

Postoperative major surgery patients developing silent deep vein thrombosis: A prospective observational study



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Surgical patients are at high risk for developing deep vein thrombosis (DVT). There are many reports concerning DVT, but little is known about silent deep vein thrombosis (sDVT). This study aimed to determine the incidence of sDVT. Secondary objective is to identify the associated factors for the use of DVT prophylaxis and Caprini risk scores among major surgery patients. This prospective observational study involved postoperative surgical patients who are at risk of developing sDVT. The Caprini risk-assessment scores were calculated, and each subject had a preoperative and postoperative compression ultrasound complemented by duplex venous ultrasonography of deep venous system. No patient from the study experienced sDVT. There were significant associations between Caprini risk score group (odds ratio, 8.16; 95% confidence interval [CI], 1.01–68.74; $P = .016$) and the use of central venous catheter (odds ratio, 6.34; 95% CI, 1.62–24.80; $P = .008$) with DVT prophylaxis. Interestingly, the use of central venous catheter resulted in more than four-point increment of Caprini risk scores (mean increment, 4.19; 95% CI, 3.16–5.21; $P < .001$). Besides that, age was also significantly associated with Caprini risk scores (β coefficient, 0.06; 95% CI, 0.02–0.11). Result from our study shows that the sDVT was nonexistent in this study setting. High-Caprini risk score group and the presence of central venous catheter were the significant predictor factors for the use of DVT prophylaxis. Significant predictor factors for Caprini risk scores were age and the presence of central venous catheter. (J Vasc Nurs 2018;36:173-180)

Venous thromboembolism (VTE) imposed a great impact on the mortality of the surgical and medical patients. It is the most preventable cause of death in surgery.^{1,2} The natural history of VTEs are resolution, propagation, recanalization, and embolization. The pathogenesis of VTE is multifactorial. There is still no single independent predictor that has a direct association with an increased occurrence of deep vein thrombosis (DVT). Rudolf Virchow, the Father of Pathologist,

postulated that thrombus development occurs via the classical Virchow's triad, that is, endothelial injury, blood stasis, and hypercoagulability.^{1,3} The presence of any component of Virchow's triad will raise the probability of thrombus formation. Endeavors have been made over the years to study its pathogenesis and also to devise a clinical scoring system to reliably predict its occurrence and outcome. Postoperative VTE is reported as one of the most preventable causes for hospital morbidity and mortality in today's practice using the antithromboprophylaxis agent.^{1,2}

In an international multicenter trial on antithrombotic prophylaxis, researchers discovered that the clinically significant DVT among the nonheparinized patients postoperatively can be as high as 31% ($n = 211$), whereas for those receiving prophylactic heparin, the rate of DVT is much lower ($n = 53$, 8.5%). They also observed that the possibility of the onset of clinically significant DVT is highest from the third to the sixth days postoperatively in both control and heparinized groups.^{1,2} Wilarusmee et al reported that the prevalence of DVT among ICU patients was 10.5%.⁴ However, the investigators did not administer the routine thromboprophylaxis to all their patients. Besides, Chua et al also reported that the incidence of clinically significant DVT was 5.01% ($n = 21$) among admissions to neurorehabilitation unit (median time to the DVT development was 14 days after events) in Singapore.⁵ They used a D-dimer assay as the marker to select the groups of patient who were clinically eligible for duplex venous ultrasound scan. Out of 251 patients, 247 patients had an elevated D-dimer assay that exceeded the normal cutoff value of 0.34 $\mu\text{g/mL}$. Out of these, only 21 patients were confirmed to have DVT at either proximal or distal deep vein

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systems. Thus, they concluded that the occurrence of silent deep vein thrombosis (sDVT) among patients admitted for neurorehabilitation is uncommon, which can be explained by the possible presence of protective genetic or ethnic factors, early walking initiation, and the timing of the admission that was during the declining period of the thrombotic risk.

In the United States, the DVT prevalence was 145 per 100,000 individuals per year, whereas the pulmonary embolism (PE) was reported approximately 69 per 100,000 individuals per year in the general population.^{6,7} The VTE accounted for 150,000–200,000 deaths per year, and one-third of the VTE-related deaths occurred after surgery.⁸

In 2007, an epidemiological model was constructed to estimate the number of VTE per annum within the six European Union countries namely France, Germany, Italy, Spain, Sweden, and United Kingdom. The estimated symptomatic VTE events per annum were 465,715 cases of clinically significant DVT, 295,982 cases of PE, and 27,473 VTE-related deaths.⁹

Furthermore, a study by Harris et al found that the incidence of proximal DVT among surgical intensive care patients was 7.5%, and the majority of these were asymptomatic.¹⁰ Based on the natural history of DVT, 40% of sDVT will become symptomatic, whereas the rest remained undiagnosed. Out of these undiagnosed thrombotic cases, 50% will eventually develop PE, and 30% will succumb to death.¹⁰

In the United Kingdom, the House of Commons Health Committee reported that an estimated 25,000 deaths occurred due to preventable hospital-acquired VTE per year in 2005.¹¹ The under usage of VTE prophylaxis regime was attributed to be the primary factor. However, most of the study subjects are Caucasians, and therefore, it would be unfair to extrapolate these findings to the Asian counterparts.

Apart from that, there was a similar study conducted in our hospital in 2004, whose research objective was to estimate the incidence of DVT among general surgical patients postoperatively. At that time, all study participants were not given any forms of thromboprophylaxis because it was not in accordance with the hospital policy. Besides, it was also believed that the incidence of DVT among the Asian population was low, a view shared by the treating clinicians. They discovered that the incidence of DVT among their study participants was 2.2%, a comparatively low estimate if comparison was made with the Caucasian populations.¹²

sDVT, also known as asymptomatic DVT, is the formation of thrombus within the deep venous system with no overt clinical manifestations such as swollen tender limbs seen in the symptomatic DVT.¹³ In the thrombosis research, efforts were undertaken to detect early thrombus formation so that the propagation of the thrombus that may eventually lead to fatal venous thromboembolic event such as PE can be prevented or halted.¹³ However, not all health-care centers can bear the high financial cost for administering thromboprophylaxis agents to all patients.

In a Japanese prospective clinical trial, they observed that the peak incidence of sDVT occurred on day 4 of postoperative period. They recruited 101 patients undergoing either total hip or knee replacement surgery, and all their patients received prophylactic fondaparinux injection from the postoperative day 1 to day 14. They noticed that in the total hip replacement surgery

group, the incidence of the asymptomatic DVT was 0% on the day of surgery, 13.6% on day 1, 27.1% on day 4, and 11.9% on day 14. On the other hand, in the total knee replacement group, they observed that the incidence of sDVT was 50% on day 1, 58.3% on day 4, and, intriguingly, 20.8% on day 14.¹³

In our cohort, the method of DVT prophylaxis used is early mobilization, which takes the forms of either mechanical (intermittent pneumatic calf pump and thromboembolic deterrent stocking [TDS]) or pharmacological approaches (daily subcutaneous fondaparinux or twice daily subcutaneous heparin injection). As our practice is gearing toward the concept of enhanced recovery after surgery, we mobilized most of our patients within the first four days during the postoperative periods.

Our study was designed to determine the incidence of sDVT and to identify the associated factors of the usage of DVT prophylaxis and the Caprini risk scores among postoperative major surgery patients at the Hospital Universiti Sains Malaysia (HUSM).

MATERIALS AND METHODS

Study design and setting

A prospective cohort study was conducted in the surgical ward of HUSM, Kubang Kerian, Kelantan, Malaysia, from December 2013 to May 2014.

Ethical approval

An ethical clearance was obtained from the Human Research Ethics Committee, Universiti Sains Malaysia in Kelantan, Malaysia (Federal Wide Assurance registration number: 00007718 and Institutional Review Board registration number: 00004494). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013.

Patient's confidentiality was safeguarded by not documenting the patient's name or any other forms of identification on the data-collection sheet. Each subject was given a random number, and only the study investigator knew how to break the random code. Besides, the data-collection sheets were kept by the principal investigator at a secured place, and the Statistical Package for Social Sciences (SPSS) file, in which all the information was stored, was protected with password to prevent any accidental or intentional breach of participant's confidentiality.

Participants

This study involved postoperative HUSM surgical patients who underwent a major surgery and are at the risk of developing sDVT. All patients who had been admitted to the surgical ward during this study period were screened according to the inclusion and exclusion criteria. All study participants who met the prerequisite selection criteria and consented to study participation were enrolled into this study.

The inclusion criteria were an age of 18 years and above, underwent surgical operations involving general or regional anesthesia for more than 45 minutes, and had consented to study participation. The exclusion criteria were any patients who were already diagnosed or on treatment for any form of VTE and those who did meet the inclusion criteria but refused to participate in the study.

A convenient sampling method was chosen because of the scarcity of potential study participants, which was attributed secondary to last-minute cancellation of the planned surgical procedures and for not fulfilling the inclusion and exclusion criteria of this study.

Sample-size estimation

The sample size was calculated using a single proportion formula for the first objective and two-proportion formula for the second objective, using PS: Power and Sample Size Calculation, version 3.0.4.3.

For the first objective, two estimates of the incidence of sDVT were used from the previous studies by Tun et al¹² and Harris et al.¹⁰ Based on these two estimates, the calculated sample sizes for the first and second objective were 82 subjects and 37 subjects, respectively.^{9,11} For this objective, the sample size calculated using the estimate from Tun et al¹² was chosen because it was based on a local estimate of sDVT, reflecting the number of new cases of sDVT encountered during the day-to-day surgical practice in the HUSM.

For the second objective, which is to investigate the association between the use of DVT prophylaxis and Caprini risk scores, the sample size was calculated using the parameter estimate obtained from Bahl et al¹⁴ for P_0 (the prevalence of DVT prophylaxis in Caprini low-risk group [≤ 4]). For P_1 , the prevalence of DVT prophylaxis in the Caprini high-risk group (Caprini risk score > 4) is set at 0.01 based on expert opinion. The final calculated sample size was 48 subjects per group (in view of 20% of attrition rate).¹⁴

Data collection

Voluntary written informed consent was obtained from each study participant, and their rights to withdraw from the study at any stage and for any reason would not jeopardize their subsequent quality of medical care. Subjects were first risk stratified according to the Thrombosis Risks Factor Scoring system as proposed by Caprini and Arcelus.^{5,7}

There are multiple risk-assessment models proposed to risk stratify the patients who are at higher risk of developing DVT. In the previous studies, Salzman and Hirsh predictive models were used to identify high-risk patients for DVT.^{15,16} However, we found that both the predictive models were less accurate in DVT risk stratification because of the subjective nature of these risk scoring systems, and this will inadvertently lead to misclassification bias. Hence, we opted for the Caprini risk-assessment model because it is more impervious to subjective clinical assessments and takes less time to risk score the patients, an obvious advantage for a busy referral center such as ours.⁷

Each subject had a preoperative duplex ultrasound of the deep venous system for bilateral lower limbs. This was subsequently followed by a postoperative ultrasound duplex of the deep venous system for bilateral lower limbs on postoperative day 4.

Based on our daily observations, most of our patients undergoing major abdominal surgery were on the average discharged from the ward on day 4 postoperatively. Hence, we arranged for the ultrasound duplex of the venous system on day 4 or on the day before their discharge.¹³ The venous duplex ultrasound with venous compression ultrasonographic assessment is used to detect DVT. It is the easiest and least invasive modality compared to contrast venography. In addition, the compression ultrasonography is a highly accurate method for detecting proximal DVT, despite a slightly less sensitivity for detecting calf DVT.¹⁷ The sensitivity and specificity of compression ultrasonography in detecting proximal DVT

were reported to be 94% and 93%, respectively.^{16,18,19} The sensitivity for detecting distal or calf DVT was reported to be 63%.¹⁹ The alternative method, contrast venography, is a highly sensitive and specific modality for detecting DVT. However, it imposes contrast-related risks and the side effects of this investigative procedure may outweigh the benefit.¹⁷

A bilateral ultrasonography of the lower extremity is performed with color-flow duplex imaging of the major proximal veins that includes the common femoral, superficial femoral, and popliteal veins. The routinely used probes are the linear probes of 9–3 MHz frequency or curved probes of 5–2 MHz frequency. The venous compressibility is evaluated at 1-cm intervals. The diagnosis of DVT is deemed positive based on the following conditions: 1) the venous segment was not fully compressible, 2) the presence of thrombus in the vein, and 3) the absence of flow or abnormal flow in the venous systems.^{10,20,21}

For venous ultrasonography, Siemens Acuson X300 premium edition ultrasound machine (Siemens, Washington DC) was used. Two different radiologists were tasked to perform the ultrasound to ensure the reliability of the results. The ultrasonography of bilateral lower extremities was performed using color-flow duplex imaging of the major veins, including the common femoral, superficial femoral, and popliteal veins. Thrombi present in these veins were recorded as confirmed DVT. Ultrasound probes of various frequencies were selected to optimize imaging according to the patient's body habitus. The routinely used probes were the linear probes of 9–3 MHz frequency or curved probes of 5–2 MHz frequency. The compressibility was evaluated at 1-cm intervals. This examination was then repeated with duplex ultrasound of the venous system to look for any other evidence of abnormal blood flow. The diagnosis of DVT was deemed confirmed when the venous segment was not fully compressible, there is thrombus in the vein, or flow or abnormal flow is absent. The interrater agreement of the results was excellent (Cohen's kappa = 1 [95% confidence interval {CI} of kappa, not applicable]).

Statistical analysis

The data were descriptively analyzed in mean and standard deviation (SD) or median and interquartile range for continuous data. For categorical data, frequency and percentage were used.

A simple logistic regression analysis was performed to examine predictors (age, body mass index [BMI], gender, Caprini risk score group, and central venous access [CVA] use) of the use of DVT prophylaxis. A multiple linear regression analysis was performed to investigate the relationships between Caprini risk scores and other variables (age, BMI, gender, ethnicity, and CVA use).

The model assumptions (linearity, independence, normality, and homoscedasticity of the residuals) were inspected and examined using scatter plots of residuals versus predicted values, Levene's test for detecting heteroscedasticity of the variances of the residuals, and Shapiro-Wilk test for residuals' normality. No obvious violations of these assumptions were detected.

Data analyses were performed using Stata version 11 (StataCorp. 2009. Stata Statistical Software: Release 11; StataCorp LP, College Station, TX). The limit of significance was set at 0.05.

RESULTS

Characteristics of study participants

Initially, 60 patients were recruited for the study as per inclusion criteria. However, five patients had to be excluded due to

procedural cancellation. All of them underwent preoperative ultrasonographic assessment of the bilateral lower limbs' deep vein system, including the common femoral, superficial femoral, and popliteal veins by two radiologists, and the scan was repeated by the same radiologists on postoperative day 4. Those who had their operation postponed or canceled were excluded; hence, no follow-up ultrasonographic scan was performed on them.

Table 1 shows characteristics of study participants. In total, 55 patients (25 males and 30 females) were included in the study. The mean age of the study participants was 51.3 years (SD, 15.18). Their mean BMI was 25.7 kg/m² (SD, 4.62).

Nearly two-third of the patients (63.6%) did not use any form of CVA, whereas for those who had it, internal jugular vein (IJV) catheter placement was the main type of CVA (80%).

With respect to DVT prophylaxis, 76.5% of the patients did not receive any mode of DVT prevention. Among those who received it, TDS was the main form of DVT prophylaxis (46.2%).

With regard to the Caprini risk-assessment score for VTE, the mean score was 6.0 (SD, 2.72; range = 3–13). More than two-third of study participants belonged to the high-Caprini risk score group (Caprini risk score > 4).

Surprisingly, the incidence of sDVT in postsurgical subjects is 0%. As a result, the population estimate of the incidence of sDVT (95% confidence interval of sDVT incidence) could not be measured. Besides, the association between sDVT and Caprini risk score groups could also not be statistically tested due to the absence of sDVT cases in this study cohort.

Associated factors for the use of DVT prophylaxis

Table 2 shows the associated factors for the use of DVT prophylaxis. Using simple logistic regression, there was an association between high-Caprini risk score group and the use of DVT prophylaxis ($P = .016$). Subjects with high Caprini risk score (Caprini risk score > 4) have 8.16 (95% CI, 1.01–68.7) times the odds of being treated with any form of DVT prophylaxis compared with those with low or moderate Caprini risk score. This concurs to our best practice guidelines that are published several months after the completion of this prospective study.²²

Apart from that, the use of CVA has been identified as one of the determinants for DVT prophylaxis (odds ratio, 6.34; 95% CI, 1.62–24.80; $P = .008$). Age, gender, and BMI groups were not associated with the use of DVT prophylaxis. Therefore, the Caprini risk score and the presence of CVA are the significant predictor factors for the use of DVT prophylaxis. In the Caprini risk score, there is no predictor factor for CVA usage. This could also be a confounding bias as the patients with CVA usually are nursed at critical care unit and immobilized; hence, their score will usually be higher.^{7,22,23} However, there is no sDVT detected in our cohort.

Relationship between age, BMI, gender, ethnicity and CVA use, and the Caprini risk scores

There was a significant moderate correlation between the age of study participants and continuous Caprini risk scores (Pearson's $r = 0.34$, $P = .026$). Based on the multiple linear regression analysis, one unit increase in the age of study participants is significantly associated with a 0.06 (95% CI, 0.02–0.11) unit increase in the Caprini risk scores.

TABLE 1

THE DISTRIBUTION OF BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS (N = 55)

| Variables | Distribution |
|---|--------------|
| Age (y), mean (SD) | 51.3 (15.18) |
| BMI (kg/m ²), mean (SD) | 25.7 (4.62) |
| Gender, n (%) | |
| Male | 25 (45.5) |
| Female | 30 (54.5) |
| Ethnicity, n (%) | |
| Malay | 52 (94.5) |
| Chinese | 3 (5.5) |
| Central venous access (CVA), n (%) | |
| Yes | 20 (36.4) |
| No | 35 (63.6) |
| CVA types*, n (%) | |
| Nil | 35 (63.6) |
| IJV | 16 (29.1) |
| Subclavian | 3 (5.5) |
| Femoral | 1 (1.8) |
| DVT prophylaxis, n (%) | |
| Yes | 13 (23.6) |
| No | 42 (76.4) |
| DVT prophylaxis type [†] , n (%) | |
| Nil | 42 (76.4) |
| PCC | 4 (7.3) |
| TDS | 6 (10.9) |
| Combined modes | 3 (5.5) |
| Disease status, n (%) | |
| Non-cancer-related diseases | 31 (56.4) |
| Cancer-related diseases | 24 (43.6) |
| Surgery duration (h), median (IQR) | 4 (3.83) |
| Caprini risk score | 6.0 (2.72) |
| Caprini risk score group, n (%) | |
| High (>4) | 37 (67.3) |
| Low/moderate (≤4) | 18 (32.7) |

SD = standard deviation; BMI = body mass index; IJV = internal jugular vein; DVT = deep vein thrombosis; PCC = pneumatic calf compression pump; TDS = thromboembolic deterrent stocking; IQR = interquartile range.

*IJV percentage as the main CVA (80%).

[†]TDS as the main mode of DVT (46.2%).

With respect to the use of the statistical relationship between CVA and Caprini risk scores, there was a significant good correlation between these two variables (Spearman's $\rho = 0.74$,

TABLE 2

FACTOR ASSOCIATED WITH THE USE OF DEEP VEIN THROMBOSIS (DVT) PROPHYLAXIS FROM SIMPLE LOGISTIC REGRESSION ANALYSES (N = 55)

| <i>Variables</i> | <i>β (S.E.)*</i> | <i>OR (95% CI)†</i> | <i>LR Statistics (df)‡</i> | <i>P value</i> |
|--------------------------|------------------|---------------------|----------------------------|----------------|
| Age | 0.01 (0.02) | 1.01 (0.97–1.06) | 0.38 (1) | .538 |
| BMI category | | | | |
| Low (<25) | | 1.00 | | |
| High (≥25) | 1.57 (1.10) | 0.48 (0.56–41.1) | 2.85 (1) | .091 |
| Gender | | | | |
| Male | | 1.00 | | |
| Female | 0.38 (0.65) | 1.46 (0.41–5.18) | 0.34 (1) | .561 |
| Caprini risk score group | | | | |
| Low/moderate | | 1.00 | | |
| High | 2.10 (1.09) | 8.16 (1.01–68.74) | 5.80 (1) | .016 |
| CVA use | | | | |
| No | | 1.00 | | |
| Yes | 1.85 (0.70) | 6.34 (1.62–24.80) | 7.75 (1) | .008 |

BMI = body mass index; CI = confidence interval; CVA = central venous access; OR = odds ratio; S.E. = standard error; LR = likelihood ratio.

Bold indicates statistical significance.

*Regression coefficients (standard errors).

†Odd ratio (95% confidence interval).

‡Likelihood ratio statistics (degree of freedom).

$P < .001$). Based on the multiple linear regression analysis, the use of CVA can result in an increment of Caprini risk score by 4.19 (95% CI, 3.16–5.21) unit.

No significant association was found between BMI groups, gender, ethnicity, and Caprini risk scores. Therefore, age and the presence of CVA are the significant predictor factors for Caprini risk scores (Table 3).

DISCUSSION

From the study, we noticed that we have found no incidence of sDVT among the study subjects. This may be because of over judicious usage of mechanical and pharmacological DVT as thromboprophylactic measure. During the study period, the usage of DVT prophylaxis is upon discretion of the treating physician. The national guidelines of DVT were only developed after the study period; hence, the standardized recommendation of best practice was not followed strictly.²²

Every 7 out of 10 selected patients have the Caprini risk scores of high-risk groups. Despite this adverse prognostic outlook, we were not been able to detect any single sDVT case in this study cohort. This is a good indicator that we have been offering an effective and optimal measure to prevent this dreaded postoperative complication. This claim is further corroborated by the results of this study which demonstrated that those with Caprini risk score above 4 were 8.16 times more likely to receive

DVT prophylaxis than those with Caprini risk score of 4 or less. As a result, it can be asserted that those with high risk of sDVT have been properly identified, and the prophylactic measures for DVT have promptly been instituted, resulting in 0% incidence of DVT.

In the current practice, the pharmacological DVT prophylaxis are recommended for five to seven days postoperatively until the patient be able to ambulate significantly, and the extend pharmacological DVT prophylaxis are recommended for up to 28 days postoperatively for patients who have had a major surgery to the abdomen or pelvis.²² From our study, 76% did not receive any form of prophylaxis, and we were not able to detect any incidence of sDVT. This may not be the best practice, but perhaps we should relook into the indication of DVT prophylaxis rather than liberal usage of DVT prophylaxis in all major surgery patients. The current clinical practice would concur us to use DVT prophylaxis liberally.

The method of DVT prophylaxis used in this study is early mobilization that takes the form of either mechanical (intermittent pneumatic calf pump and TDS) or pharmacological approaches (daily subcutaneous fondaparinux or twice daily subcutaneous heparin injection). As our practice is geared toward the concept of enhanced recovery after surgery, we managed to mobilize most of our patients within the first four days during the postoperative periods. Comparing this to a Japanese cohort who had major orthopedics surgery, they noted 58.3% of their

TABLE 3

MULTIPLE LINEAR REGRESSION ANALYSIS—ASSOCIATED FACTORS FOR HIGH CAPRINI RISK SCORES (N = 55)

| <i>Variable</i> | <i>β (S.E.)*</i> | <i>95% CI of β</i> | <i>t Statistics (df)</i> | <i>P Value</i> |
|-----------------|------------------|--------------------|--------------------------|-----------------|
| Age | 0.06 (0.02) | 0.02 to 0.11 | 2.35 (1) | .026 |
| BMI category | | | | |
| Low (<25) | | - | | |
| High (≥25) | 0.10 (0.08) | -0.06 to 0.26 | 1.03 (1) | .233 |
| Gender | | | | |
| Male | | - | | |
| Female | -1.33 (0.73) | -2.77 to 0.12 | -1.84 (1) | .071 |
| Ethnicity | | | | |
| Malay | | - | | |
| Non-Malay | -1.80 (1.61) | -5.03 to 1.42 | -1.12 (1) | .268 |
| CVA use | | | | |
| No | | - | | |
| Yes | 4.19 (0.51) | 3.16 to 5.21 | 8.22 (1) | <.001 |

CI = confidence interval; BMI = body mass index; CVA = central venous access; S.E. = standard error.

Bold indicates statistical significance.

*Regression coefficients (standard errors).

cohort developed silent DVT on postoperative day four despite giving pharmacological thromboprophylactic agent.¹³ The early mobilization measures would have contributed drastically in preventing the formations of DVT as part of preventing stasis in the vessels.

From the results, it was realized that more than one-third of our patients have a central venous catheterization due to the requirement of invasive hemodynamics' monitoring. However, none of them developed sDVT. One possible mechanistic explanation for this is that the majority of CVA was inserted at IJV, thereby negating the possibility of DVT development in the lower limb. On the contrary, the blood flow in the IJV is more constant and less viscous because of the regular heparin flushing, which explains the reason why venous thrombosis is less likely to occur.²⁴ Hence, this would conclude the formation of DVT, and the disease is due to the dynamic interplay between multiple factors within the web of causality.

We were unable to reproduce the results similar to those of the Japanese patients who have undergone total hip or knee replacements.¹³ In those patients, all had pharmacological form of DVT prophylaxis, and they have found an incidence of 58.3% at day 4 after operation. This could be accountable as they do a detailed ultrasonographic scan down to the distal deep vein system, namely below the popliteal vein and calf veins. The majority of their silent deep vein thromboses are found at the calf veins.¹³ As for our study, we emphasize on the proximal deep vein systems as they cause more catastrophic clinical sequelae of PEs.²⁵ The ultrasonographic scans of the distal deep vein systems are more challenging, and they are not readily compressible compared to those proximal ones, hence, they are more tech-

nically demanding to perform. The reported sensitivity of ultrasound scan to detect distal DVT was only 63.4% compared with 94.2% for proximal DVT.¹⁹

Tun et al published an observational study over a 30-month period (1998–2001) of a total of 54 postoperative major surgery patients with no VTE prophylaxis given.¹² In their study, they managed to detect a symptomatic DVT on day 3 and an sDVT on day 7.¹² However, the similar methodology and results were not reproducible because of several ethical issues. First, it would be unethical not to start any forms of VTE prophylaxis either in a form of mechanical or pharmacological approach in today's era of practice, especially in those who are at high risk of VTE. Second, we were doubtful of a selection bias among the patients who he has recruited over the 30-month period, as we would expect to have more surgical patients operated over that period of time, as it is the referral center.

In our center, there is no standardized protocol on VTE prophylaxis among the major surgery patients at the time of the study period. The commencement of VTE prophylaxis is up to the discretion of the managing team surgeons. However, if we look into the Japanese study by Yamaguchi et al, they reported an incidence of sDVT of 27.1% among those who were given thromboprophylactic agent of fondaparinux at day 4 of the postoperative period.¹³ Therefore, the administration of thromboprophylactic agents does not exclusively protect one from getting sDVT. This draws to the conclusion that the pathogenesis of VTE is of a multifaceted nature. It does not fully comply with Virchow's triads. However, the presence of the Virchow's triad does increase the risk of venous thromboembolic events.

A Caprini's risk-assessment tool can assist clinicians to risk stratify the patient, providing them with a better understanding on risk of VTE and the judicious use of the thromboprophylactic agents.^{7,14} In our center, we do not provide the graduated compression stockings because of financial constraints, but we will indefinitely advise our patient to purchase them from the local pharmacy, should we feel that the patient is at high risk of developing VTE postoperatively. However, some of the patients who are at high risk of DVT had been given an anticoagulant (fondaparinux) based on the surgeon's discretion as a mean of pharmacological thromboprophylaxis. This is a negative study; hence, the Caprini risk score could not be validated in terms of its predictive capability for accurate identification of patients who are at high risk of developing sDVT. With this scoring system, we can always justify the advice and the prophylaxis given to the patient with regard to the VTE, should there be a rise of any forms of legal implications.

From the results, it can be clearly seen that the presence of central venous catheter is a stronger factor for high Caprini risk scores, as evident from the larger magnitude of Caprini risk score increment if central venous catheter is present than if age increases by 1 year (β coefficient = 4.19 vs 0.06). Besides, the correlation between the presence of central venous catheter and Caprini risk score is much higher than that between age and Caprini risk scores (Spearman's $\rho = 0.74$ vs Pearson's $r = 0.34$). However, this finding adds another interesting fact to how Caprini risk score should be calculated. From the regression analysis, the presence of central venous catheter will result in a 4-point increment in Caprini risk scores. This runs contra to the number of points allotted to the presence of CVA catheter, which is two, in the present method of calculating Caprini risk scores. Hence, it is advisable that future studies should be conducted to further consider this issue.

This is a study confined to a single referral center. Owing to the rarity of sDVT, this single-center study may not be sufficiently powered to accurately obtain the true estimate of the incidence of sDVT among the major postoperative surgical patients in Malaysia. Besides, this study is only conducted for a very short follow-up period. It has been shown by Bahl et al¹⁴ that venous thromboembolic events can occur up to 30 days postoperatively or even up to 90 days according to Seruya et al.²⁶ Consequently, the incidence of sDVT occurring in outpatient setting cannot be properly captured, leading to a further underestimation of true incidence of sDVT in our population setting.

This study included all patients who underwent a major surgery that is defined as any procedure lasting more than 45 minutes, either an open surgery or minimally invasive surgery. Owing to the short duration of the study, we were not able to truly select the very high-risk groups and study the incidence of occurrence of sDVT among them. With regard to the combination of the ultrasound venous duplex scan with the conventional compressive ultrasound scan, the sensitivity is improved especially when detecting deep system of the calf.^{19,25} A more detailed scan including the distal deep vein system may yield a different result at an expert center. However, this is a meticulously tedious exercise that may show a research benefit but does not address the need of the clinical benefits. The aim of treatment of DVT is to prevent an embolic event to the

pulmonary artery. There is only a substantial amount of distal DVT that progresses to proximal DVT, and 90% of proximal DVT resolves with recanalization and collateral formation without progressing to a catastrophic PE if treated early.

Future studies should include multiple referral centers using the same criteria for patient selection, especially the nearby district general hospital and the general hospital that provides surgery services. This would strengthen the validity and the value of the study, should it yield the same results. Apart from that, a longer follow-up period is needed in view of the high probability of sDVT occurrence at 30 days or later postoperatively. A more stringent selection criterion using the Caprini risk score of more than 3 only and exclusion of all nonmalignant surgical diseases are advocated for the future studies. This would enable a much more judicious use of pharmacological and mechanical thromboprophylaxis measures. At the interest of a thrombosis research, more detailed scans should be performed to see the incidence of occurrence of sDVT at the distal deep vein system and followed by a repeated scan in a week time should it be present to see for thrombosis progression as commented in the clinical practice guidelines. However, this selection criterion will incur much ethical conflicts in view of ambiguity of treatment of distal DVT.

CONCLUSION

From this study, we found that there is no subject with any sonographic evidence of sDVT detected. Hence, the incidence rate of sDVT in this cohort is 0%. Owing to the negative findings, the Caprini risk-assessment scoring system could not be validated in terms of its predictive scoring for developing sDVT. The negative results also asserted that those with high risk of sDVT have been properly identified, and the prophylactic measures for DVT have promptly been instituted, resulting in 0% incidence of DVT.

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