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Incidence of Venous Thromboembolism after Primary Total Hip Arthroplasty with Mechanical Prophylaxis in Hong Kong Chinese

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Purpose: The incidence of deep vein thrombosis (DVT) following total hip arthroplasty (THA) without chemoprophylaxis could be as high as 50% in Caucasians. However, according to several subsequent studies, the incidence of venous thromboembolic events (VTE) in Asians was much lower. The routine use of chemoprophylaxis, which could potentially cause increased bleeding, infection, and wound complications, has been questioned in low-incidence populations. The objective of this study is to determine the incidence of VTE after primary THA without chemoprophylaxis in an Asian population using a fast-track rehabilitation protocol and to verify the safety profile for use of 'mechanical prophylaxis alone' in patients with standard risk of VTE.

Materials and Methods: This is a retrospective cohort study of 542 Hong Kong Chinese patients who underwent primary THA without chemoprophylaxis. All patients received intermittent pneumatic compression and graduated compression stockings as mechanical prophylaxis. Multimodal pain management was applied in order to facilitate early mobilisation. Routine duplex ultrasonography was performed between the fourth and seventh postoperative day for detection of proximal DVT.

Results: All patients were Chinese (mean age, 63.0±11.9 years). Six patients developed proximal DVT (incidence rate, 1.1%). None of the patients had symptomatic or fatal pulmonary embolism.

Conclusion: The incidence of VTE after primary THA without chemical prophylaxis can be low in Asian populations when following a fast-track rehabilitation protocol. Mechanical prophylaxis alone can be regarded as a reasonably safe practice in terms of a balanced benefit-to-risk ratio for Asian patients with standard risk of VTE.

Keywords: Total hip arthroplasty, Venous thromboembolism, Combined modality therapy, Hong Kong

INTRODUCTION

Deep vein thrombosis (DVT) following total hip arthroplasty (THA) has been a common complication, with a reported incidence rate of 45%-52% in Caucasians when no chemical prophylaxis was administered[1-4]. Symptomatic pulmonary embolism (PE) was reported in approximately 1% of patients[4,5] and 0.1%-0.3% died from a fatal PE[6-9]. Most international guidelines were based on the Western literature. Medications ranging from aspirin, unfractionated heparin, low-molecular weight heparin (LMWH) to oral anticoagulants have been recommended as routine chemical thromboprophylaxis for THA[10-12].

However, after several reports of significantly lower incidence of DVT when compared to Caucasians, there has been concern regarding the generalisability of these international guidelines to some Asian popula-

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tions[13-22]. Of note, the use of anti-thrombotic agents for THA resulted in wound haematoma, persistent wound drainage, failure of wound healing, risk of infection, gastrointestinal bleeding, blood loss requiring transfusion, and thrombocytopenia, etc.[21-35]. While the risk profile for chemoprophylaxis remains a constant, a smaller number of venous thromboembolic events (VTE) that can be prevented will convert to a lower benefit-to-risk ratio in low-incidence populations[23].

More specifically for Chinese patients, available literature reporting on their incidence of VTE after THA is limited[19,36]. The objective of the current study is to provide contemporary data on the incidence of proximal DVT and PE after primary THA without chemical prophylaxis in an Asian population following a fast-track rehabilitation protocol. The findings of the current study are intended to provide alternative views to surgeons worldwide for consideration in management of Asian patients. The second aim of this study is to confirm the safety profile for use of 'mechanical prophylaxis alone' for patients with standard risk of VTE, as recommended by the Asia-Pacific Consensus Group 2021 for Asian populations[37].

MATERIALS AND METHODS

1. Study Design

This is an original retrospective cohort study using the registry of a total joint replacement center located in Hong Kong. The Clinical Data Analysis and Reporting System (CDARS) and the Clinical Management System (CMS) of the Hospital Authority were used for retrieval of medical records. Records of all patients who underwent a THA procedure from October 2011 to December 2020 at our center in Yan Chai Hospital were reviewed. Revision surgeries, patients who were non-Chinese, and those with high risk of VTE who received chemical prophylaxis were excluded. Records of readmission within 90 days of the operation date were retrieved using the CDARS. The study was approved by the Research Ethics Committee, Kowloon West Cluster, Hospital Authority, Hong Kong (No. KW/EX-22-007 (167-07)), and the written informed consent was waived by the committee due to the retrospective nature of the study.

2. Fast Track Rehabilitation Protocol

Preoperative assessment of patients was performed by our multidisciplinary team, which included physiotherapists, occupational therapists, and medical social workers for patient education and management of social support to facilitate early discharge from the hospital after the operation. We encourage discharge to home, rather than to a rehabilitation facility.

Mechanical prophylaxis was prescribed as follows: postoperatively, an intermittent pneumatic compression (IPC) device (Kendall SCD 700 Sequential Compression System™; Covidien) applied to both lower limbs was prescribed for all patients from day zero to day three after the operation. This device consisted of a piece of garment fitted to the calf and the thigh. The system measured the time required for a patient's veins to refill after being compressed. The frequency of compression varied from 20 to 60 seconds based on the measured venous refill time. Sequential and graduated compression was generated for promotion of unidirectional blood flow, where the inflated pressure was 45 mmHg at the ankle, 40 mmHg at the calf, and 30 mmHg at the thigh. The device was applied for 24 hours a day except during performance of walking exercise.

Early mobilisation and walking exercise were initiated on postoperative day one, under the supervision of our team physiotherapists. Patients were instructed to wear a pair of graduated compression stockings (T.E.D.™ Anti-Embolism Stockings; Covidien) continuously for six weeks after the operation.

Multimodal perioperative pain management was applied to assist early mobilisation. An intraoperative local periarticular injection (PAI) containing a cocktail of ketorolac (30 mg), levobupivacaine (100 mg), and adrenaline (0.5 mg), made up to 100 mL of normal saline, was administered. Postoperative analgesia included oral non-steroidal anti-inflammatory drugs (etoricoxib 90 mg once daily for five days), paracetamol (1,000 mg four times daily), and tramadol (50 mg four times daily). Oral pregabalin (50 mg every eight hours) or oxycodone (5 mg four times daily) was prescribed only for inadequate pain control. Pantoprazole (40 mg once daily) was prescribed for gastrointestinal prophylaxis.

Patients were discharged after the goals of walking independently with support for 50 m and transferring independently in and out of bed and toilet had been achieved. Upon discharge, they were instructed to walk every day, while gradually increasing the distance as tolerated. All patients were provided access to an outpatient physiotherapy service, either in our hospital or any hospital under the governance of the Hospital Au-

thority that was in closer proximity to their living place.

3. Perioperative Antithrombotic Management Protocol

Referencing the 'VTE risk assessment tool' from the National Institute for Health and Care Excellence (NICE) guideline[12], patients with high risk of VTE were defined as those with previous history of VTE, active malignancy, and those on oral contraceptive pills or hormonal replacement therapy. LMWH (enoxaparin) was administered to these patients on the next postoperative day, and was continued as chemical prophylaxis for seven days. No additional chemical prophylaxis was administered to patients with standard risk of VTE.

Patients with concomitant use of antithrombotics (CUA) for other medical causes were instructed to continue taking the drugs or stop taking them preoperatively according to the protocol. The drugs were resumed as soon as postoperative day one if no signs of major bleeding or discharge were observed. These cases were not excluded as they were continuing their usual medications with no additional pharmacological intervention purely for VTE prophylaxis.

4. Definition of VTE

In general, VTE include occurrence of thromboembolism in any segment of the systemic and pulmonary venous systems. The VTE of interest in the current study included proximal DVT of the lower limbs and pulmonary arterial thromboembolism.

5. VTE Screening Protocol

Duplex ultrasonography of both lower limbs was performed routinely for all patients between the fourth and seventh day after the operation. Ultrasonography was performed by a radiologist using an ultrasound machine (LOGIQ E9™; GE HealthCare). Proximal DVT was diagnosed in cases where a vein was not fully compressible, any hyperechoic signal was observed, or when venous flow was absent or diminished either in the popliteal vein, superficial femoral vein, common femoral vein, or more proximal veins. Distal DVT was not recorded in the current study.

Postoperative assessment of patients for the signs and symptoms of DVT, including fever, thigh or calf pain, thigh and calf circumference, and prominence of superficial veins was performed daily by our team surgeon and a specialist nurse. Patients who showed clinical signs of DVT, regardless of the number of postoperative days, underwent an urgent duplex ultrasound examination. Monitoring of patients for signs and symptoms of PE, including shortness of breath, palpitation, desaturation, tachycardia, and hypotension, was also performed. An urgent contrast computed tomography scan of the pulmonary artery (CTPA) was performed in cases of clinical suspicion. PE was diagnosed in cases where filling defect(s) were observed within the pulmonary arterial vasculature, or if there was one or more observable intraluminal thrombus.

Treatment with warfarin was administered for three months to patients who developed DVT or PE.

6. Outcome Measurements

The primary outcome was the incidence of proximal DVT, while the secondary outcomes were the incidence of symptomatic PE and fatal PE.

7. Sample Size Calculation

Assuming an incidence rate of DVT of 18.1% after primary THA without chemical prophylaxis[36] in a population of 7,413,070 in Hong Kong[38], to attain a 95% confidence level and a margin of error within 5%, the required sample size is at least 228 patients[39].

8. Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software (ver. 26.0; IBM Corp.). Independent *t*-test and chi-square test were used as parametric tests, while Mann–Whitney U test and Fischer's exact test were used as non-parametric tests. Logistic regression modeling was performed for adjustment of confounding variables. A $P<0.05$ indicated a statistically significant difference. Continuous variables were expressed as mean±standard deviation, corrected to one decimal place, unless otherwise specified.

RESULTS

1. Patient Demographics and Clinical Details

The records of 557 patients were retrieved. Ten cases involving revision surgeries were excluded, and four non-Chinese patients were excluded, and one case was excluded because chemoprophylaxis had been administered for history of DVT. A total of 542 patients, 550 hips, were included in the study.

All patients were Chinese, and their mean age was

63.0±11.9 years, with a mean body mass index (BMI) of 25.2±4.2 kg/m^2. The ratio of males to females was 41:59.

Most of the patients underwent surgery for treatment of osteoarthritis (51.1%), followed by avascular necrosis (39.7%) and dysplastic hip (7.4%). Cementless THA was performed in 94.8% of cases, while the remaining cases were hybrid type (cementless cup and cemented stem). The mean length of operation was 110 minutes and more than 90% were performed under general anaesthesia. Patients were discharged from the hospital, on average, within 8.5 days.

Mechanical prophylaxis (IPC device and graduated compression stockings) was prescribed postoperatively for all patients. Among the patients, 17.5% had CUA for other medical reasons, most of which were aspirin (14.9%). None of the patients received additional chemical prophylaxis for VTE (Table 1).

Table 1. Patient's Demographic and Clinical Details (n=542)

Variable	Value
Mean age (yr)	63.0±11.9
Sex	
Male	222 (41.0)
Female	320 (59.0)
Ethnicity	
Chinese	542 (100)
Mean BMI (kg/m^2)	25.2±4.2
Concomitant use of antithrombotic agents	95 (17.5)
Aspirin	81 (14.9)
DOAC*	7 (1.3)
Plavix	5 (0.9)
Warfarin	2 (0.4)
Laterality of operation	
Left	251 (46.3)
Right	283 (52.2)
Bilateral	8 (1.5)
Type of operation	
Cementless	514 (94.8)
Hybrid (cementless cup, cemented stem)	28 (5.2)
Operative diagnosis	
Osteoarthritis	277 (51.1)
Avascular necrosis	215 (39.7)
Dysplastic hip	40 (7.4)
Others†	10 (1.8)
Mode of anaesthesia	
General	489 (90.2)
Spinal	42 (7.7)
Combined spinal-epidural	11 (2.0)
Mean operation time (min)	110.0±36.9
Length of inpatient stay (day)	8.5±6.9
Use of intermittent pneumatic compression devices	542 (100)
Use of graduated compression stockings	542 (100)

Values are presented as mean±standard deviation or number (%).
BMI: body mass index, DOAC: direct oral anticoagulant.
*DOAC included dabigatran, apixaban and rivaroxaban.
†Other diagnoses included ankylosing spondylitis, rheumatoid arthritis, fused hip, and fracture.

2. Outcomes

1) Primary outcome

Out of the 542 patients, six patients developed DVT, converting to an incidence rate of 1.1%. All except one of these patients were diagnosed during the inpatient stay for the index operation. Only one patient was diagnosed upon readmission on postoperative day 19 (Table 2). Details of the patients with DVT are shown in Table 3.

2) Secondary outcomes

No case of symptomatic PE or fatal PE was reported (Table 2).

3) 90-day mortality

Two cases of 90-day mortality (incidence rate, 0.4%) were reported: one patient died of myocardial infarction on postoperative day 17, while the other patient died of a perforated peptic ulcer at two months.

3. Subgroup Analysis

1) Comparison between VTE and No VTE groups

There was no demographic difference. No risk factor for development of VTE was identified. A longer length of inpatient stay was observed in the VTE group after adjustment (9.5 days vs. 7 days, P=0.013) (Table 4).

2) Comparison between CUA and Non-CUA groups

Patients in the CUA group were older (66.0 years vs.

Table 2. Primary and Secondary Outcomes (n=542)

Outcome	Value
Incidence of proximal DVT	6 (1.1)
Diagnosed during inpatient stay	5 (0.9)
Diagnosed upon readmission within 90 days	1 (0.2)
Incidence of symptomatic PE	0 (0)
Incidence of fatal PE	0 (0)

Values are presented as number (%).
DVT: deep vein thrombosis, PE: pulmonary embolism.

Table 3. Demographic and Clinical Details of Patients with VTE

Variable	Patient No. 1	Patient No. 2	Patient No. 3	Patient No. 4	Patient No. 5	Patient No. 6
Age (yr)	68	80	63	68	31	58
Sex	Male	Female	Male	Male	Male	Male
Ethnicity	Chinese	Chinese	Chinese	Chinese	Chinese	Chinese
BMI (kg/m^2)	26.4	24.8	28.8	21.0	25.9	23.5
Co-morbidities	Hypertension	Hypertension, hyperlipidaemia, impaired fasting glucose, ischaemic heart disease	Hypertension, hyperlipidaemia	Hypertension, renal impairment, history of NSTEMI	SLE, lupus nephritis	Good past health
Concomitant use of antithrombotics	Nil	Aspirin	Nil	Aspirin	Nil	Nil
Operative diagnosis	Dysplastic hip	Avascular necrosis	Osteoarthritis	Avascular necrosis	Avascular necrosis	Osteoarthritis
Laterality of operation	Right	Right	Left	Left	Left	Right
Mode of anaesthesia	GA	GA	GA	GA	GA	GA
Operation time (min)	125	93	84	125	180	119
Day of postoperative duplex ultrasound scan	5	5	8	3	5	3
Duplex ultrasonography findings	Thrombus detected at the upper level of right SFV	A 1.4 cm long eccentric echogenic structure adhering to mid-right SFV posterior wall, making it incompressible	Mid- and lower thirds of left SFV appear small in caliber with hyper-echoic content inside	Thrombus detected at upper right SFV	No DVT	Proximal segment of right SFV cannot be completely compressed. No Doppler flow signals are obtained.
Length of inpatient stay (day)	15	5	14	50	6	4
Outcome	Uneventful after three months of warfarin treatment	Uneventful after three months of warfarin treatment	Uneventful after three months of warfarin treatment	Developed NSTEMI with APO on postoperative day 5. Contrast CT of pulmonary artery did not show PE. Treated with warfarin together with aspirin (usual medication). Developed right thalamic haemorrhage at three months post-treatment. Succumbed from nosocomial pneumonia at six months.	Readmission due to right lower limb swelling. An extensive thrombosis was detected from proximal right SFV to popliteal vein by duplex ultrasound on postoperative day 19. Treated as antiphospholipid syndrome with long-term warfarin.	Uneventful after three months of warfarin treatment

VTE: venous thromboembolic event, BMI: body mass index, NSTEMI: non-ST elevation myocardial infarction, SLE: systemic lupus erythematosus, GA: general anaesthesia, SFV: superficial femoral vein, DVT: deep vein thrombosis, APO: acute pulmonary oedema, CT: computed tomography, PE: pulmonary embolism.

Table 4. Comparison of Key Variables between VTE and No VTE Groups

Variable	No VTE group	VTE group	Crude *P*-value†	Adjusted *P*-value‡
No. of patients	536 (98.9)	6 (1.1)	-	-
Mean age (yr)	63.1±11.8	61.3±16.6	0.984	0.877
No. of males	217 (40.5)	5 (83.3)	0.045*	0.072
Mean BMI (kg/m^2)	25.2±4.2	25.1±2.6	0.829	0.842
Concomitant use of antithrombotics	93 (17.4)	2 (33.3)	0.284	0.360
Diagnosis of avascular necrosis	212 (39.6)	3 (50.0)	0.686	0.887
Use of spinal anaesthesia	42 (7.8)	0 (0)	0.417	0.998
Mean operation time (min)	109.7±37.0	121±33.7	0.297	0.533
Length of inpatient stay (day)	7 (2-77)	9.5 (4-50)	0.488	0.013*

Values are presented as number (%), mean±standard deviation, or median (range).
VTE: venous thromboembolic event, BMI: body mass index.
*P<0.05.
†Hypothesis was tested using non-parametric test for the small sample size in the VTE group.
‡Variables were adjusted for age, sex, and BMI.

Table 5. Comparison of Key Variables between Concomitant Use of Antithrombotics Group (CUA) and Non-CUA Group

Variable	Non-CUA	CUA	Crude *P*-value	Adjusted *P*-value†
No. of patients	447 (82.5)	95 (17.5)	-	-
Mean age (yr)	62.4±11.9	66.0±11.3	0.821	0.030
No. of males	181 (40.5)	41 (43.2)	0.631	0.225
Mean BMI (kg/m^2)	25.1±4.2	25.6±4.1	0.691	0.457
Mean operation time (min)	110.5±38.1	106.4±30.9	0.222	0.410
Length of inpatient stay (day)	8.1±6.3	10.2±9.1	0.042*	0.041*
Incidence of VTE	4 (0.9)	2 (2.1)	0.284‡	0.368

Values are presented as number (%) or mean±standard deviation.
BMI: body mass index, VTE: venous thromboembolic event.
*P<0.05.
†Variables were adjusted for age, sex, and BMI.
‡Hypothesis was tested using Fischer's exact test in a 2×2 table.

62.4 years, P=0.030) and their average inpatient stay was two days longer than that of the non-CUA group (10.2 days vs. 8.1 days, P=0.041), after adjustment for age, sex, and BMI.

The incidence rate of proximal DVT in the CUA and Non-CUA groups was 2.1% and 0.9%, respectively (P=0.368) (Table 5).

DISCUSSION

Several early studies reported on the high incidence rate of DVT, up to 50%, following THA without chemical prophylaxis in Caucasians[1-4]. Symptomatic PE has been reported in approximately 1% of patients[4,5] and it could become fatal in 0.1%-0.3%[6-9]. The use of routine chemical prophylaxis for VTE in patients undergoing THA is recommended by most international guidelines, including those established by the American Academy of Orthopaedic Surgeons (AAOS), the American College of Chest Physicians (ACCP), and the NICE[10-12]. Despite their high standards, development of these guidelines was based on the epidemiology of Caucasian populations, thus there have been questions regarding their generalisability to Asian populations. Kim and Suh[13] were among the first authors to report a lower incidence (10%) of DVT following THA without chemical prophylaxis in their Korean patients. Several subsequent studies based on the Thai, Indian, Japanese, and Singaporean populations reported similarly low incidence rates of 3%-9%[14,16,17,19].

The lower incidence of VTE in Asians compared with Caucasians is believed to be multifactorial. From a genetic point of view, mutations in the factor V Leiden gene and the prothrombin promoter G20210A gene cause predisposition to higher thromboembolic risks up to 80 times[40-42]. Despite their presence in approximately

5% of White populations, they are rarely observed in Asian populations[40,43-46]. Kim and Kim[40] suggested that the low incidences of obesity, hyperlipidaemia, and venous diseases in the Korean population could be related to the low incidence of VTE. An epidemiological study conducted by Liao et al.[46] using the New Zealand database found that the relative risk of VTE (11.7 per 100,000 adults per year in Chinese, compared to 114.7 per 100,000 adults per year in Europeans) was significantly lower for Asians, particularly Chinese. An early cross-sectional study of the Hong Kong Chinese population also suggested that the incidence of PE in their local population was less than one-tenth that of Western populations[47].

Specific data on the Chinese population have been remarkedly limited. Only two relevant studies were identified by the authors in the available literature. One retrospective study conducted by Wong et al.[19] that included Chinese patients in Singapore reported a DVT rate of 8% (proximal DVT rate, specifically: 3.0%). Data heterogeneity could be a potential source of bias in the study mentioned above due to inclusion of Malay, Indian, and Eurasian races, and both primary and revision THA in their analysis. Ko et al.[36], who conducted a prospective study on the Chinese population in Hong Kong, reported a DVT rate of 18.1% (proximal DVT rate, specifically: 13.6%). However, their study included a mixed cohort of patients who underwent total knee arthroplasty (TKA) and THA, and when THA patients were considered alone, the sample size was 22, which was likely underpowered statistically to draw a robust conclusion. In our cohort including 542 Hong Kong Chinese patients in the same locality, the incidence rate of proximal DVT was 1.1% (Table 2).

Such a significant difference in the incidence rates described above is presumed to be a result of the better understanding and practice of enhanced recovery after surgery (ERAS) achieved within the past two decades. This included and was not limited to the use of mechanical prophylaxis, early postoperative mobilisation, and multi-modal perioperative pain management[21,48-56].

Mechanical prophylaxis in the form of IPC is theoretically plausible by disrupting 'venous stasis' of the Virchow's triad of coagulation. It has been repeatedly proven in randomised controlled trials as an effective alternative to chemical prophylaxis in preventing DVT after THA[26,48,50]. Warwick et al.[26], who conducted a randomised controlled trial that included 274 THA patients treated with a foot pump or LMWH, found that there was no difference in the incidence of proximal or distal DVT and concluded that use of a foot pump is an acceptable alternative to LMWH, with fewer soft tissue side effects. Similarly, in another randomised controlled trial conducted by Pitto et al.[50] including 200 THA patients, DVT was detected in 3% of patients in the foot pump group, and 6% of patients in the LMWH group, with no statistical difference. The findings of their study confirmed the safety and effectiveness of mechanical prophylaxis for DVT in THA[50]. A promising 0.3% incidence of DVT was reported in a large Korean cohort of 741 THA patients treated with an IPC device, which was significantly lower than that of their historical cohort treated with anti-embolic stockings only[57].

The practice of early mobilisation alone resulted in a 30-fold decrease in the incidence of DVT in the group of TKA patients who began walking within 24 hours of the operation[51]. In the current cohort, early mobilisation was facilitated by the application of multimodal perioperative pain management. Multimodal analgesia makes use of the synergistic effects of various analgesics, enabling the administration of smaller doses of any individual analgesic, thereby reducing unwanted side effects[54]. The authors supported the use of intraoperative PAI and the strategy of 'opioid-sparing'. Meta-analysis of comparative studies showed that the postoperative pain score was decreased at 24 and 48 hours with use of PAI in THA. Reduced consumption of opioid was observed at 24 hours[55]. The authors did not favour use of opioid in the form of intravenous patient-controlled analgesia, in order to avoid potential side effects such as respiratory depression, nausea, vomiting, ileus, urinary retention, pruritus, hypotension, bradycardia, and cognitive change[54,56]. All of these side effects can have a negative impact on patients' course of rehabilitation. Oral opioid (oxycodone, short-acting) was only administered in cases of inadequate pain control, as nausea and vomiting were common side effects.

The next question to be answered is, "Should a low-incidence population be treated the same as high-incidence ones?" Kim et al.[21], who published a review on this topic, listed the potential problems of the universal adoption of Western guidelines in treatment of Asian patients. Kim[22] also reminded that surgeons shall not easily adopt routine use of thromboprophylaxis for

Asian patients to prevent unwanted complications. Wound haematoma requiring drainage, persistent wound discharge, failure of wound healing, risk of infection, blood loss requiring transfusion, thrombocytopenia, and major bleeding leading to mortality, have all been reported in the literature[21-35]. Burnett et al.[34] reported high complication rates in association with the routine use of LMWH, including the return of 3.4% of patients to the operation room for wound incision and drainage and prolonged hospitalisation for wound drainage for 5.1%. Use of LMWH was identified by Patel et al.[35] as a risk factor for increased drain output and wound discharge. In addition, the risk of infection increased by 42% with each day of prolonged wound drainage. Warwick et al.[26] also reported more soft-tissue side effects in terms of more bruising and swelling of the thigh and more wound oozing in post-THA patients who received enoxaparin compared with those who used a foot pump. A study conducted by Sharrock et al.[31] reported significantly higher all-cause mortality in the group treated with potent anticoagulants, while there was still occurrence of clinical PE in the group.

Regarding Asian populations in particular, a meta-analysis by Xu et al.[23] reported a 5.6 times relative risk of minor bleeding events (ecchymosis, wound haemorrhage, haematoma, and epistaxis) in patients treated with LMWH when compared with the control group. Results of the subgroup analysis in the current study showed that the inpatient stay was two days longer for patients with CUA (10.2 days vs. 8.1 days, P=0.041) (Table 5).

While the risk profile for chemical prophylaxis remains a constant, a smaller number of cases of VTE that were prevented will convert to a lower benefit-to-risk ratio in low-incidence populations[23]. Therefore, the review by Kim et al.[21] supported the use of a risk-stratified approach, where a preoperative risk assessment should be performed for all patients based on the individual predisposing factors. This suggestion was adopted by the Asia-Pacific (AP) Region Venous Thromboembolism Consensus Group in 2021, and the first multi-national guideline was published specifically for Asian patients[36]. The guideline recommended stratifying patients into four groups according to their risk of VTE (classified as 'standard' or 'elevated') and their risk of bleeding (classified as 'with' or 'without'). A strong consensus (97.2%) regarding use of 'mechanical prophylaxis alone' for prevention of VTE was reached for patients with standard risk of VTE, with or without risk of bleeding (Table 6).

Our cohort only included patients with standard risk of VTE, and all patients received mechanical prophylaxis, which provides reasonable validity for verification of the safety profile of the recommendation described above. The authors would like to consider the 'non-CUA group' in our cohort (Table 5) as a surrogate for a 'mechanical prophylaxis alone' treatment group. When an IPC device and graduated compression stockings were used as the only means of prophylaxis, the incidence rate of proximal DVT was 0.9% (four cases of DVT in 447 non-CUA patients), with no case of symptomatic or fatal PE (Table 5). Referencing the meta-analysis by Xu et al.[23] that included 11,765 Asian patients, the incidence rate of proximal DVT was 2.67% in their LMWH group. Mechanical prophylaxis alone appears to be a measure that is not inferior to pharmacological prophylaxis in preventing VTE in patients with standard risk of VTE.

The authors agree with the AP Consensus guideline that a risk-stratified approach should be used in determining prophylactic measures in Asian populations[36]. However, while the AP Consensus guideline has greater validity and relevance to Asian populations than the Western guidelines, it should be noted that 'Asian populations' is still an umbrella term under which people of different ethnicities and genetic traits across

Table 6. Summary of the Risk-stratified Recommendations for Thromboprophylaxis in Asian Patients undergoing THA by the Asia-Pacific Consensus Group 2021[37]

		Bleeding risk	
		Without	With
VTE risk	Standard	Mechanical prophylaxis alone or pharmacological prophylaxis combined with mechanical prophylaxis	Mechanical prophylaxis alone
	Elevated	Pharmacological prophylaxis combined with mechanical prophylaxis	Mechanical prophylaxis alone or combined with aspirin

THA: total hip arthroplasty, VTE: venous thromboembolic event.

Asian countries show wide clinical heterogeneity. It would be worth the effort for researchers to verify the safety profile of the recommendations made in the new guidelines using their local data before application.

The authors recognise the limitations of the current study. First, there are intrinsic biases associated with its retrospective nature.

Second, venography is the gold standard for diagnosis of DVT. Duplex ultrasonography, with interobserver variability (kappa) ranging from 0.56 to 0.85, depending on the sites and number of compressions at the veins, was utilised in the current study[58]. However, because venography is considered an invasive procedure that can expose patients to unnecessary radiation and contrast allergy when used as a routine screening tool, it was not preferred by the authors. In addition, some studies have reported that duplex ultrasonography was a comparable modality to venography in detection of DVT[37,58-60]. In a study by Grady-Benson et al.[60], up to 100% sensitivity, specificity, and accuracy for detecting proximal DVT was attained; however, a slightly inferior result was obtained in the detection of distal DVT (88% sensitivity, 98% specificity and 98% accuracy).

Third, examination of thrombi in the calf veins (distal DVT) was not performed in the current study. It is believed that study of distal veins might demonstrate a higher overall incidence rate of DVT. For example, in a study of a large cohort of Korean patients reported by Kim et al.[61], the proximal rate of DVT was 1.54% (nine in 582 hips). This figure is in keeping with the finding of the current study (1.1%). The rate of distal DVT in that Korean cohort was 13.4% (78 in 582 hips). Despite this, some studies have suggested that because thrombi in the distal calf veins are securely attached to the vessel wall and resolve spontaneously they are unlikely to produce symptomatic emboli[62-64]. It is the authors' belief that thrombi in the calf veins should not be detected deliberately, in order to minimise over-treatment of clinically insignificant thrombi as well as potential patient anxiety.

Fourth, treatment with seven days of LMWH was administered to patients in the current cohort with high risk of VTE. The authors recognise that there is controversy regarding the optimal duration and choice of chemical prophylaxis for patients in high-risk groups[36]. Some Western guidelines have recommended extended use of chemical prophylaxis, up to 28-35 days[11,12]. In addition, the options have been further expanded in recent years with the more popular use of direct oral anticoagulants[65]. However, these are beyond the recommendations that can be made based on the findings of the current study.

Fifth, routine screening for detection of PE was not performed in the current study. CTPA was performed only in cases of clinical suspicion, which may have resulted in under-detection of clinically silent PE. Finally, the study did not include a control group for comparing the incidence of VTE in patients treated with chemical prophylaxis.

CONCLUSION

The incidence of VTE after primary THA without chemical prophylaxis can be low in Asian populations when following a fast-track rehabilitation protocol. Mechanical prophylaxis alone can be regarded as a reasonably safe practice in terms of a balanced benefit-to-risk ratio for Asian patients with standard risk of VTE.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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