Present practice of thrombosis prophylaxis of radical prostatectomy in a European country – a Hungarian multicenter study

Present practice of thrombosis prophylaxis of radical prostatectomy

Authors
Matyas Benyo¹, Jolan Harsfalvi², Gyorgy Pfiegler³, Zsuzsanna Molnar¹, Mihaly Muranyi¹, Tamás Jozsa¹, Tibor Flasko¹

Authors Affiliations
¹Department of Urology, ²Clinical Research Center, ³Division of Rare Diseases, Medical and Health Science Center, University of Debrecen, Hungary

Suggested key words: thrombotic event, pelvic surgery, pharmacological prophylaxis

Corresponding author
Matyas Benyo, Department of Urology, Medical and Health Science Center, University of Debrecen, Nagyerdei krt. 98, Debrecen, H-4012, Hungary. Tel: +36205140211; fax: +3652255256; e-mail: benyomatyas@gmail.com
Abstract

Venous thromboembolism is a possible fatal complication after pelvic surgery. There is a lack of trials assessing the effect of prophylactic measures in urology. The aim of the study was to evaluate the practice of thrombosis prophylaxis in a Central European country.

A questionnaire of performed radical prostatectomies, way of thrombosis prophylaxis and number of experienced thrombotic events was posted to all Hungarian departments of urology.

With a response rate of 59% 506 radical prostatectomies were reported. Low molecular weight heparin was administered by 100% of the departments. Graduated support stockings were applied by 37% of the patients. Early mobilization was the most common way of mechanic prophylaxis (57%). Thrombotic events were experienced in 1.4%, 0.2% was fatal.

The thrombosis prophylaxis of patients undergoing radical prostatectomy is not unified. Due to the potential mortality of thrombotic complications it should be evaluated and prophylaxis should be recommended in urological guidelines.

Introduction

Venous thromboembolism (VTE) – like deep vein thrombosis (DVT) and pulmonary embolism (PE) – is reported as complication after radical prostatectomy (RP) in 0.8 to 6.2% with the use of various prophylactic methods [1]. These thrombotic complications were the most common cause of death after oncological pelvic surgery according to a large population study with a ratio of 40% [2]. Guidelines were composed in order to prevent thrombotic events after surgical procedures, but these data are not supported by recent comparative studies concerning risk assessment and thrombosis prophylaxis of European centers performing radical prostatectomies [3; 4]. The role and way of the thrombosis prophylaxis is not included in the most important European urological guidelines [5]. A reason of this can be that there is still lack of randomized trials comparing the different pharmacologic interventions and ways of mechanic prophylaxis. The papers reporting the effects of thrombosis prophylaxis in urological surgery were published at least 20 years ago, and these publications don’t provide information on low molecular weight heparin (LMWH) administration [6; 7]. The cost-effectiveness of the different thromboprophylactic methods is also not evaluated regarding urological procedures. Prophylaxis of DVT was proven cost-effective in terms of gained life-years according to a study of gynecologic procedures. External pneumatic compression appeared to be the most cost-effective strategy under the authors’ baseline assumptions against LMWH and unfractionated heparin [8].

The guideline of the American Urological Association recommends the following prophylaxis in urology related to laparoscopic and major open procedures after the determination of the individual thrombotic risk of the patient. Regarding laparoscopic procedures it is recommended to use pneumatic compression boots (PCB) at the time of the surgical intervention. In high-risk and very high risk groups (like laparoscopic and open radical
prostatectomy) patients may require the use of low dose unfractionated heparin (LDUH) or LMWH, but clear recommendation cannot be done regarding the use of pharmacological prophylaxis due to the lack of RCTs in this population. Given the increased risk factors within the patients’ population undergoing open urologic procedures, more aggressive regimens combining the use of PCB with pharmacologic prophylaxis may be considered [3; 9]. The recommendation is the following for open urological procedures: high risk patients require UFH 3x or LMWH 1x daily or PCB if bleeding high, in case of very high risk patients UFH 3x and or LMWH 1x daily and PCB are recommended. In case of increased risk of bleeding mechanical prophylaxis is favored against pharmacologic prophylaxis [3].

Hypercoagulable state after radical prostatectomy was proven by a recent trial which can be a predictor of thrombotic events [10] Since the second peak of thrombotic events is present at the fourth week after radical pelvic surgery it should be considered to use the prophylactic method till the end of the first postoperative month [2].

The aims of the present study were to evaluate (a) the present practice of thrombosis prophylaxis, (b) the role of different prophylactic measures and (c) the ratio of thrombotic events in Hungary in comparison with international practice. Further aim was to advise discussion points to a guideline development work.

Materials and methods

A questionnaire was posted to every department of urology (n=37) having surgical activity in Hungary. In a covering letter the head of the division was requested to report retrospectively the number of the performed radical prostatectomies, the preferred approach, the surgeons’ experience, the length of the postoperative hospital stay, thrombotic risk assessment, the way and the length of different prophylactic methods and the number of experienced thrombotic events of the previous year. The responders were asked either to present their result by filling the questionnaire electronically (http://urology.deoec.hu/info.aspx?sp=10) or post the form back. All data was entered into a computer database and analyzed in an anonymous fashion. During the analysis Microsoft Office Excel statistics were used.

The ethics committee of the Health Scientific Committee of the Ministry of Health approved the study protocol (case number: 24098-0/2010-1018EKU). The Hungarian Association of Urology morally supported the present research.

Results

Response rate, number and approach of radical prostatectomies

A total response rate of 59% (22 departments) was achieved. Eight departments do not perform RP, so they were excluded from our study. The reported number of radical prostatectomies was 506 performed by the departments who filled the form, among these 45.9% (212) was laparoscopic, 0.9% (4) was perineal and 53.2% (245) was retropubic RPs. The high volume centers (radical prostatectomies >50/year) performed 314 radical
prostatectomies (62.1% of all) Table 1. More than 70% of the procedures were performed by a single surgeon in 93% of the institutes. The average length of hospital stay was 10 days ranging from 8 to 16.

Risk assessment and way of thrombosis prophylaxis

Pharmacological thromboprophylaxis with LMWH once daily was preferred by 100% of the departments, but the practice was different Table 2. 80% of the patients are under LMWH administration from the 1st day prior RP to the end of the 4th postoperative week. None of the institutes reported the use of UFH. Graduated support stockings were applied by 37% of the patients. Although pneumatic compression boots were available by 29% of the institutes, they didn’t use them. Early mobilization was the most common way of mechanic prophylaxis. One low volume department reported the method of planned hemodilution during the surgical procedure for the purpose of thrombosis prophylaxis.

Although dose adjustment of LMWH is performed in 93% of the departments and by 91% of the patients, risk assessment was reported only by 11 institutes. In the high-volume centers this is the task of the anesthesiologist, but in the smaller institutes it is a due of the urologist Table 3.

Modification of ongoing anticoagulant treatment

Acetylsalicylic acid drugs were stopped by 97% of the patients (487), and in 58% (287) they were replaced by LMWH. In case of thienopyridins these drugs were switched to LMWH in 82% (416). Kumarins were replaced in 100%. The highest variation was experienced regarding the timing of modification of ongoing anticoagulant treatment of the patients. The responders reported stopping the therapy in the range of 10th to 1st day prior to surgery, and the drugs were re-administered in the range of 1st to 30th postoperative day.

Thrombotic events

According to the self-report of the institutes clinical thrombotic events were experienced in 1.4% of the cases (7 patients): 4 were deep vein thrombosis (DVT) and 3 were pulmonary embolism (PE). Two DVT events occurred during the 4th postoperative week, the others were experienced within two weeks after the surgical procedure. Two thrombotic events were reported by high volume center (>50 RP/year) and two by low - volume department (<20 RP/year). Six patients were under constant LMWH prophylaxis at the time of the thrombotic event. The start of the pharmacological prophylaxis varied from 1 day prior surgery to the first postoperative day. GSS was also applied in the first few postoperative days by 5 patients. Five patients underwent risk assessment and dose adjustment prior surgery, 3 of them were rated as high risk, the others as very high risk patients. One of the 7 events was fatal (0.2% referring to the whole study population) and this event was reported by a low volume department (3 weeks of LMWH + GSS).

Limitations
The data entered by the responders regarding the thrombotic events were self-reported and couldn’t be verified. There were some centers in Hungary, who didn’t answer the questionnaire.

Discussion

The number of the reported radical prostatectomies represents the current practice in Hungary. The most experienced centers in the country prefer the laparoscopic approach. Since more than 70% of the procedures were performed by a single surgeon in 93% of the institutes thus we could draw the conclusion, that especially in the high volume centers the surgeons are experienced enough where most of the patients were treated (62%), which is the most important factor regarding the oncological and functional outcome independent from the preferred approach [11; 12]. Experienced centers can even perform RP in selected locally advanced cases with satisfactory results. [13]. Proper skill of the surgeon can also decrease blood loss during RP so the departments can better focus on thrombosis prophylaxis.

The most common method of prevention is pharmacological prophylaxis in the studied Hungarian hospitals, although the timing of LMWH administration is not unified. These results were similar to the practice of UK centers as reported by Galvin [4]. In case of increased risk of bleeding the pharmacological prophylaxis should be replaced by the PCB, what wasn’t characteristic to the Hungarian departments. By almost 20% of the patients the LMWH administration was stopped before the end of the second week. According to different studies the risk of thrombotic events are present till at least the end of the first postoperative month [2; 10]. The role of different ways of mechanic prophylaxis was minor except the early mobilization. The PCBs are available in almost 30% of the departments, but they do not use them. The reason of this is yet to be evaluated.

The urologist determines the way and length of the thrombosis prophylaxis in 43% of the departments. Therefore it’s essential for the urological community to know the different methods, the presence of risk assessment and dose adjustment.

The majority of the departments had stopped any other anticoagulant therapy or prophylaxis before surgery, and many of them replaced it with LMWH. The timing was really various as the results shows. The acetylsalicylic acid is for prevention and not for anticoagulant therapy, so it is not absolutely necessary to replace [14]. Thienopyridins can lead to excessive bleeding during surgical procedures so it is recommended to replace it with LMWH 8 days before operation (lifetime of the thrombocytas is that long), and to switch back only when risk of bleeding is over [15]. Perioperative antiplatelet drugs may not increase the risk of on bleeding complications in urological surgery according to a recent meta-analysis, but still more high-quality trials with larger samples and longer follow-ups are required. [16].

The ratio of the reported thrombotic events is similar to the international results [1]. The fact that all 7 patients were administered LMWH and 6 of them were still protected by the drug raises the question that is pharmacological prophylaxis alone or in combination with early mobilization and GSS appropriate for preventing venous thromboembolism? Should
urologists use PCB in every case? These questions will remain unanswered till more papers will be published regarding this topic. But as urologists it is essential to know the different prophylactic methods, and to evaluate the effectiveness of the known ones. It would be beneficial if the European Association of Urology (EAU) Guidelines – which is a bible for all European urologists – would include recommendation of thrombosis prophylaxis in urology like it is presented by the American Urological Association [5]. An all European study – or at least presented by each country – of the present practice of thrombosis prophylaxis would reveal the effectiveness of the different ways of prophylaxis.

**Conclusion**

The thrombosis prophylaxis of patients undergoing radical prostatectomy is not unified. Due to the potential mortality of thrombotic complications as urologists it is essential to know the different prophylactic methods, and to evaluate the effectiveness of the known ones. It would be beneficial that urological guidelines would include a chapter of thromboprophylaxis as well.

**Acknowledgements**

The author would like to thank the efforts of the Hungarian urological departments of the following institutes who answered the questionnaire:

- Istvan Tisza Hospital (Berettyoujfalu), Semmelweis University (Budapest), Saint Stephan Hospital (Budapest), Bajcsy-Zsilinszky Hospital (Budapest), Saint John Hospital (Budapest), Uzsoki street Hospital (Budapest), University of Debrecen (Debrecen), Saint Pantaleon Hospital (Dunaujvaros), Mor Kaposi Hospital (Kaposvar), Hospital of Bacs-Kiskun County (Kecskemet), Semmelweis Halasi Hospital (Kiskunhalas), Hospital of Borsod-Abauj-Zemplen County (Miskolc), Ignac Semmelweis Hospital (Miskolc), University of Pecs (Pecs), Saint Lazar Hospital (Salgotarjan), University of Szeged (Szeged), Hospital of Tolna County (Szekszard), Istvan Bugyi Hospital (Szentes), Markusovszky Hospital of Vas County (Szolnok), Odon Javorszki Hospital (Vas), Ferene Csonoky Hospital (Veszprem), Hospital of Zala County (Zalaegerszeg).

The technical work of Mr. Pal Orosz is highly appreciated.

**References**


### Table 1: Centers experience according to the performed RPs

<table>
<thead>
<tr>
<th>Number of RPs/year</th>
<th>Number of departments</th>
<th>Number of patients</th>
<th>Number of retropubic RPs</th>
<th>Number of perineal RPs</th>
<th>Number of laparoscopic RPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>6</td>
<td>81</td>
<td>77</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>20-50</td>
<td>4</td>
<td>111</td>
<td>104</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>&gt;50</td>
<td>4</td>
<td>314</td>
<td>109</td>
<td>0</td>
<td>205</td>
</tr>
</tbody>
</table>
Table 2: Administration of the different prophylactic methods

(GSS: graduated support stockings, PCB: pneumatic compression boots)

*availability of PCB in the institute/hospital but none of them were used

<table>
<thead>
<tr>
<th>Method</th>
<th>Nr. of patients</th>
<th>Percentage (%)</th>
<th>Nr. of centers</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LMWH start</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 day prior RP</td>
<td>409</td>
<td>80,8</td>
<td>10</td>
<td>71,4</td>
</tr>
<tr>
<td>on the day of RP</td>
<td>52</td>
<td>10,3</td>
<td>3</td>
<td>21,4</td>
</tr>
<tr>
<td>1st postop. day</td>
<td>45</td>
<td>8,9</td>
<td>1</td>
<td>7,1</td>
</tr>
<tr>
<td><strong>LMWH stop</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5th postop. day</td>
<td>15</td>
<td>3,0</td>
<td>1</td>
<td>7,1</td>
</tr>
<tr>
<td>10th postop. day</td>
<td>84</td>
<td>16,6</td>
<td>1</td>
<td>7,1</td>
</tr>
<tr>
<td>21st postop. day</td>
<td>12</td>
<td>2,4</td>
<td>1</td>
<td>7,1</td>
</tr>
<tr>
<td>28th postop. day</td>
<td>395</td>
<td>78,1</td>
<td>11</td>
<td>78,6</td>
</tr>
<tr>
<td><strong>GSS</strong></td>
<td>187</td>
<td>37,0</td>
<td>8</td>
<td>57,1</td>
</tr>
<tr>
<td>Mobilisation on 1st postop. day</td>
<td>353</td>
<td>69,8</td>
<td>8</td>
<td>57,1</td>
</tr>
<tr>
<td><strong>Mobilisation on 2nd postop. day</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(PCB*)</td>
<td>196</td>
<td>38,7</td>
<td>4</td>
<td>28,6</td>
</tr>
</tbody>
</table>
Table 3: Ratio of dose adjustment and risk assessment

<table>
<thead>
<tr>
<th>Risk assessment category</th>
<th>Nr. of patients</th>
<th>Percentage (%)</th>
<th>Nr. of centers</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose adjustment</td>
<td>461</td>
<td>91,1</td>
<td>13</td>
<td>92,9</td>
</tr>
<tr>
<td>Risk assessment</td>
<td>381</td>
<td>75,3</td>
<td>11</td>
<td>78,6</td>
</tr>
<tr>
<td>Risk assessment by</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anesthesiologist</td>
<td>279</td>
<td>55,1</td>
<td>4</td>
<td>28,6</td>
</tr>
<tr>
<td>urologist</td>
<td>95</td>
<td>18,8</td>
<td>6</td>
<td>42,9</td>
</tr>
<tr>
<td>together</td>
<td>37</td>
<td>7,3</td>
<td>2</td>
<td>14,3</td>
</tr>
<tr>
<td>not reported</td>
<td>95</td>
<td>18,8</td>
<td>2</td>
<td>14,3</td>
</tr>
</tbody>
</table>