Chicago Pritzker School of Medicine, Chicago, IL, USA; [2]Department of Urology, University of Minnesota, Minneapolis, MN, USA

Correspondence to: Joseph J. Pariser, MD. Department of Urology, University of Minnesota, 420 Delaware St. SE, MMC 394, Minneapolis, MN 55455, USA. Email: pariserj@gmail.com.

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Radical cystectomy (RC) is the gold standard treatment for muscle invasive and select high-risk non-muscle invasive bladder cancers. The operation is well known to pose significant perioperative morbidity (1). Venous thromboembolic events (VTE) remain a major and increasingly acknowledged complication of RC. Until recently, there have been several obstacles to clear guidance on perioperative thrombophylaxis, including concerns regarding standardized reporting of VTE and questions about the risks of anticoagulation (2-4).

In a timely review by Tikkinen *et al.*, procedure-specific VTE and bleeding risks after urologic surgery were outlined after a comprehensive literature review, with a clear demonstrable benefit of extended-duration thromboprophylaxis after RC (5). The question remains whether there has been adequate widespread adoption of post-discharge prophylaxis.

In a recent article published in *Journal of Urology*, Klaassen and associates assert the answer is no (6). They systematically expound on several key concepts. First, retrospective institutional series and large multi-institutional databases reveal that symptomatic VTE occurs in 3–12% of patients undergoing RC (4-12). Importantly, more than half of these VTE occur after hospital discharge. Next, the article thoroughly reviews Level 1 evidence and a meta-analysis from the general surgery literature supporting the use of extended-duration thrombophylaxis, showing a greater than 50% reduction in VTE (7-9).

The specific benefit of extended-duration (post-discharge) VTE prophylaxis after RC has been evaluated at high-volume centers where it was initially adopted. We and others have previously described experiences instituting regimens consisting of post-discharge enoxaparin, which were associated with decreased VTE rates (10-12). Specifically, we reported a decrease in the rate of VTE from 12% to 5% with benefits predominantly in post-discharge events (6% *vs.* 2%) (10). Fortunately, bleeding rates did not measurably increase with post-discharge thromboprophylaxis in any of these series. The recent Tikkinen report further dispels fears of major bleeding requiring reoperation, estimating its incidence after RC is roughly 0.3% (5). While not yet clearly recommended from the American Urological Association (AUA), numerous other societies recommend approximately 4 weeks of "extended-duration" thrombophylaxis following RC.

While enoxaparin is generally safe and effective, novel low molecular weight heparin agents (Tinzaparin) and Factor Xa inhibitors (e.g., Apixaban) remain alternatives that warrant further investigation in this population, especially given the potential for oral administration and decreased risks in patients with renal insufficiency. Finally, the authors discuss data from an electronic AUA

survey showing that 31% of respondents do not use any thrombophylaxis at all following RC, let alone an agent for an extended-duration (13).

In summary, this article acts as a timely and useful review of the rationale for aggressive VTE prophylaxis following RC. Hopefully, it will serve to educate and improve utilization for extended-duration regimens to decrease the longstanding high perioperative morbidity associated with RC.

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Footnote

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