

## **Patients Experience and Preference Regarding Subcutaneous Venous Thromboembolic Prophylaxis Following Robotic Assisted Radical Cystectomy**

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### **Abstract**

#### **Aim**

The European Association of Urology recommend venous thromboembolic (VTE) prophylaxis for 28 days following radical cystectomy (RC). The aim of this study was to assess patients experience with VTE prophylaxis.

#### **Methods**

A review was performed of the last 100 patients who underwent RC at our centre.

#### **Results**

80 patients responded, 59 (73.8%) patients self-administered, 16 (20%) had it administered by a family member and 5 (6.3%) required a daily visit by a district nurse. 22 (27.5%) patients reported mild pain, 18 (22.5%) moderate pain while 9 (11.3%) reported severe pain. 33 (41.3%) patients described some bruising. 4 (5%) patients reported haematomas and 3 (3.8%) skin irritation. 4 (5%) patients described difficulty with injecting. 69 (86.3%) patients reported they would prefer an oral agent if possible. No patient developed a VTE.

#### **Conclusion**

Patients who receive extended VTE would prefer an oral agent if possible.

### **Introduction**

The incidence of venous thromboembolism (VTE) following radical cystectomy (RC) is reported to be up to 17% (open cystectomy 2.9–11.6% and robotic assisted radical cystectomy (RARC) 2.6–10.3%)<sup>1</sup>. The European Association of Urology recommends 28 days VTE prophylaxis following RC<sup>2</sup>. The current standard is subcutaneous low molecular weight heparin (LMWH).

There have been concerns regarding patient compliance and physician adherence with the extended regimen<sup>3</sup>. Data from orthopaedic literature suggest that extended VTE prophylaxis with direct oral anticoagulants (DOACs) may be as effective in VTE prevention<sup>4</sup>. The aim of this study was to assess patients experience and preference regarding subcutaneous VTE prophylaxis following RARC.

## Methods

A retrospective review was performed of the last 100 patients who underwent RARC. All patients received dalteparin post operatively commencing the night of the procedure and continued for 28 days. Patients are managed according to an enhanced recovery program which emphasises early mobilisation<sup>5</sup>.

## Results

80 patients agreed to take part in our survey. The clinical and pathological characteristics of the cohort are detailed in Table 1.

n=	80
<b>Median Age, years (range)</b>	72 (48-87)
<b>Sex (%)</b>	
Male	57 (71.3)
Female	23 (28.7)
<b>Histological subtype</b>	
Urothelial Cancer	70 (87.5)
Variant	10 (12.5)
<b>Indication for surgery</b>	
Non muscle invasive disease	35 (43.8)
Muscle invasive disease	45 (56.2)
<b>Pathological Stage</b>	
T1	29 (36.3)
T2	31 (38.8)
T3	14 (17.5)
T4	6 (7.5)
<b>Nodal Status</b>	
N0	75 (93.8)
N1	5 (6.2)
<b>Neo-adjuvant chemotherapy</b>	24 (30)
<b>Median pre-operative Haemoglobin, g/L (range)</b>	130 (81-163)
<b>Median operative time, mins (range)</b>	320 (200-500)
<b>Median blood loss, mls (range)</b>	200 (50-800)

**Table 1:** Patient demographics and histopathological details of patients who underwent robotic assisted radical cystectomy.

59 (73.8%) patients self-administered, 16 (20%) had it administered by a family member and five (6.3%) required a daily visit by a district nurse. 31 (38.9%) patients reported no pain over the course, 22 (27.5%) mild pain, 18 (22.5%) moderate pain while 9 (11.3%) reported severe pain. 33 (41.3%) patients described some degree of bruising. 4 (5%) patients reported haematomas and three (3.8%) skin irritation. Four (5%) patients described difficulty with injecting. No patient reported stopping dalteparin injections early.

69 (86.3%) patients reported they would prefer an oral agent if possible.

No patient developed a thrombo-embolic event by 90 days. No patient was readmitted with a haemorrhagic event.

## **Discussion**

Our study demonstrates no issue with compliance with extended VTE prophylaxis following RARC. There were also no significant complications associated with extended VTE prophylaxis. Despite this the majority of patients in our cohort would prefer an oral alternative if possible.

Contrary to our findings, numerous studies have demonstrated that patient compliance can be an issue<sup>3,6</sup>. Marchocki et al, reported on 62% of patients completed their 28-day regimen<sup>3</sup>. Furthermore, physician adherence to prescribing extended regimens needs to be improved, Bergqvist demonstrated only 80% of over 3000 high risk orthopaedic patients received the appropriate prescription for extended VTE prophylaxis in a multi-centre registry across 17 European countries<sup>6</sup>.

The concern regarding extended VTE prophylaxis is the increased risk of bleeding. One of the advantages of RARC is less blood loss (200mls in our series)- the risk of a secondary haemorrhage is low (no patient was readmitted with a haemorrhage in our series). In a review of over 400 open RC, Pariser et al, demonstrated no increase in bleeding events or transfusion rates following the introduction of an extended VTE regimen<sup>7</sup>.

The use of an oral agent would be preferable for patients- avoiding the need to self-inject. Several randomized controlled trials in the orthopaedic literature have compared the use of direct oral anticoagulants (DOACs), factor Xa inhibitors such as apixaban to LMWH. The ADVANCE-2 trial compared Apixaban and Enoxaparin VTE prophylaxis following knee replacement. Apixaban 2.5 mg twice daily, starting on the morning after total knee replacement, offers a convenient and more effective orally administered alternative to 40 mg per day enoxaparin, without increased bleeding<sup>8</sup>. In the ADVANCE-3 trial 5,407 patients were randomized similarly for 35 days after hip replacement. Thromboprophylaxis with apixaban, as compared with enoxaparin, was associated with lower rates of venous thromboembolism (1.4% vs 3.9%,  $p < 0.001$ ), without increased bleeding<sup>9</sup>. Furthermore, similar to LMWH no therapeutic monitoring is required with DOACs.

The current 2021 EAU guidelines for radical cystectomy suggest pharmacological prophylaxis such as LMWH- there is a slight discrepancy with the 2020 EAU VTE guidelines which suggest alternate prophylaxis regimens can be used such as DOACs <sup>2</sup>. Despite this LMWH is standard practice.

There is also an economic advantage to the use of DOACs instead of LMWH<sup>10</sup>.

Although no serious adverse events were reported with 28 days of dalteparin use following radical cystectomy, the majority of patients would prefer an oral alternative.

#### **Ethical Approval:**

The study was approved by the ethical committee at the Royal Surrey (RS2021-1252).

#### **Declaration of Conflicts of Interest:**

There are no conflicts of interest to declare.

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#### **References:**

1. Tikkinen KAO, Craigie S, Agarwal A, Violette PD, Novara G, Cartwright R, et al. Procedure-specific Risks of Thrombosis and Bleeding in Urological Cancer Surgery: Systematic Review and Meta-analysis. *Eur Urol.* 2018 Feb;73(2):242-251.
2. Tikkinen KAO, Cartwright R, Gould MK, et al. Thromboprophylaxis. EAU guidelines 2019. <https://uroweb.org/guideline/thromboprophylaxis>. Accessed September 2nd 2021
3. Marchocki Z, Norris L, O'Toole S, Gleeson N, Saadeh FA. Patients' experience and compliance with extended low molecular weight heparin prophylaxis post-surgery for gynecological cancer: a prospective observational study. *Int J Gynecol Cancer.* 2019 Apr 16:ijgc-2019-000284.
4. Forster R, Stewart M. Anticoagulants (extended duration) for prevention of venous thromboembolism following total hip or knee replacement or hip fracture repair. *Cochrane Database Syst Rev.* 2016 Mar 30;3:CD004179.

5. Collins JW, Patel H, Adding C, Annerstedt M, Dasgupta P, Khan SM, et al. Enhanced Recovery After Robot-assisted Radical Cystectomy: EAU Robotic Urology Section Scientific Working Group Consensus View. *Eur Urol*. 2016 Oct;70(4):649-660.
6. Bergqvist D, Arcelus JJ, Felicissimo P; ETHOS investigators. Post-discharge compliance to venous thromboembolism prophylaxis in high-risk orthopaedic surgery: results from the ETHOS registry. *Thromb Haemost*. 2012 Feb;107(2):280-7.
7. Pariser JJ, Pearce SM, Anderson BB, Packiam VT, Prachand VN, Smith ND, et al. Extended Duration Enoxaparin Decreases the Rate of Venous Thromboembolic Events after Radical Cystectomy Compared to Inpatient Only Subcutaneous Heparin. *J Urol*. 2017 Feb;197(2):302-307.
8. Lassen MR, Raskob GE, Gallus A, Pineo G, Chen D, Hornick P; ADVANCE-2 investigators. Apixaban versus enoxaparin for thromboprophylaxis after knee replacement (ADVANCE-2): a randomised double-blind trial. *Lancet*. 2010 Mar 6;375(9717):807-15.
9. Lassen MR, Gallus A, Raskob GE, Pineo G, Chen D, Ramirez LM; ADVANCE-3 Investigators. Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. *N Engl J Med*. 2010 Dec 23;363(26):2487-98.
10. Brockbank J, Wolowacz S. Economic Evaluations of New Oral Anticoagulants for the Prevention of Venous Thromboembolism After Total Hip or Knee Replacement: A Systematic Review. *Pharmacoeconomics*. 2017 May;35(5):517-535.