## ORIGINAL ARTICLE

# VENOUS THROMBOEMBOLISM PROPHYLAXIS FOR SURGICAL PATIENTS IN AN ASIAN HOSPITAL

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**Background:** Venous thromboembolism (VTE) is increasingly recognized as a significant postoperative complication in Asian hospitals. Recommendations have been published for VTE prophylaxis. We conducted a prospective survey of the risk profile and measures used for VTE prophylaxis in elective surgical patients in our hospital.

**Methods:** All patients who underwent elective general or orthopaedic surgery over a 4-week period were included. Information collected included demographic data, presence of risk factors, type and duration of surgery, perioperative use of VTE prophylaxis and any diagnosis of deep vein thrombosis or pulmonary embolism during the current admission as well as in any readmissions in the 6 weeks after discharge. The patients were classified based on their age, risk factors and type of surgery into low, moderate, high or highest risk and the prophylactic measures they received compared with published recommendations.

**Results:** Two hundred and twenty-six patients underwent 227 elective surgeries over the 4-week period. There were 7 low, 16 moderate, 45 high and 55 highest risk patients. One hundred and three patients could not be classified. Postoperative prophylactic measures were omitted in 93.8%, 81.8% and 31.5% of patients in moderate, high and highest risk groups, respectively. One patient developed clinical deep vein thrombosis preoperatively and one postoperatively. There were no cases of pulmonary embolism.

**Conclusions:** VTE prophylaxis is underutilized in our survey. Further studies are required to identify the reasons for omission and to develop hospital specific protocols to increase appropriate use of prophylaxis.

**Key words: Asian, deep vein thrombosis, prophylaxis, pulmonary embolism, venous thromboembolism.**

Abbreviations: ACCP, American College of Chest Physicians; DVT, deep vein thrombosis; LMWH, low molecular weight heparin; PE, pulmonary embolism; VTE, venous thromboembolism.

## INTRODUCTION

Venous thromboembolism (VTE), previously thought to be rarer in Asian populations than in Caucasian populations, is increasingly recognized as a significant postoperative complication in Asian hospitals.[1–7] Evidence based recommendations for prophylaxis against VTE based on risk stratification have been proposed by the American College of Chest Physicians (ACCP) since 1986, with the latest consensus statement published in 2001.[8] However, a survey in our surgical intensive care unit and other surveys on adherence to published guidelines and hospital protocols for prevention of VTE have found that practice often deviates from the ideal.[2,9–16] We conducted this prospective survey on patients admitted for elective surgery in our hospital to determine the risk profile of our patients and compare the perioperative prophylactic measures used with the Sixth ACCP consensus conference recommendations with the aim of identifying deviations that may indicate need for improvement of practice.

## METHODS

Our hospital is an 801 bed acute care hospital that provides surgical services including general, orthopaedic, otorhinolaryngeal, urological and ophthalmic surgery.

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With the approval of the hospital ethics committee and consent of the heads of the general and orthopaedic surgical departments, we included all in-patients who underwent elective general or orthopaedic surgery over a 4-week period. Patients undergoing ambulatory surgery were excluded. The patients were identified in the operating room. Verbal consent was obtained from the patient. They were followed up in the ward in the postoperative period until they were discharged. The two investigators, who were not involved in the patients' daily care, collected the postoperative data. Medical staff not involved in data collection were not informed of the purpose of the survey. Information collected on a standardized survey form included demographic data, presence of any risk factors or medical conditions, the type and duration of surgery, the perioperative use of prophylactic measures against VTE, time to first ambulation and discharge and any clinical diagnosis of deep vein thrombosis (DVT) or pulmonary embolism (PE). The hospital's computer database was searched subsequently to identify any readmissions in the 6 weeks following discharge due to DVT or PE.

After completion of data collection, the patients were classified, based on their age, risk factors and type of surgery, into low, moderate, high or highest risk groups according to published guidelines (Table 1).[8] Surgery lasting longer than 30 min was considered as major surgery.[17] Orthopaedic patients who did not suffer from major trauma or who underwent orthopaedic surgery other than hip or knee arthroplasty or hip fracture surgery were considered to have unclassified risk. Prophylactic measures used were then compared with the recommendations. Appropriateness of the measures with respect to the modalities used, time of implementation and duration of therapy (at least 7–10 days or until ambulation) was determined. Nadroparin (Fraxiparine,

SanofiWinthrop, Notre Dame de Bondeville, France), 9500 IU anti-Xa activity per mL, at 0.3 mL once daily was the low molecular weight heparin (LMWH) used. Venous foot pumps and elastic stockings were the mechanical means of prophylaxis available in our hospital. Statistical analysis was performed using SPSS for Windows Release 10.0 (SPSS, Chicago, IL, USA) and confidence interval (CI) analysis software.[18]

## RESULTS

A total of 226 in-patients underwent 227 general surgical and orthopaedic procedures during the survey period (Table 2). The most common risk factors were major trauma (13.3%), immobility beyond 3 days (10.6%), malignancy (8.8%), obesity with body mass index greater than 30 kg/m$^2$ (6.7%), infection (4.9%) and varicose veins (3.1%). Others included stroke with paralysis, cardiac failure, previous DVT, inflammatory bowel disease, central venous lines and use of oestrogen for hormone replacement therapy.

One hundred and three patients underwent orthopaedic surgery other than hip or knee arthroplasty, hip fracture surgery and surgery for major trauma. They were considered to have unclassified risk and were excluded from further analysis of appropriateness of perioperative prophylaxis. Three of these patients had received elastic stockings as a means of prophylaxis.

One patient was started on i.v. heparin infusion to treat arterial thrombosis and one developed DVT preoperatively. They were excluded from further analysis of appropriateness of perioperative prophylaxis.

Most patients did not receive any form of prophylaxis – 93.8% (95% CI 71.7–98.9%), 81.8% (95% CI 68–90.5%) and 31.5% (95% CI 20.7–44.7%) for patients in moderate, high and highest risk groups, respectively (Table 3). After excluding patients who were ambulating within 24 h of surgery, the proportion of patients receiving prophylaxis increased. Of those that remained immobilized longer than 24 h, only two patients (3.0%, 95% CI 0.8–10.2%) received prophylaxis that met the ACCP consensus recommendations. The commonest reason for inappropriateness of prophylaxis was failure to start prophylaxis preoperatively (Fig. 1). Prophylactic measures were inadequate for two or more reasons in 29 patients. One patient in the moderate risk group and five patients in the highest risk groups had epidural catheters placed for postoperative analgesia. None received pharmacological prophylaxis. All patients with hip fractures received elastic stockings within 24 h of admission.

One patient developed distal DVT in the ipsilateral leg following a hip fracture 7 days after admission but before surgery. She had used elastic stockings for prophylaxis. Subcutaneous nadroparin 0.6 mL twice daily was started upon diagnosis. The patient underwent fracture fixation after 1 week of treatment. Subcutaneous nadroparin was continued until hospital discharge 16 days after surgery. Another patient, after knee arthroplasty, developed calf vein thrombosis which resolved without pharmacological therapy. This patient had used elastic stockings and a

**Table 1.** Classification of thromboembolism risk and recommended prevention strategies.†

| Level of risk | Examples | Recommended prevention strategies |
|---|---|---|
| Low | Minor general surgery in patients <40 years with no additional risk factors | Early mobilization |
| Moderate | Minor general surgery in patients with additional risk factors; non-major general surgery in patients aged 40–60 years with no additional risk factors; major general surgery in patients <40 years with no additional risk factors | LDUH q12h, LMWH, ES.‡ or‡ |
| High | Non-major general surgery in patients >60 year or with additional risk factors; major general surgery in patients >40 years or with additional risk factors | LDUH q8 h, LMWH or IPC‡ |
| Highest | Major general surgery in patients >40 years plus prior VTE, cancer, or molecular hypercoagulable state; hip or knee arthroplasty, hip fracture surgery; major trauma§; spinal cord injury | LMWH, oral anticoagulants, IPC/ES‡ + LDUH/LMWH or ADH |

VTE, venous thromboembolism; LDUH, low dose unfractionated heparin; LMWH, low molecular weight heparin; ES, elastic stockings; IPC, intermittent pneumatic compression; ADH, adjusted dose heparin; q8 h, every 8 h; q12 h, every 12 h. †Modified from Sixth ACCP Consensus Conference on Antithrombotic Therapy; ‡to start immediately before surgery and continue until fully ambulatory; §major trauma defined as multisystem trauma, lower extremity or pelvic fractures, major head injury.

**Table 2.** Demographic data and use of prophylactic measures

| Level of risk | Low | Moderate | High | Highest | Unclassified |
|---|---|---|---|---|---|
| Number | 7 | 16 | 45 | 55 | 103 |
| Age (years)† | 24 ± 6 | 37 ± 8 | 56 ± 15 | 62 ± 20 | 35 ± 15 |
| Sex (M/F) | 7/0 | 9/7 | 24/21 | 26/29 | 79/24 |
| ASA physical status (1/2/3/4) | 5/2/0/0 | 7/8/1/0 | 12/20/12/1 | 8/33/14/0 | 60/34/8/1 |
| Number who received central neuraxial blockade | 1 | 4 | 12 | 25 | 10 |
| Time to ambulation (<24 h/24–48 h/ >48 h postoperatively) | 7/0/0 | 13/3/0 | 28/5/12 | 6/7/42 | 68/21/14 |
| Surgery classification (Minor or non-major general surgery/major general surgery/knee arthroplasty/hip fracture surgery/other orthopaedic surgery) | 7/0/0/0/0 | 6/10/0/0/0 | 1/44/0/0/0 | 0/16/9/16/14 | 0/0/0/0/103 |

ASA, American Society of Anesthesiologists. †Mean ± SD.

**Table 3.**   Venous thomboembolism prophylactic measures used for patients

| Level of risk | Low | Moderate | High | Highest |
|---|---|---|---|---|
| Postoperative immobility up to 24 h | | | | |
|   Number | 7 | 13 | 28 | 6 |
| Type of prophylaxis | | | | |
|   None | 7 | 12 | 28 | 6 |
|   ES only | 0 | 1 | 0 | 0 |
| Postoperative immobility beyond 24 h | | | | |
|   Number | 0 | 3 | 16 | 48 |
| Type of prophylaxis | | | | |
|   None | – | 3 | 8 | 11 |
|   ES stockings only | – | 0 | 5 | 14 |
|   LMWH only | – | 0 | 0 | 1 |
|   ES with VFP | – | 0 | 2 | 8 |
|   ES and LMWH | – | 0 | 0 | 5 |
|   ES, VFP and LMWH | – | 0 | 1 | 7 |
|   Other measures | – | 0 | 0 | 2† |
| Appropriateness of therapy | | | | |
|   Yes | – | 0 | 0 | 2 |
|   No | – | 3 | 16 | 46 |

†One patient received aspirin, one patient received VFP, ES and subcutaneous unfractionated heparin. VFP, venous foot pump; ES, elastic stockings; LMWH, low molecular weight heparin.
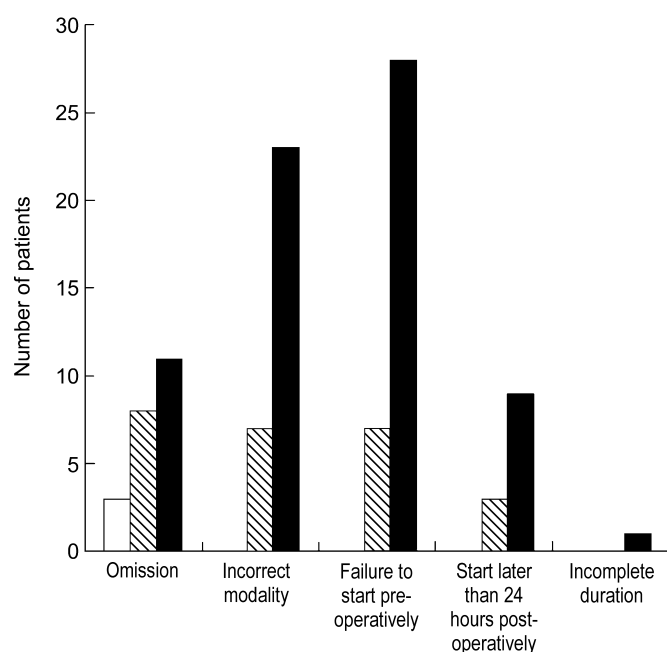


**Fig. 1.**   Reason for inadequate prophylaxis among patients who were immobilized longer than 24 h postoperatively. □, medium risk; ▨, high risk; ■, highest risk.

venous foot pump for prophylaxis. DVT was suspected in both patients clinically and confirmed by Doppler ultrasonography. There were no cases of postoperative diagnosis of PE.

There were four deaths, attributed to acute myocardial infarction (one each from the high and highest risk groups), sepsis from urinary tract infection (1) and pneumonia (1). No autopsy was performed.

Eighteen patients were readmitted in the 6 weeks following discharge. None of them was readmitted with DVT or PE. One patient returned to his home country and was lost to follow up.

## DISCUSSION

In our survey, prophylactic measures used were inadequate when compared with recommendations published by the ACCP. There are several possible reasons for this, including perception of the low incidence of DVT and PE in our local population, failure to recognize at risk patients, unfamiliarity with published recommendations, lack of equipment and concerns regarding complications from anticoagulation.

The incidence of DVT in Asians has been variably reported as lower than or equal to that in Caucasians.[1,19,20] Postulated explanations include a lower incidence of Factor V Leiden mutations among patients of Asian descent compared with those of Caucasian descent.[21–23] Recent literature, however, suggests an increasing incidence of DVT among hospitalized patients in Asian populations, from 2.8 per 10 000 patient admissions in 1990 to 15.8 per 10 000 patient admissions in 2002.[19,20] The incidence of postoperative DVT among unprotected Asian surgical patients range from 0.3% to 76.5% and that of clinical PE range from 0.5–6% depending on the type of surgery and the diagnostic method.[3–7,24,25] There is considerable overlap with incidence of 0.4–80% for DVT and 0.2–10% for PE among Caucasian patients.[8] With the possible lower incidence of VTE among Asians, the cost effectiveness of various prophylactic measures has yet to be determined.

As the recommendations were derived from studies that were largely conducted in Caucasian populations, they may not be directly applicable to Asian patients. However, there are studies that have shown the safety and effectiveness of LMWH in reducing the incidence of VTE in Asian patients undergoing colorectal surgery, total hip and knee arthroplasty and support its use as prophylactic measure.[24–26]

The failure to stratify patients according to the appropriate risk category may contribute to the less frequent use of prophylactic measures.[11] There is also ambiguity in the consensus in the criteria for risk stratification. There are no precise definitions for minor, non-major, major surgery or major trauma. Recommendations for minor, non-major and major surgery were for general surgical patients. Orthopaedic patients who did not undergo hip/knee arthroplasty, hip fracture surgery or suffer from major trauma could not be classified, even though some had sufficient risk factors, such as prolonged immobility caused by lower limb amputation, to likely warrant prophylaxis. There were no firm recommendations for this group of patients because of lack of supportive evidence. Further education of medical personnel and use of a checklist will allow the patient at risk to be correctly identified and given appropriate prophylaxis.

Most patients in moderate and high risk groups were ambulating within 24 h of surgery and did not receive any prophylaxis. The recommendations state that patients in these groups require prophylaxis and that most of these prophylaxis should be started preoperatively, or within 24 h postoperatively and continued until the patients were ambulating. However, it is unclear if patients who mobilized early still required prophylaxis and if so, for what duration.

The mechanical means of prophylaxis recommended were intermittent pneumatic compression and elastic stockings. Venous foot pumps such as those used in our hospital were not recommended because of the lack of evidence of their effectiveness in preventing VTE. As such, patients who could have used intermittent pneumatic compression but were placed on venous foot pumps were considered to have not received appropriate prophylaxis.

Pharmacological means of prophylaxis were used less often than mechanical means and when used, usually started postoperatively. The specific recommendation concerning nadroparin stated that the effective regime was a weight-based dose started 12 h preoperatively. This deviation is possibly due to surgeons' and anaesthetists' concern with haemorrhagic complications.[27] Central neuraxial blockade is commonly used in our patients. The use of spinal anaesthesia may also contribute to a delay in administration or avoidance of anticoagulants, especially in the presence of an haemorrhagic aspirate during needle placement. Unfortunately, we did not collect data to determine if this was a reason for the omission of anticoagulation. While FDA guidelines caution against the use of LMWH in the presence of an epidural catheter, the consensus statement supports the use of LMWH in patients with indwelling epidural catheter, provided precautions are taken.[28]

Delay in the start of LMWH might have been influenced by clinical protocols currently used in our hospital. These protocols consist of a set of preprinted orders for patients undergoing certain surgeries that need to be endorsed each day by the managing team. These orders are not all encompassing nor to the exclusion of other instructions. Current protocols for hip fractures, knee arthroplasty and acute spinal cord injury include LMWH only in the orders for days following surgery. However, the inclusion of elastic stockings in the orders for the day of admission likely accounts for utilization of elastic stockings for all patients with hip fractures.

We did not collect data from the primary physician regarding the reasons for choice of prophylactic measures because we did not want to influence current practices during the period of survey. Subsequent studies should address the reasons for choice of prophylaxis and consider them in the development of hospital specific protocols.

In this survey of patients for elective surgery, the incidence of clinically significant DVT was 0.44% in the preoperative period and 0.44% in the postoperative period. This could either reflect the truly low incidence of clinically significant DVT in this population, or be a sampling error due to the small study population. We did not assess for asymptomatic DVT as determination of incidence of VTE was not a primary aim of this study. As no postmortem was performed, it is possible that out of the four deaths, the deaths attributed to myocardial infarction could have been caused by undetected PE. As we searched only our hospital's computer database for readmission data, we might have missed patients who presented to other hospitals with DVT after initial discharge from our hospital.

In conclusion, most elective surgical in-patients have at least moderate risk of developing VTE. Prophylactic measures against DVT are underutilized in our surveyed population. Further study is required to identify the reasons for this. A larger study screening for DVT will also help to determine if the incidence of VTE is lower in an Asian surgical population. This survey also highlighted difficulties with applying published recommendations to daily practice because of ambiguity of certain recommendations, especially with regards to our local population, and lack of equipment. Education of medical staff to raise awareness and development of an in-house protocol with unambiguous criteria for risk stratification would encourage appropriate use of prophylaxis, and hopefully result in a reduction in the incidence of VTE.

## REFERENCES

1. White R, Zhou H, Romano P. Incidence of idiopathic deep vein thrombosis and secondary thromboembolism among ethnic groups in California. *Ann. Intern. Med.* 1998; **128**: 737–40.
2. Tan SM, Ng KS. Pulmonary embolism in an Asian surgical intensive care unit: a series of 4 cases and a review of the practice of prophylaxis. *Crit. Care Shock* 2001; **4**: 211–16.
3. Kum CK, Sim EKW, Ngoi SS. Deep vein thrombosis complicating colorectal surgery in the Chinese in Singapore. *Ann. Acad. Med. Singapore* 1993; **22**: 895–7.
4. Dhillon KS, Askander A, Doraisamy S. Postoperative deep-vein thrombosis in Asian patients is not a rarity. A prospective study of 88 patients with no prophylaxis. *J. Bone Joint Surg.* 1996; **78-B**: 427–30.
5. Nandi PL, Li WS, Leung R, Chan J, Chan HT. Deep vein thrombosis and pulmonary embolism in the Chinese population. *Hong Kong Med. J.* 1998; **4**: 305–10.
6. Lee HM, Suk KS, Moon SH, Lim DJ, Wang JMJ, Kim NH. Deep vein thrombosis after major spinal surgery. Incidence in an East Asian population. *Spine* 2000; **25**: 1827–30.
7. Lee FY, Chu W, Chan R *et al.* Incidence of deep vein thrombosis after colorectal surgery in a Chinese population. *ANZ J. Surg.* 2001; **71**: 637–40.
8. Geerts WH, Heit JA, Clagett GP *et al.* Prevention of venous thromboembolism. *Chest* 2001; **119**: 132S–75S.
9. Arnold DM, Kahn SR, Shrier I. Missed opportunities for prevention of venous thromboembolism. An evaluation of the use of thromboprophylaxis guidelines. *Chest* 2001; **120**: 1964–71.

10. Lepaux DJ, Charpentier C, Pertek JP *et al.* Assessment of deep vein thrombosis prophylaxis in surgical patients: a study conducted at Nancy University Hospital, France. *Eur. J. Clin. Pharmacol.* 1998; **54**: 671–6.

11. Ahmad HA, Geissler A, Maclellan DG. Deep vein thrombosis prophylaxis: are guidelines being followed? *ANZ J. Surg.* 2002; **72**: 331–4.

12. Gillies TA, Ruckley CV, Nixon SJ. Still missing the boat with fatal pulmonary embolism. *Br. J. Surg.* 1996; **83**: 1394–5.

13. George BD, Nethercliff J, Cook TA, Galland RB, Franklin IJ. Protocol violation in deep vein thrombosis prophylaxis. *Ann. R. Coll. Surg. Engl.* 1998; **80**: 55–7.

14. Bratzler DW, Raskob GE, Murray CK, Bumpus LJ, Piatt DS. Underuse of venous thromboembolism prophylaxis for general surgery patients. *Arch. Intern. Med.* 1998; **158**: 1909–12.

15. Stratton MA, Anderson FA, Bussey HI *et al.* Prevention of venous thromboembolism. Adherence to the 1995 American College of Chest Physicians consensus guidelines for surgical patients. *Arch. Intern. Med.* 2000; **160**: 334–40.

16. Williams HR, MacDonald DA. Audit of thromboembolic prophylaxis in hip and knee surgery. *Ann. R. Coll. Surg. Engl.* 1997; **79**: 55–7.

17. Thromboembolic Risk Factors (THRIFT) Consensus Group. Risk of and prophylaxis for venous thromboembolism in hospital patients. *BMJ.* 1992; **305**: 567–74.

18. Altman DG, Machin D, Bryant TN, Gardner MJ (eds). *Statistics with Confidence: Confidence Intervals and Statistical Guidelines*, 2nd edn. London: BMJ Publishing Groups, 2000.

19. Lee LH, Gu KQ, Heng D. Deep vein thrombosis is not rare in Asia – the Singapore General Hospital experience. *Ann. Acad. Med. Singapore* 2002; **31**: 761–4.

20. Lee LH. Clinical update on deep vein thrombosis in Singapore. *Ann. Acad. Med. Singapore* 2002; **31**: 248–52.

21. Price DT, Ridker PM. Factor V Leiden mutation and the risks for thromboembolic disease: a clinical perspective. *Ann. Intern. Med.* 1997; **127**: 895–903.

22. Ridker PM, Miletich JP, Hennekens CH, Buring JE. Ethnic distribution of Factor V Leiden in 4047 men and women: implications for venous thromboembolism screening. *JAMA* 1997; **277**: 1305–7.

23. Rees DC, Cox M, Clegg JB. World distribution of factor V Leiden. *Lancet* 1995; **346**: 1133–4.

24. Ho YH, Seow-Choen F, Leong A, Eu KW, Nyam D, Teoh MK. Randomized, controlled trial of low molecular weight heparin vs. no deep vein thrombosis prophylaxis for major colon and rectal surgery in Asian patients. *Dis. Colon Rectum* 1999; **42**: 196–203.

25. Fong YK, Ruban P, Lee BPH, Lo NN, Seow KH, Ng SCK. Use of low molecular weight heparin for prevention of deep vein thrombosis in total knee arthroplasty – a study of its efficacy in an Asian population. *Ann. Acad. Med. Singapore* 2000; **29**: 439–41.

26. Yoo MC, Kang CS, Kim YH, Kim SK. A prospective randomized study on the use of nadroparin calcium in the prophylaxis of thromboembolism in Korean patients undergoing elective total hip replacement. *Int. Orthop.* 1997; **21**: 399–402.

27. Levine MN, Raskob G, Landefeld S, Kearon C. Hemorrhagic complications of anticoagulant treatment. *Chest* 2001; **119**: 108S–21S.

28. Lumpkin MM. FDA Public Health Advisory. *Anesthesiology* 1998; **88**: 27A–8A.