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ORIGINAL ARTICLE

Epidemiological updates of venous thromboembolism in a Chinese population

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KEYWORDS
deep vein thrombosis;
epidemiology;
Han Chinese;
mortality;
pulmonary embolism

Summary *Background/Objective:* Deep vein thrombosis (DVT) was thought to be uncommon in Asians and routine thromboprophylaxis in the form of anticoagulation for surgical patients was considered to be unnecessary. The current study aims to provide a contemporary epidemiology of venous thromboembolism in a population-based scale.
Methods: Information from January 1, 2010 to December 31, 2011 was retrieved from a centralized computer public healthcare database serving mainly an ethnic Han Chinese population of 7.1 million. The incidence, demographics, and hospital mortality rates of DVT and pulmonary embolism (PE) were obtained, and analyzed for different surgical categories.
Results: The overall annual incidences of DVT, PE alone, and PE with DVT were 30.0 per 100,000 population, 8.7 per 100,000 population, and 3.0 per 100,000 population, respectively. Overall male to female ratio was 1:1.24. Venous thromboembolic disease was more common with increasing age in both sexes. Thirty days' mortality rates associated with DVT, PE alone, and PE with DVT were 9.0%, 17.4%, and 13.3% respectively. Among the patients who received 103,023 major and intermediate surgical procedures in the study period, the mean incidence of postoperative DVT, PE alone, and PE with DVT were only 0.20% (203.5 patients), 0.08% (85.5 patients), and 0.04% (40.5 patients) respectively.
Conclusion: Compared with a similar study 10 years ago, there seemed to be a general increase in incidence of DVT and PE. This study showed that postoperative thromboembolic events were not uncommon, with DVT occurring in up to 0.2% of patients and PE in 0.12% of patients in this longitudinal survey.

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1. Introduction

Venous thromboembolism is a major contributor to the global disease burden.[1] Deep vein thrombosis (DVT) and pulmonary embolism (PE) were thought to be rare in the Asian population when compared with the Caucasian population. In the Caucasian population, recent studies quoted the annual incidence rate of DVT was between 65 per 100,000 population and 152 per 100,000 population[2–5] and that of PE was between 45 per 100,000 population and 189 per 100,000 population.[2–7] By contrast, the annual incidence rates among Asians were between 5.3 per 100,000 population and 17.1 per 100,000 population for DVT[8,9] and between 3.9 per 100,000 population and 7.0 per 100,000 population for PE.[8,9] However, an autopsy study showed a 4.7% prevalence rate of pulmonary thromboembolism among 12,421 postmortem examinations in the Han Chinese population.[10] The incidence of venous thromboembolism may be undetected or underestimated in Orientals.

We previously published a comprehensive epidemiology study of venous thromboembolism in a Chinese population for the years 2000–2001.[8] The overall incidence of DVT and PE was 17.1 per 100,000 population and 3.9 per 100,000 population at the time. Hospital mortality rates associated with DVT and PE were 7.3% and 23.8%, respectively. Mean incidence of postoperative DVT and PE was 0.13% and 0.04%, respectively. We have in our territory a dedicated, reliable pan-territory electronic registration of patients' morbidity and mortality of venous thromboembolism over a long period of time. The Clinical Management System (CMS) and Electronic Patient Record (ePR), built in-house since 1991 in all the public hospitals, stores essential clinical database of $>$ 7 million patients who had attended these hospitals. Since 1999, data could be extracted through the Clinical Data Analysis and Report System (CDARS), which allowed a direct evaluation of the prevalence of DVT and PE in a predominately Chinese community.

The aim of this current study is to provide an update on the epidemiology of deep venous thromboembolism in the Han Chinese population in Hong Kong.

2. Methods

Hong Kong had a population of 7,071,576 in 2011. The population continued to grow older compared with the preceding 10 years. The median age rose from 36.7 in 2001 to 39.6 in 2006 and further to 41.7 in 2011. Approximately 94% of the population were of Han Chinese ethnicity.[11] Our Hospital Authority is a public healthcare institution that manages 42 hospitals and provides over 90% of all in patient services in Hong Kong. Since 1999, patient data from all public hospital could be retrieved through the CDARS including the hospitalization rate, demographics, diagnosis, surgical procedures, and outcomes. A unique personal identifier allows retrieval of individual data for review.

Hospital admission and discharge statistics for the years 2010 and 2011 were included in the current analysis. All patients with discharge diagnosis of: (1) DVT; (2) PE alone; and (3) PE together with DVT were searched for their International Classification of Diseases codes 9th version (DVT: 451.1, 451.8, 453.8; PE: 415.1) through the CDARS. Information on patients' age, sex, diagnosis, surgery (if any), 30 days mortality, and the cause of death were collected. The incidence of postoperative DVT and PE were determined by cross-reference to surgical codes and categorized as cardiothoracic surgery, dental, general surgery, neurosurgery, obstetrics and gynecology, ophthalmology, orthopedic surgery, and urology.

The annual overall and age-specific incidences of DVT and PE in Hong Kong were calculated from new hospital admission rates per 100,000 population, and stratified according to sex and age groups using population census data from 2011. Patients with PE were further categorized into those without or with evidence of DVT.

Comparisons between groups were made with Chi-square test and a p value < 0.05 was accepted as significant.

3. Results

3.1. Patient demographics

During the 24 months from January 2010 to December 2011, there were 2,898,107 admissions (of 1,348,097 patients) to all public hospitals in Hong Kong. An electronic medical record search yielded 4238 patients with diagnosis of DVT, and 1665 with PE, of which 430 (25.8%) were associated with DVT.

Figure 1 shows age distribution of DVT, PE alone, and PE with DVT for all patients. Venous thromboembolism increased over age with incidence peaked at age group of 75–84 years. The median age of patients with DVT at presentation was 73 years and that of PE was 70 years. Venous thromboembolism demonstrated a slight female predominant. Overall male to female ratio is 1:1.24 (1:1.27 for DVT and 1:1.15 for PE).

3.2. Incidence and mortality

The overall annual incidences of thromboembolic disease in Hong Kong were 30.0, 8.7, and 3.0 per 100,000 population for DVT, PE alone and PE with DVT respectively (Table 1). These figures were lower than those reported in Western countries (Table 3). However, significant growth in incidences were noted comparing to a similar study 10 years previously using the same hospital database and statistical methods.[8] Annual incidence of DVT increased almost doubly from 17.1 per 100,000 in the years 2000–2001 to 30.0 per 100,000 in years 2010–2011. Incidence of PE increased triply from 3.9 per 100,000 in years 2000–2001 to 11.7 per 100,000 in years 2010–2011.

Table 2 showed the age-specific incidence and mortality rates from DVT, PE alone, and PE with DVT. The annual age-specific incidences of DVT, PE alone, and PE with DVT were 0.4 per 100,000 population, 0.2 per 100,000 population, and 0.1 per 100,000 for those aged 0–14 years; 1.6 per 100,000 population, 0.7 per 100,000 population, and 0.3 per 100,000 for ages 15–24 years: 6.6 per 100,000 population, 1.5 per 100,000 population; 0.6 per 100,000 for ages 25–34 years, 12.7 years, 2.9 years; 1.6 per 100,000 for ages 35–44 years, 21.5 years, 6.2 years; 2.4 per 100,000 for ages 45–54 years, 31.5 years, 12.4 years, 3.9 per 100,000 for ages 55–64 years, 72.2 years, 22.6 years; 8.9 per 100,000 for ages 65–74 years, 159.7 years, 53.0 years; 14.5 per 100,000 for ages 75–84

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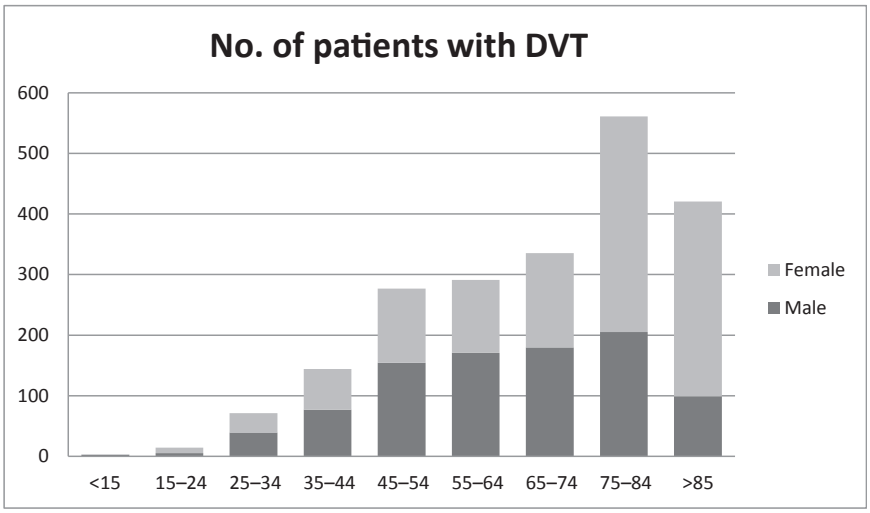
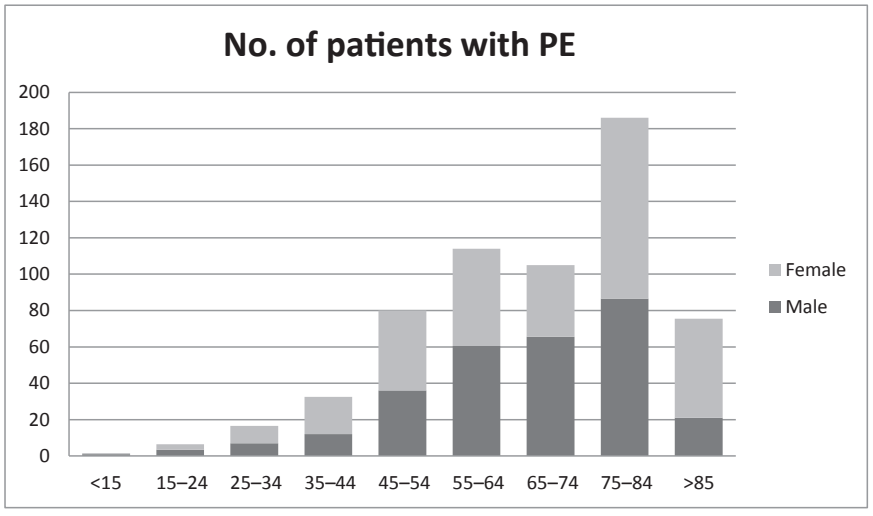
A



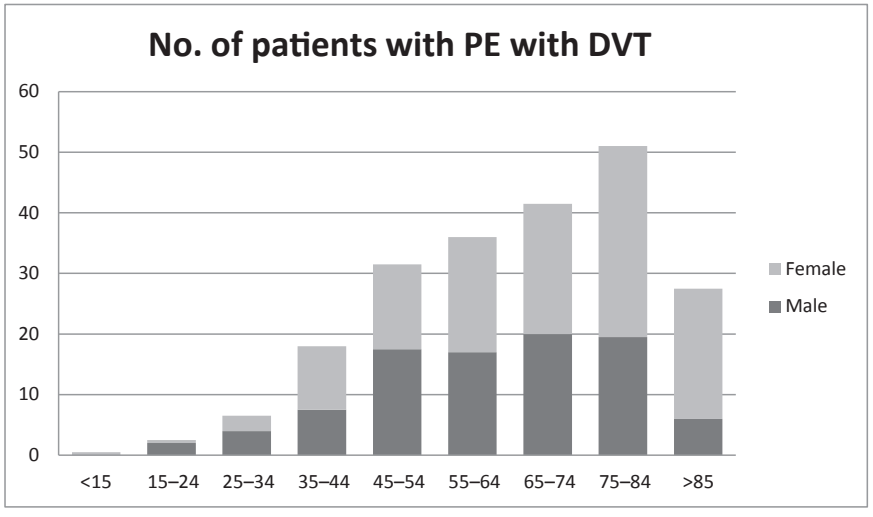
DVT = deep vein thrombosis; PE = pulmonary embolism.

B



DVT = deep vein thrombosis; PE = pulmonary embolism.

C



DVT = deep vein thrombosis; PE = pulmonary embolism.

Figure 1 Age distribution of patients with (A) deep vein thrombosis (DVT); (B) pulmonary embolism (PE) alone; and (C) PE with DVT (averaged over the years 2010 and 2011).

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Table 1 Age specific incidence and mortality from deep vein thrombosis and pulmonary embolism (averaged over the years 2010 and 2011).

	Per 100,000 population									
	All ages	Age group (y)								
		0–14	15–24	25–34	35–44	45–54	55–64	65–74	75–84	≥ 85
DVT										
Male	28.3	0.6	1.3	8.7	16.1	25.4	37.3	75.5	128.7	243.2
Female	31.4	0.2	2.1	5.1	10.2	18.0	25.9	68.7	185.5	379.9
All	30.0	0.4	1.7	6.6	12.7	21.5	31.5	72.2	159.7	335.5
PE										
Male	8.9	0.2	0.8	1.5	2.5	5.9	13.2	27.5	54.3	51.6
Female	8.6	0.1	0.7	1.5	3.1	6.5	11.5	17.4	51.8	64.4
All	8.7	0.2	0.7	1.5	2.9	6.2	12.4	22.6	53.0	60.2
PE with DVT										
Male	2.8	0	0.5	0.9	1.6	2.9	3.7	8.4	12.2	14.7
Female	3.2	0.1	0.1	0.4	1.6	2.1	4.1	9.5	16.4	25.4
All	3.0	0.1	0.3	0.6	1.6	2.4	3.9	8.9	14.5	21.9
DVT mortality (% of incidence)										
Male	2.7 (9.6)	0 (0)	0 (0)	0 (0)	0.4 (2.6)	1.7 (6.8)	3.4 (9.1)	7.3 (9.7)	19.1 (14.9)	33.2 (13.6)
Female	2.7 (8.5)	0 (0)	0 (0)	0 (0)	0.3 (3.0)	1.4 (7.8)	2.2 (8.3)	5.1 (7.4)	14.8 (8.0)	46.1 (12.1)
All	2.7 (9.0)	0 (0)	0 (0)	0 (0)	0.4 (2.8)	1.6 (7.2)	2.8 (8.8)	6.2 (8.6)	16.8 (10.5)	41.9 (9.0)
PE mortality (% of incidence)										
Male	1.7 (19.3)	0 (0)	0.1 (14.3)	0.1 (7.1)	0.3 (12.5)	1.2 (19.4)	1.9 (14.0)	5.7 (20.6)	12.6 (23.1)	12.3 (23.8)
Female	1.4 (15.7)	0 (0)	0 (0)	0 (0)	0.5 (17.1)	1.0 (14.8)	1.6 (14.0)	2.6 (15.2)	9.6 (18.6)	10.6 (16.5)
All	1.5 (17.4)	0 (0)	0.1 (7.7)	0 (3.0)	0.4 (15.4)	1.0 (16.9)	1.7 (14.0)	4.2 (18.6)	11.0 (20.7)	11.2 (18.5)
PE with DVT mortality (% of incidence)										
Male	0.3 (11.2)	0 (0)	0 (0)	0 (0)	0.2 (13.3)	0.3 (11.4)	0.4 (11.7)	0.4 (5)	1.6 (12.8)	4.9 (33.3)
Female	0.5 (14.8)	0 (0)	0 (0)	0 (0)	0.2 (14.3)	0.4 (17.9)	1.0 (23.7)	0.7 (7.0)	2.3 (14.3)	4.1 (16.3)
All	0.4 (13.3)	0 (0)	0 (0)	0 (0)	0.2 (13.9)	0.3 (14.3)	0.7 (18.1)	0.5 (6.0)	2.0 (13.7)	4.4 (20.0)

DVT = deep vein thrombosis; PE = pulmonary embolism.

Table 2 Annual incidence of postoperative deep vein thrombosis and pulmonary embolism in different groups of surgeries (averaged over years 2010 and 2011).

	No. of operations	No. of postoperative DVT	No. of postoperative PE	No. of postoperative PE with DVT
Cardiothoracic surgery	2957	3.0 (0.10)	4.0 (0.14)	0.5 (0.02)
Dental	1391	0.5 (0.04)	1 (0.07)	0.5 (0.04)
General surgery	34295	53 (0.15)	31.5 (0.09)	14 (0.04)
Neurosurgery	2940	19 (0.64)	14.5 (0.49)	3.5 (0.12)
Obstetrics and gynecology	12882	17 (0.13)	5 (0.03)	4 (0.03)
Ophthalmology	16858	8 (0.05)	1.5 (0.01)	1 (0.01)
Orthopedics	24436	91.5 (0.37)	21.5 (0.09)	15.5 (0.06)
Urology	7264	11.5 (0.16)	6.5 (0.09)	2 (0.03)
Overall	103023	203.5 (0.20)	85.5 (0.08)	40.5 (0.04)

Values in parentheses are %.
DVT = deep vein thrombosis; PE = pulmonary embolism.

years, and 335.5 years, 60.2 years; and 21.9 per 100,000 for ages 85 or older (Chi-square test, $p < 0.001$). Incidence peaked at those aged > 85 years old. Within the study interval, 380 patients died within 30 days of DVT, 215 patients died within 30 days of PE, and 57 patients died within 30 days of PE with DVT. Corresponding 30 days mortality rates associated with DVT, PE alone, and PE with DVT were 9.0%, 17.4%, and 13.3% respectively. Age-specific mortality rates for DVT and PE were also highest in elderly people, amounting to around 10% and 20% in those older than 75 years.

3.3. Postoperative thromboembolism

Postoperative DVT may be important as patients had immobility and malignancy. Within the 24 months, there were a total of 206,046 intermediate, major or ultramajor surgical operations performed in all our surveyed hospitals. A total of 407 DVTs (9.6% of all DVTs), 171 PEs (13.8 % of all PEs), and 81 PE with DVTs (18.8 % of all PE with DVTs) were postoperative events. The mean annual incidences of postoperative DVT and PE in relation to different surgical

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specialties are summarized in Table 2. The mean annual incidence of postoperative DVT, PE alone, and PE with DVT were only 0.20%, 0.08%, and 0.04% respectively. Incidence of postoperative DVT was highest in neurosurgery (0.64 %) and lowest in dental (0.04 %). Similarly, incidence of postoperative PE was highest in neurosurgery (0.61 %) and lowest in ophthalmology (0.02 %).

4. Discussion

We performed a contemporary literature search using PubMed, OVID MEDLINE, and EMBASE to summarize all population-based incidences of venous thromboembolism around the world. Search keywords comprised deep vein thrombosis, venous thromboembolism, venous thrombosis, vein thrombosis, pulmonary embolism, together with keywords of epidemiology, incidence, and prevalence. Only most recent studies published between the years 2010 and 2014 were included, and the result is tabulated in Table 3. Our study reconfirmed a relatively low incidence of venous thromboembolism in a Chinese population compared with Caucasians.

This was an updated pan-territory survey on the incidence of DVT in the Han Chinese in Hong Kong, and compared with our study 10 years previously using an

Table 3 Incidence of deep vein thrombosis and pulmonary embolism reported in different population.

Author	Year of publication	Study site	Study type	Incidence of DVT	Incidence of PE
Present study		Hong Kong	Retrospective study of 7,100,000 residents based on regional hospital database	30.0 per 100,000 population	11.7 per 100,000 population
Cheuk et al[8]	2004	Hong Kong	Retrospective study of 6,700,000 residents based on regional hospital database	17.1 per 100,000 population	3.9 per 100,000 population
Chau et al[10]	1997	Hong Kong	Autopsy review included 12,421 death	—	4.7%
Jang et al[9]	2011	Korea	Retrospective analysis of a national health insurance database	5.3 per 100,000 population	7.0 per 100,000 population
Lee et al[30]	2010	Taiwan	Retrospective analysis of a national health insurance database	Venous thromboembolism incidence 15.9 per 100,000 population	
Yusuf et al[5]	2012	United States	Retrospective analysis of the national hospital database 2007—2009	152 per 100,000 population	121 per 100,000 population
Wiener et al[7]	2011	United States	Retrospective analysis of Nationwide Inpatient Sample (NIS) of Healthcare cost & Utilization Project (HCUP) 1998—2006	—	112 per 100,000 population
Tagalakis et al[4]	2013	Canada	Retrospective analysis of a provincial healthcare database	78 per 100,000 population	45 per 100,000 population
Hald et al[31]	2013	Norway	Prospective study of 29,967 patients	Venous thromboembolism incidence 148 per 100,000 population	
Holst et al[32]	2010	Denmark	Prospective study of 18,954 patients	Venous thromboembolism incidence 269 per 100,000 population	
Severinsen et al[3]	2010	Denmark	Prospective study of 56,014 patients aged 50—64 y	65 per 100,000 population	51 per 100,000 population
Moretti et al[33]	2010	Italy	Retrospective analysis of regional hospital database	—	189 per 100,000 population
Shiraev et al[6]	2013	Australia	Retrospective analysis of national hospital databases	—	53 per 100,000 population
Vazquez et al[2]	2013	Argentina	Prospective study within a health maintenance organization	130 per 100,000 population	64 per 100,000 population

DVT = deep vein thrombosis; PE = pulmonary embolism.

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identical database and research methods,[8] it showed a significant surge in incidence of both DVT and PE. Incidence of DVT increased almost doubly from 17.1 per 100,000 in the years 2000–2001 to 30.0 per 100,000 in the years 2010–2011. Incidence of PE increased triply from 3.9 per 100,000 in the years 2000–2001 to 11.7 per 100,000 in the years 2010–2011. Another Asian country Korea had similar observations.[9] An aging population may partly explain the picture but raising trends was still witnessed if age-specific incidences were compared. Etiology of venous thromboembolism is multifactorial with both genetic[12] and environmental risk factors. Genetic compositions of a population should be more or less static over time. Preference towards a more Westernized diet may increase venous thromboembolic disease.[13] It has been suggested that the difference in diet and hence gut flora protects Asian from DVT and PE.[14] A more plausible explanation was better reporting of the condition over the years. Better detection, with advances in diagnostic technology[15] and increased awareness may account for the apparent rise. Attributed to lifestyle changes, aging population, and increasing awareness, we might expect more occurrence of venous thromboembolism in China, where ethnic origin is predominant Han Chinese similar to our locality.

Irrefutable evidence has shown that thromboprophylaxis reduced postoperative DVT or PE in Caucasians.[16–18] A meta-analysis of 46 randomized control trials in general surgery compared thromboprophylaxis using low dose unfractionated heparin versus placebo.[16] The rate of DVT was significantly reduced [from 22% to 9%; odd ratio (OR), 0.3; number needed to treat (NNT), 7], as were rates of symptomatic PE (from 2.0% to 1.3%; OR, 0.5; NNT 143), fatal PE (from 0.8% to 0.3%; OR, 0.4; NNT 182), and all-cause mortality (from 4.3% to 3.2%; OR, 0.8; NNT 97). There was a small increase rate of bleeding events (from 3.8% to 5.9%; OR, 1.6; NNT 47). Well-developed guidelines were available in the West.[19] Use of thromboprophylaxis in Asia, however, is more controversial[20] due to lack of well-designed multicenter randomized controlled trials as well as nonstandardized research designs. Our study showed that the overall postoperative risk of DVT was 0.20% and that of PE was 0.12%. A recent review[21] of postoperative thromboembolic risk in Asian general surgery patients revealed similar risk. Median incidence of above-knee DVT was 0.08% (range, 0–2.9%), whereas median incidence of PE was 0.18% (range, 0–0.58%) among those observational studies. In comparative studies, overall rates of DVT and PE were 2.5% (range, 0–7.4%) and 1.9% (range, 0–1.9%) in control groups, whereas rates of DVT and PE were both 0% in low molecular weight heparin groups. Baseline risk of venous thromboembolism in Asian surgical patients was indeed low, and hence the number needed to treat by means of pharmacological thromboprophylaxis would be high. Routine pharmacological thromboprophylaxis in the form of heparin is therefore not worthwhile in our population.

Neurosurgical patients had the highest incidence of postoperative DVT and PE, 0.64% and 0.61% respectively. This was consistent with worldwide studies.[22–24] They were prone to clotting because of long operating times, paralysis, prolonged bed rest, hypercoagulability, posttraumatic status, and old age. The latest guidelines recommended intermittent pneumatic compression.[19] Controversy existed concerning the use of low dose unfractionated heparin or low molecule weight heparin. As heparin rose the rate of major postoperative intracranial hemorrhage,[25,26] neurosurgeons must weigh the balance among pharmacological prophylaxis and[25,26] bleeding complications.

Venous thromboembolism is often clinically silent. Our study included only symptomatic postoperative patients. Prospective trials undertaken in Asian countries have demonstrated the rate of asymptomatic DVT up to 59% after orthopedic surgery and up to 16% after major general surgery. Symptomatic patients only constituted a small minority.[27] An autopsy study in our territory also showed a 4.7% prevalence rate of pulmonary thromboembolism.[10] Postoperative venous thromboembolism may be an unrecognized and undertreated condition in Asia. Japan[28] and Korea[29] developed their own guidelines on prevention of venous thromboembolism. Both incorporated stratification of patients into low, moderate, and high risk with different recommendations. Local guidelines are lacking in Hong Kong and there is a prompt need for its development.

There are a few limitations to our study. A prospective interpretation of retrospectively collected clinical data may have inherent flaws. This study was based on hospital admissions, and on the presumed accurate electronic entering of the diagnosis. Patients who died of their venous thromboembolism may not have full autopsy examination to pinpoint the precise cause of death, or there may be misdiagnosis. Out of hospital deaths and those cared by private hospitals have not been included. Our public hospitals provide ~90% inpatient care of the whole population. Excluding those cared by private hospitals and out of hospital deaths would inevitably underestimate the incidence of thromboembolism. The CDAR system also had limitations in the search for comorbidities. Only age, sex, and postoperation status were included. Other important risk factors such as malignancy, infection, obesity, pregnancy, estrogen therapy, and thrombophilia could not be retrieved. Otherwise, subgroup analysis could have been performed to see their individual incidences.

Although the incidence of thromboembolism in the Chinese population was still low compared with Caucasians, there was a general trend of increase in incidence of DVT and PE over time. Postoperative thromboembolic events were not common.

Conflicts of interest

No conflict of interests declared, no financial gains or external funds received. Abstract was presented in UIP Chapter Meeting Seoul, Korea as a free paper (AB-0113) on August 29, 2015.

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