REVIEW

Procedure-Specific Thromboprophylaxis in Urological Surgeries: A Narrative Review

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Purpose: Postoperative pulmonary embolism is a leading cause of mortality in patients undergoing major urologic surgeries, presenting a complex challenge in balancing the risks of venous thromboembolism (VTE) and perioperative bleeding. This study examines the current evidence on thromboprophylaxis in urological procedures, focusing on procedure-specific considerations.

Methods: Literature on thromboprophylaxis in urological procedures was reviewed during the past decade.

Results: Various mechanical thromboprophylaxis methods, such as compression stockings, pneumatic compression devices, foot pumps, mobilization, and exercises, are available preventive measures. Additionally, unfractionated heparin (UFH) and low molecular weight heparin (LMWH) are commonly used pharmacological agents for VTE prevention, with the choice between mechanical, pharmacological, or combined approaches tailored to individual patient characteristics and surgical requirements. Patient risk stratification into low, medium, and high-risk categories based on age, BMI, and VTE history guides the selection of thromboprophylaxis strategies. Surgical procedures are categorized as oncological or non-oncological, with uro-oncological surgeries posing a higher VTE risk than non-oncological procedures. Consequently, a combination of pharmacological and mechanical prophylaxis is typically recommended for uro-oncological patients, while pharmacological prophylaxis is reserved for high-risk individuals undergoing non-oncological surgeries. Mechanical prophylaxis is advised for high-risk patients undergoing procedures with elevated VTE risk.

Conclusion: This study summarized an optimal thromboprophylaxis protocol taking into account patient risk factors and the specific urological procedure.

Keywords: robotic-assisted surgery; laparoscopic surgery; radical prostatectomy; quality of life

INTRODUCTION

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a serious complication that can occur after urological surgeries. It is a leading cause of preventable hospital-related morbidity and mortality in surgical patients [(1)]. In urological surgeries, VTE remains a serious complication and a significant challenge[(2)] and PE is considered as the most common cause of postoperative death in patients undergoing major urologic surgery[(3)]. The decision to use thromboprophylaxis in urological surgeries involves weighing the reduction in VTE risk against the potential increase in perioperative bleeding [(4)]. However, there is a lack of procedure-specific evidence about thromboprophylaxis in urologic surgeries. Therefore, we have reviewed the available evidence on thromboprophylaxis in urological surgeries and we have tried to summarized this evidence in a procedure specific context.

Epidemiology and risk factors

Available literature reported that the incidence of symptomatic postoperative VTE is between 0.05% to 4.3% based on surgery type. The incidence of symptomatic postoperative VTE varies based on the type of surgery, with orthopedic and abdominal cancer surgeries associated with the highest rates[(5,6)]. In patients undergoing urological surgeries, the rates of DVT and PE range from 0.2% to 7.8% and 0.2% to 7%, respectively[(7)]. In previous studies about the incidence of VTE in urological operations, urological surgeries divided in two major groups; urological cancer and non-cancer surgery. In the study by Tikkinen et al. researchers performed a systematic review to estimate the absolute risk of symptomatic VTE in urological non-cancer and cancer surgeries[(8,9)]. They included 71 eligible studies reporting on 14 urological malignancy surgeries and 37 observational studies reporting on 11 urological non-cancer procedures. They reported that cystectomies and open simple prostatectomy are related to the highest risk of VTE in oncological and non-oncological urology surgeries, retrospectively. Other studies, showed similar results about VTE risk in patients who underwent surgery for urological cancer. In a review of 196,915 urological

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Table 1. Rate of VTE in common urological procedures

Urological procedure	Risk of VTE%
Non oncologic procedures	
Ureteroscopic surgery (TUL, RIRS)	0-0.4
Male urethral reconstructive surgery	0.3-1.1
open simple Prostatectomy	2.7-10.8
TURP 0.2-0.8	
Donor nephrectomy (laparoscopic or open)	0.3-1.4
Recipient nephrectomy	1.3-5.3
PCNL 0.2-0.7	
Female reconstructive pelvic surgery	0.1-0.7
Oncologic procedures	
RP without PLND	
Open	1-3.9
Laparoscopic	0.4-1.5
Robotic	0.2-0.9
RP with standard PLND	
Open	2-7.9
Laparoscopic	0.8-3
Robotic	0.5-1.9
Partial nephrectomy	1-4.4
Radical nephrectomy	0.7-4.4
Radical nephrectomy with thrombectomy	2.9-11.6
Radical cystectomy	6-24.4
RPLND	2.3-9.1

malignant surgical cases entered into the Nationwide Inpatient Sample (NIS) database between 2010 to 2019, Garcia and colleagues found that the overall VTE rate was the highest among patients undergoing radical cystectomy[10]. Rate of VTE in common urological procedures has been presented in **Table 1**[8,9,11]

Various risk factors for VTE in surgical patients have been identified, including preoperative, intraoperative, and postoperative factors. These risk factors are summarized in **Table 2**[11-14].

Several risk stratification models have been introduced to help clinicians determine prophylactic strategies for preventing VTE[15]. Some of these models include the Caprini Score for Venous Thromboembolism[16], Padua Prediction Score for Risk of VTE[17], Geneva Risk Score for Venous Thromboembolism (VTE) Prophylaxis[18], IMPROVEDD (International Medical Prevention Registry on Venous Thromboembolism Risk Assessment Model)[19], Khorana Risk Score for Venous Thromboembolism in Cancer Patients[20], Michigan Risk Score for peripheral inserted central catheter-Related Thrombosis[21].

The Caprini risk score is the most commonly used tool for predicting VTE and has been validated in over 100 clinical trials in various medical and surgical settings. However, the detailed patient information required for the Caprini risk assessment model makes it difficult for urologists to use in their clinical practice[15,22]. As a result, urologists prefer to use a valid, short, and quick risk assessment model in their daily practice, such as those developed by the American Urological Association (AUA) and European Association of Urology (EAU) based on patient risk factors[2,3].

Types of thromboprophylaxis

Mechanical thromboprophylaxis

There are different types of thromboprophylaxis, including mechanical methods such as graduated compression stockings (GCS), intermittent pneumatic compression (IPC), venous foot pump (VFP), early ambulation, and foot and ankle exercises[22]. These methods are recommended alone or in combination with pharmacologic thromboprophylaxis based on patients' risk factors and the type of surgery[23,24].

The most common mechanical methods for preventing DVT include IPC and GCS. While both are considered mechanical prophylaxis, they have different methods of action[25].

Graduated Compression Stockings

Originally designed to manage chronic conditions like venous leg ulcers and lymphedema, but studies have demonstrated that GCS is effective in preventing VTE (26). These devices apply graded circumferential pressure from the distal to proximal regions of the leg, improving venous flow velocity and preventing venous stasis. These effects of the GCS increased by muscular activity of the limb, so, their effectiveness may be reduced in patients who are immobile[27,28,29].

The most important challenge with these stockings is patient compliance. Poor fit or excessive compression can lead to complications like skin marking, blistering, ulceration, pain, discomfort, and peroneal nerve palsy [27,30]. GCS is contraindicated in patients with sensory impairment like peripheral neuropathy[27].

Intermittent Pneumatic Compression

Traditionally used for the treatment of chronic lower extremity venous disease and lymphedema, but now,

Table 2. Various risk factors for VTE in surgical patients

Pre-operative risk factors	Intraoperative risk factors	Post-operative risk factors
- Malignancy	- Central venous catheterization	- Immobility
- Chemotherapy	- Prolonged operation	- Sepsis
- Radiation	- Blood loss	- Myocardial infarction
- VTE history	- Lack of prophylaxis	- Prolonged hospital stay
- Diabetes mellitus	- Reoperation	- Lack of thromboprophylaxis
- Increasing age		- Malnutrition
- Pregnancy		- Lymphocoele
- Postpartum period		
- Hormone replacement therapy		
- Heart failure		
- Inflammatory bowel disease		
- Nephrotic syndrome		
- Myeloproliferative disorders		
- Paroxysmal nocturnal hemoglobinuria		
- Obesity		
- Smoking		
- Serious lung disease		
- Varicose veins		
- Inherited or acquired thrombophilia		

Table 3. presented alternative regimens for prophylaxis of VTE

Unfractionated heparin (UFH)	**5000 IU subcutaneous injection twice daily**
Low molecular weight heparin (LMWH):	
enoxaparin	40mg subcutaneous daily
Dalteparin	standard prophylactic dose 5000 units subcutaneous once daily; 5000 units twice daily
Tinzaparin	standard prophylactic dose 3500 units once daily
	Weight 30-50 kg 2500 units once daily
	Weight 50-70 kg 3500 units once daily
	Weight 70-130 kg4500 units once daily
Bemiparin	(standard prophylactic dose 2500 units; subcutaneous once daily
Certoparin	3000 units daily
Nadroparin	standard prophylactic dose 2850 units; subcutaneous once daily
Parnaparin	standard 3200 units once daily subcutaneously
Reviparin	minimum 1750 units once daily to maximum 4200 units once daily
Vitamin K Antagonists:	
Fondaparinux	2.5 mg subcutaneous injection once daily
Direct acting oral anticoagulants	
Apixaban	2.5mg tablet twice daily
Dabigatran	220 mg tablet once daily
Rivaroxaban	10 mg tablet once daily
Edoxaban	30 mg tablet once daily

it is a reliable method for preventing VTE events. IPC mechanism is pressure to empty deep veins, producing a pulse of blood that travels proximally and preventing stasis led to DVT prevention[31]. A systematic review found that while there is weak evidence to differentiate between the effectiveness of IPC and GCS, using IPC is related to the lower DVT rate in comparison with GCS [25]. In clinical view, IPC offers improved tolerability compared to GCS and avoids the bleeding risks associated with pharmacologic prophylaxis[30]. However, symptomatic congestive heart failure and preexisting DVT are potential contraindications for IPC use[27].

Pharmacologic thromboprophylaxis

Pharmacological thromboprophylaxis agents include aspirin, adjusted dose vitamin K antagonists, synthetic pentasaccharide factor factor Xa inhibitor, unfractionated heparin (UFH), low molecular weight heparin (LMWH) and direct acting oral anticoagulants[32]. The choice of pharmacological thromboprophylaxis agent depends on several factors, including the patient's underlying medical conditions, the severity of their condition, and their risk of bleeding. Aspirin is an inexpensive, safe and effective VTE thromboprophylaxis following some orthopedic surgeries, but aspirin is not recommended for VTE prophylaxis in surgical patients in the field of urology[33,34].

The main antithrombotic agents currently used for VTE prophylaxis in urological surgeries are unfractionated heparin (UFH) and low molecular weight heparin (LMWH)[7].

Fondaparinux sodium (FPX) is the first agent in a new group of anticoagulant compounds, which specifically inhibits factor Xa without directly affecting thrombin[35,36]. There are some studies directly evaluated (FPX) for prophylaxis of VTE after surgery other than urology.[37,38]. To the best of our knowledge, there are limited studies that evaluated the safety of postoperative FPX in urological surgeries. Hata and colleagues [39] evaluated the safety of postoperative FPX in comparison with LMWH in patients undergoing uro-oncological surgery. They found that FPX is non-inferior to low molecular weight heparin with respect to risk of bleeding. They recommended prophylactic use of PFX as an alternative to LMWH for high- to highest-risk patients after surgery for urological malignancy. Based on this limitation of evidence, urology guidelines have not FPX as a recommended drug for VTE prophylaxis. Table 3 presented alternative regimens for prophylaxis of VTE[40,41]

Procedure-specific thromboprophylaxis in urology

Due to low rates of VTE in urology patients, studies often suffered from lack of power. Therefore, studies cannot make definitive conclusions. Some international and national clinical guidelines provide some recommendations for the prevention of DVT in urological surgeries, but they often lack high-level evidence and are primarily based on expert panel recommendations. In our previous study, we used the AGREE II instrument to assess VTE clinical guidelines. We included six clinical guidelines in our study, in fact, the Canadian Urological Association Guideline is an adaptation of the EAU guideline. Between remained 5 guidelines, our study indicated that NICE, CHEST, and EAU clinical guidelines received higher overall assessment scores and were recommended for use in practice. Although the EAU guideline ranked third in terms of overall assessment score, but this guideline is urology procedure-specific. Therefore, we felt EAU guidelines would be appropriate to use by urologists[42].

In this part of our review, we tried to summarize the best evidence of previous studies and guidelines in patients who underwent urological surgeries (**Table 4**). We classified the risk of VTE for the urological procedures based on Tikkinen study (**Table 5**)[2].

Uro-oncological procedures

Radical cystectomy

With a one-month post-operative mortality rate of about 5.2 %, radical cystectomy is one of the most formidable urological procedures. Venous thromboembolism (VTE) is the bulk of these mortalities, with a post-operative rate of 4.2 to 24 %. However, the rate of VTE after robot-assisted radical cystectomy was reported to be about 2.6 % to 5%[43-46]. Neoadjuvant chemotherapy, overweighting, previous history of thromboembolic events, chronic obstructive pulmonary disease (COPD), more extended hospital stays, and lymphadenectomy

Table 4. Summarized best evidence for VTE prophylaxis in patients who underwent urological surgeries

Surgery type	Pharmacological			Mechanical		
Oncological procedures:						
Radical cystectomy						
Robotic or Laparoscopic Radical prostatectomy						
- Without PLND						
- Standard PLND						
- Extended PLND						
Open radical prostatectomy with or without PLND						
Laparoscopic partial and radical nephrectomy						
Open partial and radical nephrectomy						
Radical nephrectomy with thrombectomy or nephroureterectomy						
RPLND (Retroperitoneal lymph node dissection)						
Penectomy with inguinal lymph node dissection						

Surgery type	Pharmacological			Mechanical		
Non oncological procedures:						
- Ambulatory surgery						
- Ureteroscopic surgery						
- Open or laparoscopic Donor nephrectomy						
- Recipient nephrectomy						
- TURP						
- Prolapse						
- Reconstructive pelvic surgery						
- PCNL						
- Open simple prostatectomy						

Low risk:	Patients without any risk factor	**×1**
Medium risk:	**Any one of the following:** Age ≥ 75 BMI ≥ 35 Having a first-degree relative with a history of VTE	**×2**
High risk:	Personal history of VTE Patients with 2 or more risk factors	**×4**

Red: High risk. Yellow: medium Risk. Blue: Low risk (based on Table 5)
PLND: Pelvic Lymph node dissection
TURP: Transurethral resection of the prostate
PCNL: Percutaneous Nephrolithotomy

are associated factors with increased risk of post-cystectomy VTE[43,47]. Furthermore, patients who experience VTE after radical cystectomy develop a higher rate of post-operative complications, except VTE[45]. According to the VTE frequency after radical cystectomy, embolism prevention should be performed more strictly in patients who underwent cystectomy. Also, the results of recent studies are in line with prolonged thromboprophylaxis. Previous studies showed that patients who were prescribed LMWH (40 mg Daily) for 28 days after surgery, 5.3 to 7 %, have less VTE experience compared to those who do not receive prolonged prophylaxis. 21-day Apixaban (2.5 mg BD) is another option for post-cystectomy thromboprophylaxis, which doesn't have a significant difference compared to enoxaparin (48). According to the latest European Association of Urology (EAU) guideline, for over 45-year-old patients with a Caprini score ≥ 5, the perioperative subcutaneous heparin (SCH) and mechanical prophylaxis followed by 28 days of LMWH after discharge is the optimal thromboprophylaxis protocol[49,50].

Radical prostatectomy

The rate of VTE after open radical prostatectomy ranges from 0.9% to 15.7%; however, performing radical prostatectomy by a robot-assisted approach can reduce the risk of VTE to 0.2%[43,51,52]. A combination of 28-day enoxaparin and intermittent pneumatic compression of the thigh has been shown to be safe and effective, while mechanical prophylaxis tolerance is not feasible for all patients[53]. In addition, a 15-day post-discharge Dabigatran (220 mg daily) was reported as a safe option in patients who underwent laparoscopic prostatectomy [54]. In another study, authors concluded that many patients who underwent radical prostatectomy will benefit from extended post-operative thromboprophylaxis[55]. Nevertheless, due to the absence of a significant difference and increased risk of bleeding, other studies suggest only mechanical prophylaxis for patients who underwent radical retropubic prostatectomy[56,57].

Radical and partial Nephrectomy

About 2.2% of patients who underwent open nephrectomy develop VTE after surgery, although laparoscopic nephrectomy patients have a low rate of VTE compared to other cancerous urological surgeries. However, post-nephrectomy patients develop VTE with a shorter time interval (median 7-day interval)[58]. For patients who underwent radical nephrectomy, pharmacological thromboprophylaxis is considerable; however, in partial nephrectomy patients, pharmacological thromboprophylaxis should be avoided due to the increased bleeding risk[56]. Nevertheless, EAU recommends both pharmacological and mechanical thromboprophylaxis for patients who underwent open radical or partial nephrectomy. In the case of laparoscopic partial and radical nephrectomy, the EAU guideline suggests pharmacological thromboprophylaxis only for high-risk patients. Also, in patients who require thrombectomy or urethrectomy, pharmacological thromboprophylaxis is required[41].

Non- oncological procedures

Percutaneous nephrolithotomy (PCNL)

2.8 % of patients who underwent (PCNL) are favorable to developing VTE after surgery. According to the pharmacological thromboprophylaxis's limitations in PCNL, some studies suggested a 12-hour post-operative D-dimer comparison with the pre-operative test for early detection of VTE[59,60].

Open simple prostatectomy and transurethral resection of the prostate (TURP)

The risk of VTE after open prostatectomy was reported from 2.7 % (low-risk patients) to 10.8 % (high-risk patients). In contrast, TURP patients had significantly less risk of VTE (from 0.2% to 0.8 %). Previous studies showed post-operative heparin prophylaxis can significantly reduce VTE rate after open prostatectomy, so pharmacological thromboprophylaxis should be considered in cases of having VTE risk factors[61,62]. However, according to the low VTE risk after TURP, early mobilization is the cornerstone, although mechanical thromboprophylaxis can be a choice[63]. Furthermore, early mobilization is the American Urology Association (AUA) recommendation for transurethral urological surgeries. However, high-risk patients are recommended for mechanical or pharmacological prophylaxis in cases of having advantages[34]. Also, the American Society of Hematology (ASH) recommends against the use of pharmacological prophylaxis in patients who underwent TURP. Also, they suggest in cases of using heparin for TURP and open prostatectomy patients, low molecular weight heparin (LMWH) is superior to unfractionated heparin (UFH)[64].

Nephrectomy

Recipient nephrectomy by the open approach has the highest rate of post-operative VTE among non-cancerous procedures, with a VTE rate of 1.3 % to 5.3 %. Although, donor nephrectomy patients have less risk of VTE (0.4 % to 1.4 %)[9]. For other non-cancerous urological procedures, even high-risk patients for developing VTE are at low or shallow risk of post-operative VTE[9].

Other non-oncological surgeries

Urinary sphincter procedures (VTE risk: 0.3% to 1 %), urethroplasty (risk: 0.3 to 1.1 %), open prolapse surgery (risk: 0.2 to 0.7 %), and reconstructive pelvic surgery (risk: 0.1 to 0.5 %) are the urological surgeries with the lowest risk of post-operation VTE so, pharmacological prophylaxis is not beneficial according to increased risk of bleeding. However, in high-risk patients who underwent pelvic reconstructive surgery, AUA recommends a combination of mechanical and pharmacological thromboprophylaxis[9,34].

Implication for practice

Previous studies have shown that urologist's adherence to thromboprophylaxis guideline is low. In addition, based on our review, studies about thromboprophylaxis in urological surgery are limited and recommendations are derived from existing evidence from other clinical field like orthopedic and general surgeries. Despite this limitation in evidence, we can conclude that in patients who underwent urological surgeries, thromboprophylaxis may reduce the incidence of symptomatic VTE. When urologists schedule patients for urologic surgery, they should determine the patient's risk of VTE and use risk-stratification models. Using thromboprophylaxis should be decided based on patient risk group.

Implication for research

The strength of the available evidence about thromboprophylaxis in urological surgery was not high; there-

fore, clinical trials should be conducted to compare different thromboprophylaxis methods.
future studies should assess the adverse events of pharmacological prophylaxis, the risk-to-benefit ratio of procedure-specific thromboprophylaxis, optimal doses and duration of thromboprophylaxis, quality of life, and cost-analysis.

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