Research Review Speaker Series™

Minimising the risk of venous thromboembolism post-surgery: perspectives of urological and colorectal surgeons

July 2014

Mr Ben Challacombe, MS FRCS (Urol) Consultant Urological Surgeon & Honorary Senior Lecturer Guy's and St Thomas' Hospitals and KCL, London, UK. Associate Editor BJUI.

Mr Alexis M.P. Schizas, BSc MBBS MSc FRCS (Gen Surg) Consultant Colorectal Surgeon, Guy's and St Thomas' NHS Foundation Trust, London, UK.

Mr Challabombe has been involved with and presented research findings on the behalf of Sanofi, Intuitive Surgical, Ethicon/Johnson and Johnson, GlaxoSmithKline, and Takeda.

Sanofi Australia engaged Messers Challacombe and Schizas to attend and present at this meeting, by funding the travel and honoraria for their services. Sanofi also funded the production of this publication. The content or opinions expressed in this publication may not reflect the views of Sanofi. Please consult the full product information before prescribing any of the medications mentioned in this publication. Some medicines or indications may not currently be licensed in New Zealand.

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SANOFI

This publication is a summary of recent presentations by Mr Ben Challacombe (a Consultant Urological Surgeon) and Mr Alexis Schizas (a Consultant Colorectal Surgeon), who both practice at Guy's and St Thomas' Hospitals in London, UK. They were the guest speakers on a tour that hosted presentations in Melbourne and Sydney in March 2014. Their talks addressed the benefits of extended venous thromboembolism (VTE) prophylaxis, assessment and risk stratification, current international guidelines, logistics and cost. Following these talks, an expert panel discussion delineated important aspects of VTE prophylaxis with examples from case studies.

Minimising the risk of VTE post-surgery

Ben Challacombe

In 2010, the National Institute for Health and Clinical Excellence (NICE) published guidance on the care and treatment of all adults (aged ≥18 years) who are at risk of developing VTE (deep vein thrombosis and pulmonary embolism) while in hospital in the NHS in England and Wales.[1] It advised extending pharmacological VTE prophylaxis to 28 days postoperatively for patients who have had major cancer surgery in the abdomen or pelvis.

Currently, Guy's and St Thomas' Hospitals mandate extended prophylaxis is given as follows:

- All abdominal and pelvic cancer cases, whether open, laparoscopic, or robotic
- All major pelvic surgery benign cases
- Risk stratified for abdominal benign surgery (i.e., on a case by case basis)

NHS England has mandated the risk assessment of VTE according to the national risk assessment tool in all adult admissions through the CQUIN (Commissioning for Quality and Innovation) process. VTE assessment performance at Guy's and St Thomas' Hospitals meets CQUIN targets, which were increased to >92% for risk assessment and appropriate thromboprophylaxis in April 2012. Guy's and St Thomas' Hospitals have achieved 97% hospital compliance on electronic patient records. The CQUIN framework provides incentives on the achievement of certain quality goals (VTE risk assessment, dementia diagnosis and falls prevention). Failure to achieve these goals is tied to a loss of £2 million annual incentive payments.

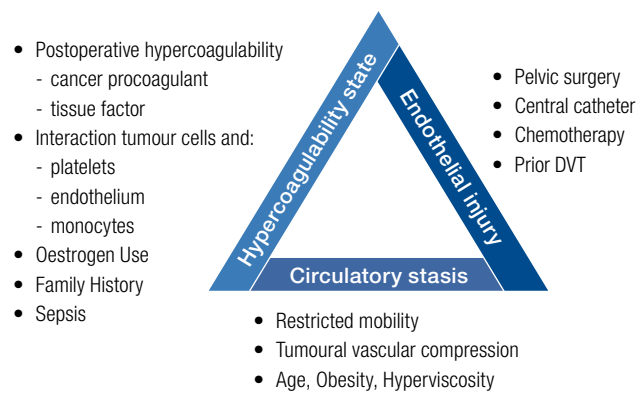
The Importance of VTE in Surgery

VTE is the most common cause of death at 30 days after cancer surgery.[2] It is estimated that in the UK, 25,000 patients die from preventable hospital-acquired VTE each year.[3] The association between thrombosis and malignant disease was first recognised by Trousseau in 1865.[4] He observed that patients presenting with gastrointestinal symptoms and thrombophlebitis could immediately be diagnosed as having cancer as the underlying cause of those GI symptoms. Since that time, numerous studies have confirmed this association.[5-10]

In 1856, German pathologist Rudolf Virchow proposed a pathophysiological basis for the development of VTE (see Fig. 1).[11] Virchow's triad postulates that the interplay of three processes – hypercoagulable state, endothelial injury, and circulatory stasis – are the major factors predisposing to formation of venous thrombosis.

- Factors that contribute to a hypercoagulable state:
  Postoperative hypercoagulability favours a procoagulant state, especially in the presence of cancer procoagulants and activation of the coagulation cascade due to release of tissue factor from damaged tissues, tumours, or cytokine stimulation
  Different interactions are observed between tumour cells and platelets, the endothelium, and monocytes
  Oestrogen use
  Family history
  Sepsis
- Endothelial injury can occur from:
  Pelvic surgery (trauma to blood vessels)
  Central venous catheterisation
  Localised cytotoxic effects from systemic chemotherapy
  Deep vein thrombosis (DVT) prior to surgery
- Circulatory stasis is the predominant causative factor for the development of thrombosis:
  Restricted mobility postoperatively
  Tumoral vascular compression
  Age
  Obesity (body mass index [BMI] >30 kg/m^2)
  Hyperviscosity

Figure 1. **Virchow's triad** [11]



Patients with malignant disease are profoundly hypercoagulable. Significantly higher plasma levels of tissue factor (TF), Factor VIIa, Factor XIIa, thrombin-antithrombin complex (TAT), and prothrombin fragments 1+2 (PF 1+2) have been described in cancer patients compared with healthy volunteers.[12] In particular, TF levels were 67% higher and Factor VIIa levels were 46% higher in the patients with cancer.

An analysis of data from a large administrative database in California describes a high incidence of symptomatic VTE within a 3-month period after different elective or urgent surgical procedures.[13] Regardless of the anatomical site of operation, presence of a malignancy predicted a higher incidence of VTE after hospital discharge compared with no malignancy.

Patients with cancer are at greater risk of pulmonary embolism (PE) post-surgery. In an analysis of data from 28,953 patients admitted during a 10-year period, the rate of postoperative PE (within 30 days of discharge) was remarkably higher in patients with cancer than in those without cancer (~2.3% vs 0.3%; odds ratio [OR] 6.7).[14] Among patients on the medical ward, the risk of developing PE was 7 times higher for cancer patients compared with non-cancer patients (0.73% vs 0.10%; OR 7.3).

Research has confirmed a significantly higher incidence of autopsy-confirmed fatal PE among cancer surgical patients compared with noncancer surgical patients (0.33% vs 0.09%; p=0.0001), despite the use of heparin prophylaxis (either a low-molecular-weight heparin [LMWH] once daily or low-dose unfractionated heparin [UFH] three times daily) for the duration of hospital stay.[15] Perioperative mortality was also significantly higher in cancer patients than in noncancer patients (3.1% vs 0.7%; p=0.0001).

- Cancer surgery appears to have 2 times the risk of postoperative DVT.[14]
- It has 3 times the risk of fatal PE compared with similar noncancer patients.[15]
- Presence of malignancy increased the risk across all specialties.[13]

An analysis of registry data from 2373 patients who had undergone laparotomy for abdominal or pelvic malignancy and were followed for 30 days postoperatively identified that the following factors were associated with a greater risk for the development of VTE in the cancer setting: age ≥60 years (OR 2.6); previous VTE (6.0); anaesthesia lasting >2 hours (4.5); an advanced tumour (2.7); and ≥4 days postoperative bed rest (4.4).[2] Mr Challacombe suggested that it might be prudent to reassess patients if they experience a complication and stay longer in hospital than planned.

Surgical risk factors for VTE include:

- Stage of disease[2]
- Anatomical site of tumour[2]
- Tumour histology (e.g. adenocarcinoma is more likely to lead to clots than a squamous cell carcinoma)[16]
- Obesity[17]
- History of VTE[2]
- Duration of procedure[2]
- Pneumoperitoneum[18]
- Lymph node dissection (particularly in the pelvic area)[19]

Medical risk factors for VTE include:

- Active cancer or cancer treatment[16]
- Age >60 years[2]
- Critical care admission[16]
- Dehydration[20]
- Known thrombophilias[17]
- Obesity (BMI >30 kg/m^2)[17]
- One or more significant medical comorbidities (e.g. heart disease; metabolic, endocrine or respiratory pathologies; acute infectious diseases; inflammatory conditions)[16]
- Personal history or first-degree relative with a history of VTE[2,17]
- Use of hormone replacement therapy[17]
- Use of oestrogen-containing contraceptive therapy[21]
- Varicose veins with phlebitis[17]

Importantly, surgeons often fail to recognise VTE in their patients: Australian research has shown that over 70% of patients were admitted under a different consultant and that fewer than half of these patients had documented evidence that the previous surgeon was aware of the readmission.[22]

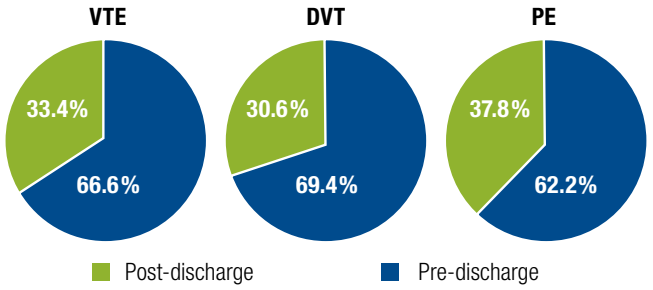
Graduated compression stockings are routinely used in the prevention of postoperative VTE and are effective in decreasing the risk of DVT in hospitalised patients, but the data are uncertain as to their effect on PE.[23]

Rationale for Extended Prophylaxis of VTE

It is usual to stop prophylaxis of most surgical patients at hospital discharge, in the belief that VTE events occur mainly in hospital. However, recent evidence has shown that overall, one-third (33.4%) of VTE events in cancer surgery patients occurred post-discharge (from 17.9% for esophagogastric to 100% for endocrine operations) (see Fig. 2).[24] The study researchers suggest that routine post-discharge VTE prophylaxis should be considered for high-risk patients.

Figure 2. **Post-discharge VTE** [24]

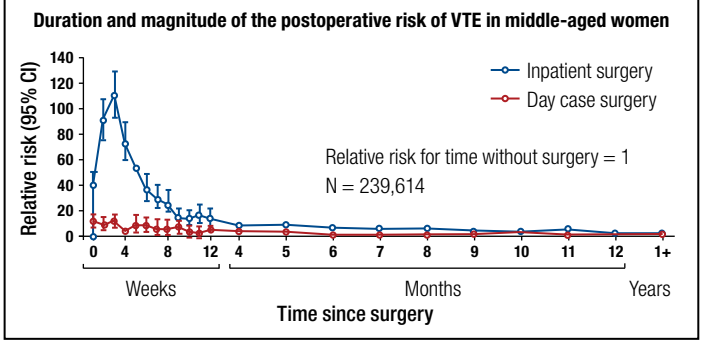
- One-third of VTE events in cancer surgery patients occured post-discharge.
- Routine post-discharge VTE prophylaxis should be considered for high-risk patients.



The time-course of postoperative VTE has been evaluated in different surgical procedures. The RIETE initiative is an ongoing, international, prospective registry of consecutive patients presenting with symptomatic acute VTE confirmed by objective tests.[25] Pharmacological thromboprophylaxis was used in 96% of those undergoing major orthopaedic surgery and in 76% of those undergoing cancer surgery, for a mean of 17 and 13 days, respectively. The use of thromboprophylaxis was suboptimal in many patients: most cases (55%) of symptomatic postoperative VTE occurred beyond the first 15 days following surgery, and 53% of patients receiving prophylaxis had their VTE event diagnosed after withdrawal. These findings are supported by data from a urology study showing that VTE events are much more common between day 14 and day 28 than it is between day 0 and day 14.

VTE risk continues for months after major surgery: a prospective cohort study (Million Women study) examined the duration and magnitude of increased risk of VTE after different types of surgery in middle-aged women (see Fig. 3).[26] Compared with not having surgery, women were 70 times more likely to be admitted with VTE in the first 6 weeks after an inpatient operation and 10 times more likely after a day case operation. The risks were lower but still substantially increased 7–12 weeks after surgery. A similar pattern of risk was seen for PE and DVT.

Figure 3. **VTE risk continues for months after major surgery**[26]



In further analyses of VTE cases occurring within 91 days of surgery from the California Patient Discharge Data Set, approximately 50% occurred post-discharge after general surgery.[13] Urological surgery was associated with even higher post-discharge rates (73% after radical prostatectomy and 54% after radical cystectomy), while the VTE post-discharge rate was 58% after gynaecological surgery (hysterectomy).

- The majority of VTE occur post-discharge in major surgical patients.
- Surgical patients with a malignancy are still at real risk of a VTE post-discharge.

Postoperative VTE has major consequences: surgical cancer patients who experience a VTE have a significant 6-fold increase in mortality in the year following the event (8.0% vs 1.3%; p<0.001).[24]

- 66% of VTE occur in the first month after surgery
- The mean time to VTE is 24 days post-cancer surgery
- The use of thromboprophylaxis is currently suboptimal in patients undergoing cancer surgery

Role of Extended Prophylaxis

The Enoxacan II study compared a 4-week with a 1-week regimen of enoxaparin prophylaxis in 332 patients undergoing elective surgery for abdominal or pelvic cancer.[27] Study participants received enoxaparin (40 mg subcutaneously) daily for 6 to 10 days and were then randomly assigned to receive either enoxaparin or placebo for another 21 days. At follow-up at 30 days and 3 months, prolonged prophylaxis was associated with a 60% risk reduction for VTE (p=0.02 at 30 days and p=0.01 at 3 months). Moreover, there was no increase in haemorrhagic complications with enoxaparin (3.6% with placebo vs 5.1% with enoxaparin; p=0.51).

A similar benefit has been demonstrated by the FAME trial; 4 weeks' administration of the low-molecular-weight heparin (LMWH) dalteparin after major abdominal surgery was associated with a 55% risk reduction for VTE on day 30 (p=0.012) and 77% risk reduction for proximal DVT (p=0.009), compared with 1 week of dalteparin thromboprophylaxis.[28] Bleeding events were not increased with prolonged compared with short-term thromboprophylaxis.

Some have questioned the value of extended VTE prophylaxis in cancer surgical populations undergoing minimally invasive surgical approaches in the management of their cancers. However, there is no clinical evidence showing a lower risk for VTE in such patients. Provision of prophylaxis is recommended for the equivalent open procedure.[29]

Laparoscopic/robotic surgery is associated with decreased risks for VTE, including shorter hospital stay, rapid mobilisation, and reduced blood loss.[30] However, increased risks include a longer procedure, use of the Trendelenburg position, and presence of a pneumoperitoneum.[31]

The optimal duration of thromboprophylaxis with LMWH after surgery has been questioned. A systematic Cochrane review established that the 30-day incidence of overall VTE after major abdominal or pelvic surgery was 14.3% in the control group (patients given thromboprophlaxis in hospital only) versus 6.1% in the patients receiving prolonged thromboprophylaxis with LMWH for at least 1 month (RRR = 57%; Peto OR 0.41; p<0.0005).32

Extended prophylaxis with LMWH (enoxaparin 40 mg) for at least 1 month after major abdominal/pelvic surgery can significantly reduce the risk of VTE at 30 days post-discharge.

- Number needed to treat N=13[32]
- Number needed to harm N=250[32]
- The dramatic reduction in VTE risk is not accompanied by any increased risk of bleeding[32]

Conclusions

- Surgical patients have a higher risk of VTE[32]
- Cancer patients have a higher risk still[32]
- Extended prophylaxis with LMWH for at least one month can significantly reduce the incidence of VTE after major abdominal and pelvic surgery[32]
- There is minimal risk of excessive bleeding[32]

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Minimising the risk of thromboembolism post-surgery

Alexis M.P. Schizas

VTE is a common complication among hospital patients and contributes to longer hospital stays, morbidity and mortality.[1] The UK Government has emphasised that there are too many preventable deaths from VTE in hospitalised patients.[2] Thousands of deaths annually are attributed to VTE and the financial cost is estimated to be in excess of £600 million per annum.[2]

VTE Assessment and Risk Stratification

NICE (UK) has published seven quality standards for VTE prevention:[3]

1. Admission assessment of VTE and bleeding risk (must be performed on 97% of patients)
2. Patients/carers offered verbal & written information regarding VTE prophylaxis
3. Patients provided with anti-embolism stockings
4. Patients are re-assessed within 24 hours of admission
5. Patients assessed to be at risk of VTE are offered VTE prophylaxis
6. Patients/carers are offered verbal & written information
7. Patients are offered extended (post-hospital) VTE prophylaxis

- NICE guidelines advise continued prophylaxis with LMWH and anti-embolism stockings until mobility returns to normal (usually 5–7 days) and for higher-risk patients having major abdominal/pelvic surgery and surgery for cancer, prophylaxis should be extended for 28–35 days.[3]
- All surgical patients, as well as medical patients with significantly reduced mobility, should be considered for risk assessment.[3] Rates of post-discharge VTE are 5–6 times higher among cancer surgery patients than in the general population (ORs by cancer site: 5.1 for colon; 6.00 for rectum; and 5.00 for prostate).
- All patients must be assessed for the risk of bleeding before being offered VTE prophylaxis.[3] This underlines the importance of reassessing patients within 24 hours of admission. Any tick should prompt clinical staff to consider if bleeding risk is sufficient to preclude pharmacological intervention.

Table 1. **Risk of bleeding**

- The risk of bleeding must always be considered before prevention steps are taken.
- Any tick should prompt clinical staff to consider if bleeding risk is sufficient to preclude pharmacological intervention.

Bleeding risk			
Patient-related	**Tick**	**Admission-related**	**Tick**
Active bleeding		Neurosurgery, spinal surgery or eye surgery	
Acquired bleeding disorders (such as acute liver failure)		Other procedure with high bleeding risk	
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR >2)		Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours	
Acute stroke		Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours	
Thrombocytopaenia (platelets <75×10^9/L)			
Uncontrolled systolic hypertension (230/120 mmHg or higher)			
Untreated inherited bleeding disorders (such as haemophilia and von Willebrand's disease)			

- VTE prophylaxis is broadly classified as static (anti-embolism stockings) or dynamic (intermittent pneumatic compression). Anticoagulants (unfractionated heparin [UFH] and LMWH) prevent venous thrombus formation and/or restrict its extension by directly altering the process of blood coagulation. In certain cases, anti-embolism stockings are contraindicated, mostly due to peripheral vascular disease or to incorrect fit.
- Timing of prophylaxis for VTE in surgical patients: when epidural/spinal anaesthesia is used, VTE prophylaxis should be initiated postoperatively. The first LMWH dose should be administered between 6 and 12 hours after surgery. Anticoagulants must be carefully timed to reduce the risk of bleeding at the catheter site.

Table 2. **Timing of doses with epidural**

- Preoperative LMWH
- Timing of first postoperative dose
- Anticoagulants must be carefully timed to reduce the risk of bleeding at the catheter site

	UFH	LMWH	fondaparinux	rivaroxaban	dabigatran
Hours post-dose before catheter removal/insertion	4h	12h	36h	18h	avoid
Hours after removal/ insertion before next dose	1h	4h	8h post-insertion 12h post-removal	6h	avoid

Preoperative prophylaxis should be given 12 hours before surgery.

Hospital-acquired VTE

Any VTE occurring while the patient is in hospital or up to 90 days from admission is classed as a hospital-acquired VTE.[4] The standard hospital contract in England requires NHS Trusts to perform local audits of appropriate thromboprophylaxis and also root cause analysis of all cases of hospital-acquired VTE.[4]

Extended VTE guidelines

In Australia, the National Health and Medical Research Council (NHMRC) has released guidelines on the prevention of VTE similar to those issued by NICE (UK):[5]

- Step 1: assessment of VTE risk factors (patient- and condition-based); surgical patients are acknowledged as being at higher risk
- Step 2: consideration of other risk factors or conditions that may warrant VTE prophylaxis for any hospital admission
- Step 3: assessment of possible contraindications to pharmacological prophylaxis
- Step 4: if pharmacological prophylaxis is contraindicated, consider mechanical prophylaxis
- Step 5: select appropriate thromboprophylaxis

- The NHMRC guidelines make recommendations on the use of LMWH prophylaxis for admitted hospital patients in general surgery, urological surgery, gynaecological surgery and abdominal surgery[5]
- NHMRC recommendations for cancer patients (surgical and non-surgical) include this advice:

  Consider using extended thromboprophylaxis with LMWH for up to 28 days after major abdominal or pelvic surgery for cancer, especially in patients who are obese, slow to mobilise or have a past history of VTE.

The Australian and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism has issued similar guidelines on VTE prevention.[6] The advice on out-of-hospital and extended prophylaxis notes that many clinical trials were based on hospital stays of 7–10 days. Increasingly, fewer patients stay as long as 10 days and after discharge may spend a considerable amount of time recuperating at home. They may not be truly ambulant and thus may be at increased risk of VTE. The guidelines state that it is important to be cautious with early discharge patients as they may still be at risk and may need continued prophylaxis.

These guidelines describe patient groups where the value of extended prophylaxis should be considered:

- High-risk patients for at least 10 days
- Patients with knee replacement for 10 days or more
- Patients following hip fracture or hip replacement surgery and major abdominal and pelvic surgery for cancer for 28–35 days

The American Society of Clinical Oncology (ASCO) has issued clinical practice guidance on VTE prophylaxis and treatment in patients with cancer:[7]

- Most hospitalised patients with cancer require thromboprophylaxis throughout hospitalisation.
- Thromboprophylaxis is not routinely recommended for outpatients with cancer.
- It may be considered for selected high-risk patients.
- Patients undergoing major cancer surgery should receive prophylaxis, starting before surgery and continuing for at least 7 to 10 days.
- Extending prophylaxis up to 4 weeks should be considered in those with high-risk features.
- Use of novel oral anticoagulants is not currently recommended for patients with malignancy and VTE.

Where ASCO differs slightly from the above-mentioned guidelines relates to the risk factors that can be used to evaluate risk in oncology inpatients. Cancer histology matters (risk is higher for adenocarcinoma than squamous cell), as does time after initial diagnosis (highest in first 3 months).[7] Among treatment-related markers, surgery lasting >60 minutes is an important risk factor.[7]

The American College of Chest Physicians suggest the same VTE prophylaxis for selected high-risk general surgery patients, including some who have undergone major cancer surgery or have previously had a VTE – the recommendation is to consider continuing thromboprophylaxis with LMWH for up to 28 days after hospital discharge.[8]

The Canadian Agency for Drugs and Technologies in Health (CADTH) has released evidence-based guidelines on VTE prophylaxis for patients in hospital settings:[9]

- Prolonging VTE prophylaxis with tinzaparin, dalteparin, enoxaparin, or bemiparin for up to 4 weeks postoperatively in patients undergoing major abdominal surgery or pelvic surgery for cancer may reduce the incidence of VTE events without increasing the incidence of bleeding complications.
- Evidence is limited and current guidelines only weakly recommend extended thromboprophylaxis for select high-risk patients undergoing major cancer surgery in the abdomen or pelvis.

VTE and Cancer: Burden

- Major contributor to morbidity and mortality[7,10]
- Prognostic risk factor for overall survival – the risk of death is 3-fold higher within the first year of diagnosis[10,11]
- A high clot burden is associated with a greater rate of post-thrombotic syndrome, higher rate of recurrence, higher bleeding rates on anticoagulant therapy, and requirement for longer-term therapy[12]
- Impacts on delivery of cancer therapy: adjuvant chemotherapy may be delayed in patients who develop a DVT or PE post-surgery[12]
- Excess utilisation of health resources: "cost", in addition to use of LMWH[12]

The Importance of being Proactive in VTE Prevention

- Epidemiological data have revealed that VTE is a bad prognostic sign in cancer and has a major impact on quality of life and delivery of anticancer therapy. Proactive strategies prevent index and recurrent VTE events; evidence indicates that such strategies may prolong survival (not just due to prevention of VTE).[12]
- Clinical data have shown that antithrombotic strategies prevent VTE and suppress tumour growth[12]

Disadvantages associated with proactive VTE prophylaxis include excess bleeding rates, requirement for closer monitoring, administration of the drug, and cost.[10,12]

Bleeding Complications: Thromboprophylaxis

- In an analysis of 33 randomised controlled trials involving 33,813 patients undergoing general surgery, minor bleeding complications were more frequent with DVT prophylaxis (LMWH or UFH [low-dose vs high-dose]) than with placebo (2.0–6.9% vs 0.8–2.8%, respectively).[13] Major bleeding complications were infrequent with pharmacological prophylaxis (0.08–0.8%).
- Similarly, an analysis of 59 randomised studies of 54,144 general surgical patients that received LMWH, UFH, or placebo/control for VTE prophylaxis found that LMWH significantly reduced the risk of DVT, PE, and clinical VTE compared with no treatment or placebo.[14] Bleeding episodes were minor in 10.3% of cases and major in 0.3–0.7%.
- In the MEDENOX, PREVENT, ARTEMIS, and PRINCE studies, LMWH prophylaxis was associated with rates of major bleeding of between 0.2% and 1.5%.

The evidence shows that pharmacological thromboprophylaxis is associated with an increased rate of bleeding, albeit a small increase. Clinicians have to balance risks of VTE and bleeding. At Guy's and St Thomas' Hospitals, clinical practice is to administer prophylaxis in colorectal surgery and major abdominal/pelvic cancers unless there is a known contraindication.

Notably, in 2009, a Cochrane systematic review reported that prolonged thromboprophylaxis with LMWH for at least 1 month significantly reduces the risk of VTE compared to thromboprophylaxis during hospital admittance only, without increasing bleeding complications after major abdominal or pelvic surgery.[15]

Logistics of Implementing Extended VTE Prophylaxis

Concerns have been expressed about the logistic difficulties of implementing extended VTE prophylaxis. Guy's and St Thomas' Hospitals have been doing this since 2011, without encountering any significant problems in teaching patients how to self-inject. A small percentage (<10%) of patients cannot self-inject or lack family members to administer the injection. These patients can either be injected by their practice nurse or caregivers.

In 2012, the British Committee for Standards in Haematology removed the requirement to screen for heparin-induced thrombocytopenia in patients discharged home from hospital on LMWH.

Cost of Extended Prophylaxis

In the UK, the cost of extended prophylaxis is low and may well turn out to be cost-negative.[16] Prevention costs of proximal DVT in Sheffield are about £140 per patient or £3500 per proximal DVT prevented. The cost of treating the initial episode is not so clearly defined but appears to exceed this in some cases. Long-term cost benefits are at present incompletely understood.

The cost of extended prophylaxis is lower in Australia, which would translate into a greater benefit:

Cost to deliver (20 doses):

- Government: $AU109 – $AU5.45/day
- Consumer: $AU36.90 – $AU1.84/day
- Safety net: $AU6.00 – $AU0.30/day

American clinicians recently reported that thromboprophylaxis for 21 days after discharge following abdominal surgery is more cost-effective than 7 days of inpatient thromboprophylaxis.[17] The comparison incorporated base case assumptions based on an abdominal oncologic resection without complications in an otherwise healthy individual. The analysis indicated that extended-duration thromboprophylaxis with LMWH for 3 weeks after discharge should be recommended whenever VTE risk is estimated at 0.88% to 2.39%; patient preferences regarding costs and medication administration, including the need for self-administered injection of LMWH, should be considered in these cases. Furthermore, based on the predetermined probabilities, and assuming an annualised cost of $US23,248 for PE, $US21,540 for DVT, $US14,363 for post-thrombotic syndrome, $US706 for generic LMWH, and $US872 for brand-name LMWH, the threshold for the relative cost-effectiveness of extended-duration thromboprophylaxis was VTE probability of 1.65% for brand-name LMWH, and 0.88% for generic LMWH.

Conclusion

- VTE is a major contributor to morbidity and mortality in patients requiring cancer surgery[7]
- Conduct an initial Assessment and Risk Stratification in VTE prophylaxis[3]
- Guidelines encourage the use of extended prophylaxis[5-9]
  - ➢ Patients identified as being at high risk
  - ➢ Extended VTE prophylaxis for at least 28 days after surgery
    - Extended prophylaxis poses no logistical problems (in clinical experience at Guy's and St Thomas' Hospitals)
    - Cost effective if risk assessed[17]

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Panel Discussion and Case Studies

An interdisciplinary expert panel gathered to discuss the treatment and prophylaxis of VTE in a variety of interesting and difficult cases. The panel consisted of Mr Challacombe, Mr Schizas, Dr Greg Gard (Gynaecological Oncologist, Royal North Shore Hospital, Sydney) and Dr Tim Brighton (Haematologist, Prince of Wales Hospital, Sydney).

Mr Challacombe presented 3 urological case studies – laparoscopic radical prostatectomy, open radical nephrectomy, and robotic partial nephrectomy. Each case illustrated various features that are scored on risk assessment when deciding whether or not to provide VTE prophylaxis. Increasingly, Mr Challacombe has become convinced of the importance of lymph node (i.e. high risk of clot with lymphadenectomy) as a complicating factor in this risk assessment. Such features have to be taken into account. His final case described a patient requiring treatment for an acute post-surgical bleed complicated by several risk features (active cancer, age >60 years, obesity, significant medical comorbidities, history of VTE, significantly reduced postoperative mobility, total anaesthetic + surgical time >90 minutes, critical care admission). The priority is to manage the haemostatic issues in the first 48 hours. Therapeutic anticoagulant prophylaxis would be withheld until deemed safe to do so without risk of bleeding.

The first of 2 general surgical case studies presented by Mr Schizas was a 45-year-old Caucasian male with rectal adenocarcinoma given external beam radiation to the rectum over a period of 5 weeks. After developing rectal bleeding the patient underwent a low anterior resection with diverting ileostomy (3 hours of surgery, rectal cancer stage T3N1M0). LMWH was not given either immediately after or within 6–12 hours after surgery. Post-surgical VTE prophylaxis was initiated the day after surgery and pharmacological prophylaxis was continued for the duration of the hospitalisation (8 days). Extended pharmacological VTE prophylaxis was not given after discharge from the hospital. Twenty-five days after surgery, he was diagnosed as having extensive DVT of the left saphenous and popliteal veins.

The second case described an at-risk patient (78-year-old female with a previous medical history of stroke, ischaemic heart disease, hypertension and diabetes, BMI 36, poor mobility, falls risk), with an ascending colon tumour scheduled for a right hemicolectomy (T2N0). Should thromboprophylaxis be given to such a patient, who is also receiving aspirin or clopidogrel? The general consensus was that prophylaxis is still required, as aspirin and clopidogrel do not effectively protect against DVT. Clopidogrel would be stopped preoperatively and recommenced as soon as possible after surgery (after the initial period of haemostasis) in combination with the thromboprophylaxis.

There was general discussion around the rationale of prophylaxis and cost-effectiveness. Despite acknowledging the expense involved in providing prophylaxis to all patients, in the light of certain VTE events (e.g. fatal PE and symptomatic/nonfatal PE) being rare occurrences, it was generally agreed that the prophylaxis rationale is 'give to many to save a few'. The argument was that it is impossible to foretell which patients will develop a thrombus.

The appropriateness of oral anticoagulants in surgical prophylaxis was discussed. Scant clinical data exist as to the efficacy of such treatment in this setting, but it was felt that these agents would be effective.

It was generally agreed that it is wise to tailor prophylactic dosing according to body weight (e.g. the Royal College of Obstetricians & Gynaecologists guideline on LMWH after C-section recommends enoxaparin doses of 60 mg in patients weighing >90 kg and 80 mg for >130 kg).[1] Clinical evidence is currently lacking in support of this practice. However, accumulating data in bariatric surgery indicate lower event rates with more appropriate weight-adjusted prophylaxis.[2]

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