



Experimental Research

The necessity of routine screening for deep vein thrombosis before surgery



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ABSTRACT

Background: Pulmonary embolism (PE) from deep venous thrombosis (DVT) can be a fatal postoperative complication. Preventive measures for venous thromboembolism (VTE) was evaluated in this hospital.

Materials and methods: Preoperative DVT screening following surgery under general anesthesia in 2009–2016 was examined, and then, 217 patients diagnosed with DVT by preoperative leg-ultrasound (US) between 2014 and 2016 were retrospectively analyzed.

Results: There were 24,826 operations under general anesthesia in the study period. Preoperative leg-US was performed in 5345 (21.5%) patients, and 648 (12.1% of patients, 2.6% of total operations) were diagnosed with DVT. In 2014–2016, 217 patients, which is 11.7% of patients undergoing leg-US, were diagnosed with DVT. DVT was found in the proximal veins (upper popliteal vein) in 86 (39.6%) patients. A total of 143 (62%) patients were considered to have organized thrombi, no patient developed pulmonary embolism, and 133 (58%) patients were discharged without follow-up examination for DVT. Ninety-six patients were evaluated for changes on leg-US, with no difference in the results with and without anticoagulant use. On multivariate logistic regression analysis, anticoagulants appeared effective for non-organized thrombi, higher D-dimer levels (≥ 10 $\mu\text{g/mL}$), or orthopedic surgery.

Conclusion: Preoperative screening for DVT did not appear useful, and treatment of asymptomatic DVT was not always necessary.

1. Introduction

The incidence of perioperative symptomatic pulmonary thromboembolism (PSPTE) is 2.2–4.4 per 10,000 cases, with the number of PSPTE cases and the fatality rate reported to have decreased in the past 10 years in Japan [1]. Guidelines of the National Institute for Health and Care Excellence recommend mechanical prophylaxis of venous thromboembolism (VTE), such as anti-embolism elastic stockings (ES), foot impulse devices, and intermittent pneumatic compression (IPC) devices, for patients who undergo gastrointestinal, gynecological, thoracic,

urological, and neurological (cranial or spinal) surgery [2–4]. Although adding pharmacological VTE prophylaxis for patients who have a low risk of major bleeding has been recommended, it is difficult to judge whether the risk of major bleeding is low. For orthopedic surgery (elective hip or knee replacement and hip fracture), VTE prophylaxis could be performed using edoxaban, fondaparinux, or low-molecular-weight heparins (LMWHs, enoxaparin) in Japan. However, there is no contraindication to initiating pharmacological VTE prophylaxis several hours before and after surgery.

We organized a working group for the prevention of death from acute

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pulmonary thromboembolism in 2008 and analyzed the data for 8 years. This study primarily aimed to evaluate the results of screening for preoperative deep vein thrombosis (DVT). The secondary aim was to assess the development of postoperative VTE with or without subsequent additional pharmacological prophylaxis in addition to routine mechanical prophylaxis.

2. Materials and Methods

2.1. Study design and data collection

This was a single-institution, case-control study approved by the Institutional Review Board (R201604-02). This study has also been registered in the Research Registry with the number 'UMIN000046740' (https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?receptno=R000053271). The study was performed in accordance with the ethical standards laid down in the most recent version of the Declaration of Helsinki. The need for written informed consent was waived, and brief information on this study was disclosed on the hospital website to guarantee a patients' opportunity to refuse their participation in the study (opt-out method). The work has been reported in the line with the STROGSS criteria [5].

The patient records/information was anonymized and de-identified before analysis. The total number of patients who underwent surgery under general anesthesia between 2009 and 2013 in Saku Central Hospital and between 2014 and 2016 in Saku Central Hospital Advanced Care Center, Japan, was 24,826. Of the patients who planned to have surgery under general anesthesia, 5345 underwent an ultrasound of the leg (leg-US) to examine for DVT after D-dimer screening.

In 2008, we participated in the Japanese collaborative action for safe medical treatment, in which we aimed at the reduction of mortality from VTE. One of the main endeavors was the prevention of VTE after surgical treatment, and another challenge was the early detection and screening tests before surgery. We then began D-dimer screening for perioperative patients.

All patients who planned to undergo surgery under general anesthesia were referred to the perioperative examination and care center in the hospital, and the VTE risk score was evaluated according to the Japanese Thrombosis Association guidelines for diagnosis, treatment, and prevention of pulmonary thromboembolism and deep vein thrombosis (Japanese Circulation Society 2017) [2]. Patients at intermediate to higher risk for VTE were managed using ES or IPC devices in the postoperative period, and additional anticoagulant medications (heparin calcium) were recommended for high-risk patients. As there was concern that thrombus might float up into the pulmonary artery by IPC during the perioperative period if DVT was found before the operation, DVT screening was performed preoperatively and ES, not IPC, was used more commonly for PE prophylaxis.

First, the measurement of D-dimer was initiated, a cut-off value was not clearly defined, and the number of patients with values more than 3.0 µg/mL was selected. For approximately 10% of all test samples, whole leg-ultrasound (US) could be performed in our examination room. Patients whose D-dimer was greater than 3.0 µg/mL underwent leg-US to check for thrombus in the femoral, popliteal, saphenous, or soleus muscle (soleal) vein. However, the D-dimer test was discontinued due to an inspection by the medical insurance regime in 2011, and since then, only leg-US without d-dimer screening has been performed for almost all patients indicated as preoperative screening according to risk evaluation. If DVT into the femoral vein was found, enhanced computed tomography was ordered, and a cardiologist was consulted. If DVT was found in the distal popliteal vein, an IPC device was prohibited.

2.2. Analysis of the outcomes of DVT cases

The medical records of the 217 patients who were diagnosed with DVT using leg-US between 2014 and 2016 were analyzed

retrospectively. In all general anesthesia surgery cases, DVT echo selection criteria were set by the evaluation score of each department of surgery and risk score as follows: predicted operation time, age over 60 years, operation for patients with cancer, prior VTE, preoperative bed rest over 48 h (recumbency), and edema of lower limbs or swollen legs. Leg-US was performed by a laboratory technician and the result with detailed findings including organized thrombus when it appeared hyperechoic and stuck, and pictorial images were reported to surgeons. The prevention method was selected by each surgeon and the mechanical method (ES or IPC) was performed with/without a therapeutic dose of anticoagulants if DVT was found. The location of the thrombus was assigned to the most proximal vein if multiple thrombi were detected. The use of anticoagulant agents (yes/no), the frequency if used, and the performance if a follow-up examination within 3 months after the operation were examined. In Japan, although only edoxaban is approved DOAC for prophylaxis for DVT in orthopedic surgery, 217 cases were diagnosed with DVT and another DOAC (rivaroxaban, apixaban) also could be used. The mortality rate and the need for intensive care due to PE before discharge from the hospital were also investigated.

2.3. Statistical analysis

The Mann-Whitney *U* test was used to examine differences in continuous variables, and the chi-square test was used for categorical variables. Multivariate logistic regression analysis was performed to identify significant clinicopathological variables to differentiate improvement of thrombi using leg-US, in which each variable had a *p*-value <0.1. For analyses, *p* < 0.05 was considered significant. JMP software (13.1.0, SAS Institute, Cary, NC, USA) was used for all analyses.

3. Results

3.1. Screening for DVT before surgery

In 2009, the first year of DVT screening, D-dimer screening with a cut-off value of 3.0 µg/mL was initiated, and 341 patients (11.5% of cases planned for surgery under general anesthesia) were screened as leg-US candidates. Shortly after, more than 30% of all surgical cases were screened using leg-US independently of the D-dimer values according to their risk evaluation. Moreover, D-dimer screening was discontinued in the latter 4 of the 8 years due to an inspection by the medical insurance regime. Approximately 9.5%–18.4% of tested cases (1.4–4.0% of all surgical cases underwent general anesthesia) were diagnosed with DVT, and the results were independent of D-dimer screening (Suppl. Fig. 1). Over the 8 years, a total of 5345 patients underwent leg-US, and DVT was found in 648 patients (12.1%). In this period, no deaths due to postoperative PE were reported.

3.2. Prognosis of patients who underwent surgery with DVT

Next, the prognosis of patients with DVT diagnosed preoperatively by leg-US between 2014 and 2016 was examined. In this period, 1849 of the total 10,346 patients who underwent surgery under general anesthesia were examined using leg-US, and 217 patients (11.7%) were diagnosed with DVT.

The demographic characteristics of the patients analyzed in this study are shown in Table 1. When DVT location was divided into two groups (proximal type for the external iliac, femoral, or superficial femoral veins; or distal type for popliteal, gastrocnemius, or soleal veins) with 74 being of the proximal type and 154 of the distal type. The most common location of DVT was the soleal vein (53.7%), followed by the femoral vein (22.1%). Overall, 70% of patients were operated on at the department of digestive or general surgery and department of orthopedic surgery. Laboratory technicians recorded the thrombus as organized thrombus when it seemed hyperechoic and stuck; 136 cases (62.7%) were determined to be organized thrombi. D-dimer was measured in 171

Table 1
Demographic characteristics of 217 patients with positive US screening for DVT.

Variable	No. Of patients
Age (y)	29-95 (median 78)
Sex	
Female	123
Male	94
Leg Side	
Bilateral	53
Right	84
Left	80
DVT position	
Central (above popliteal vein)	86
External iliac vein	2
Femoral vein	48
Superficial femoral vein	18
Popliteal vein	18
Peripheral	131
Gastrocnemius vein	8
Soleal vein	123
Surgical categories	
Digestive and general surgery	78 (2.5%)
Orthopedic surgery	73 (4.2%)
Cardiovascular surgery	16 (1.7%)
Plastic surgery	11 (2.2%)
Urology	8 (2.9%)
Neurosurgery	7 (2.9%)
Obstetrics and gynecology	7 (1.4%)
Breast/Respiratory	5/2 (1.1/0.4%)
Thyroid/Otolaryngology	1/1 (0.6/0.1%)
ESD/Nephrology/others	1/4/3 (0.6/12.5/25%)

US: ultrasound, DVT: deep venous thrombosis, ESD: endoscopic submucosal dissection, * (frequency (%) of occurrence in each surgery).

patients; the mean value was 12.7 µg/mL, and the median was 5.9 µg/mL. It was found that 28.7% of patients with DVT had a low D-dimer level (<3 µg/mL), and the same number of patients had a high D-dimer level (>10 µg/mL). The D-dimer level of all patients with DVT varied; thus, DVT was not necessarily associated with D-dimer elevation (Fig. 1).

Of the total 217 patients, all were managed using anti-embolism ES; and 111 patients took anticoagulants: 44 heparin with/without warfarin, 21 fondaparinux, 18 enoxaparin, 12 therapeutic doses of direct oral anticoagulants (DOACs; edoxaban, rivaroxaban, apixaban), eight warfarin only, and eight other consumed oral antiplatelet

medications (aspirin, clopidogrel). The treatment period for heparin, fondaparinux, or enoxaparin in 83 patients was 1–60 days (median 6 days), and 52% of the patients subsequently received warfarin or DOACs in therapeutic doses. Fig. 1 and Table 2 show that there was no selection bias in anticoagulant agent use, such as the D-dimer level and organized thrombus, except for proximal thrombus and no malignant disease.

Follow-up leg-US was performed in 88 patients to determine whether there was an improvement or no change after several days or months. Although 129 patients did not undergo follow-up examination, no patient developed PE or died. Of the follow-up patients, 40 patients were considered improved, whereas 48 showed no change. Moreover, the numbers with improvement and without change were not very different in all categories, including with or without medications, and any kinds of medications except fondaparinux (Table 3). The chi-square test examining the category related to improvement on the follow-up leg-US also showed that anticoagulant use for DVT discovered before surgery was not related to shrinkage of thrombi. In this analysis, significant differences in thrombus improvement were found for DVT with non-organized thrombus, orthopedic surgery, cases with D-dimer elevation, and fondaparinux use (Table 4). Multiple logistic regression

Table 2
Categories of medical intervention for patients with VTE risk.

Anticoagulant	Yes	No	P
	103	114	
Sex			0.5133
Female	56	67	
Male	47	47	
Age (y)			0.5566
≤78	51	61	
>78	52	53	
Site			0.0047
Proximal	51	35	
Distal	52	79	
Bilateral			0.9605
Bilateral	78	86	
Unilateral	25	28	
Organizing			0.4730
–	41	40	
+	62	74	
Surgery			0.0926
Orthopedic	40	32	
Others	63	82	
Malignancy			0.0188
Cancer	31	52	
Benign	72	62	
D-dimer ^a (µg/ml)			0.8004
<10	62	57	
≥10	26	26	

VTE: venous thromboembolism.

^a D-dimer was determined for 171 cases.

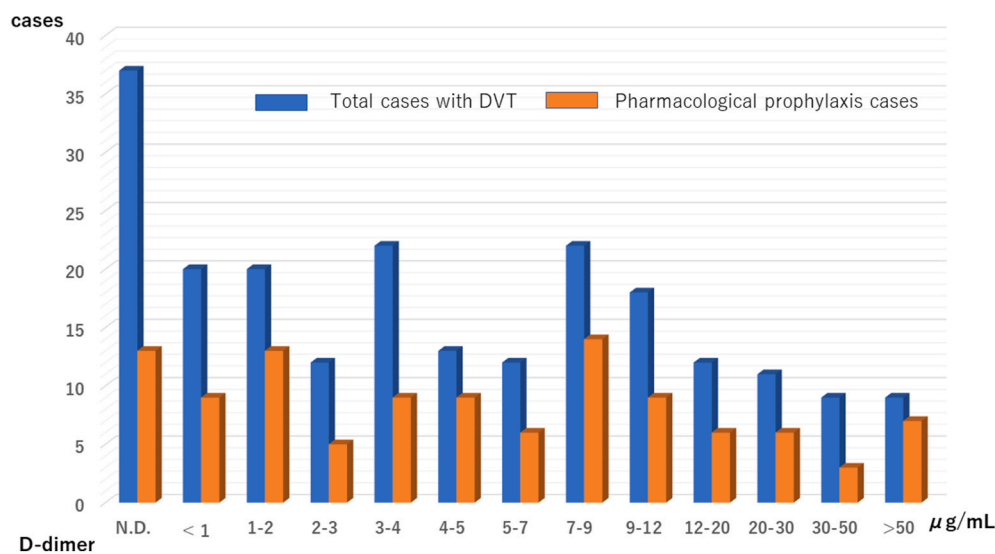


Fig. 1. D-dimer levels before operation of 217 deep vein thrombosis (DVT) cases between 2014 and 2016. Blue column: number of DVT diagnoses Orange column: cases of pharmacological prophylaxis for DVT. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Outcomes after medical intervention for patients with VTE risk.

Prognosis	Improved	No change	No follow-up	Total
No medication	40	48	129	217
Antiplatelet ^a	13	15	78	106
Anticoagulant	1	1	6	8
Fondaparinux	26	32	45	103
Enoxaparin	13	5	3	21
Heparin	2	6	10	18
DOAC	7	14	23	44
Warfarin	3	6	3	12
	1	1	6	8

VTE: venous thromboembolism, DOAC: direct oral anticoagulant (edoxaban, rivaroxaban, apixaban).

^a Antiplatelet: aspirin, clopidogrel, cilostazol.

Table 4
Chi-squared test for improvement of DVT on follow-up (total 88 cases).

Prognosis		Improved	No change	P
Sex	Female	40	48	0.9371
	Male	23	28	
Age (y)	≤78	19	25	0.6685
	>78	21	23	
Site	Proximal	18	20	0.7533
	Distal	22	28	
Bilateral	Bilateral	9	18	0.1287
	Unilateral	31	30	
Organizing	-	22	12	0.0040
	+	18	36	
Surgery	Orthopedic	29	13	<0.0001
	Others	11	35	
Malignancy	Cancer	7	19	0.0238
	Benign	33	29	
D-dimer (µg/ml)	<10	14	30	0.0018
	≥10	20	9	
Anticoagulant use	-	14	16	0.8695
	+	26	32	
Injection duration (days)	<4	23	32	0.3765
	≥4	17	16	
Fondaparinux	Yes	13	5	0.0106
	No	27	43	

DVT: deep venous thrombosis

analysis to identify clinical variables related to DVT shrinkage identified non-organized thrombus, D-dimer >10 µg/mL, and orthopedic surgery as significant (Table 5). Pharmacological prophylaxis such anticoagulant was not related to DVT improvement; however, might be useful for DVT with the findings described above.

4. Discussion

In this study, the avoidance deaths caused by acute PE (thrombosis) in our hospital for 8 years was reviewed, and no death was reported. This study aimed to analyze whether screening for DVT was meaningful; and whether asymptomatic DVT found by preoperative testing should be treated. DVT screening is important for VTE prevention; however, recently, screening was not evaluated positively as asymptomatic cases

Table 5
Multivariate logistic regression analysis to identify clinicopathological variables related to DVT shrinkage.

Variable	Odds ratio	95%CI	p-value
Organized, No/Yes	4.614	1.469–16.13	0.0084
D-dimer, >10/≤10 µg/ml	3.595	1.098–12.61	0.0343
Orthopedic surgery/others	6.528	1.466–38.80	0.0127
Malignancy, Yes/No	2.025	0.378–13.45	0.4174
Fondaparinux, Yes/No	1.969	0.457–8.957	0.3622

DVT: deep venous thrombosis

were observed with unexpected frequency.

In these cases, the D-dimer levels varied widely, and they were often high, particularly in cardiovascular and orthopedic surgery cases. Sun reported that 86.4% of patients with stroke had a D-dimer level of 500 ng/mL, and 9.5% were diagnosed with DVT using US [6]. Osaki reported that the incidence of DVT was 4.4% (7/160) and 7.2% (11/153) before and after gastric cancer surgery, respectively [7]. A multinational Asian study based on postoperative screening reported a VTE incidence comparable to that reported in Western patients [8].

The second concern was whether anticoagulants should be used after surgery, and the answer might be “no.” Heparin was used safely based on the surgeon’s decision in some cases, and no use of medication might be selected with a report of organized thrombus. Some patients might be rescued from PE by injection of anticoagulant agents; however, no patient was reported to be admitted to an intensive care unit even if no medication was given for preoperatively identified DVT or no follow-up examination was performed. Nakagawa et al. reported a randomized, controlled study for preventing VTE after laparoscopic colorectal cancer surgery with or without enoxaparin [9]. There was no difference in the incidence of VTE between the enoxaparin group (12.3%) and the IPC group (11.9%). Enoxaparin was initiated 24–36 h after surgery and skipped on the morning of removal of the epidural catheter 2 or 3 days after surgery. Epidural anesthesia after surgery is generally performed and concomitant use with anticoagulants is debatable. Another Japanese randomized, controlled study reported that the incidence of VTE in the enoxaparin group was 1.2% [10]. Whether there is a difference in asymptomatic VTE between Japanese and Western populations is controversial [11]. Loh et al. reported that pharmacological prophylaxis in addition to mechanical prophylaxis (IPC pumps) after total knee arthroplasty surgery does not reduce the incidence of VTE [12]. The use of mechanical and pharmacological prophylaxis did not lower the risk of developing DVT (incidence of 5.9% compared with mechanical prophylaxis incidence of 4.6%).

Patients who undergo total knee arthroplasty have been shown to have a high risk for VTE, leading to recommendations in international guidelines to use a combination of mechanical and pharmacological thromboprophylaxis before and after the procedure [13]. Pharmacological thromboprophylaxis of VTE has been recommended to reduce the prevalence of postoperative DVT on that assumption. The practice of routine postoperative pharmacological thromboprophylaxis has primarily been based on Western literature to date, and the recent acknowledgment of studies showing a lower incidence of thromboembolism in Asia has led to questions regarding the need for routine pharmacological thromboprophylaxis for patients undergoing surgery [14]. In contrast, Colwell et al. showed that intermittent pneumatic compressive IPC devices (IPCDs) were just as effective as enoxaparin in preventing proximal and distal DVT and PE events in hip arthroplasty patients; however, resulted in a much lower bleeding risk (1.3% IPCD and 4.3% LMWH) in a multicenter, randomized, controlled trial comparing IPCD to enoxaparin [15]. In this study, postoperative thrombus shrinkage was more common in orthopedic cases. This might be owing to the use of fondaparinux in such cases with adequate treatment duration, without the use of epidural anesthesia with fresh thrombus formation possibly common.

Singh et al. recommended full anticoagulation until the patient is ambulatory or the follow-up duplex scan is negative [16]. In their study, the incidence of clot propagation into proximal veins was approximately 7%. Of the present cases, postoperative PE occurred in cases that did not show preoperative DVT (data not shown), and none of the known DVT cases developed PE.

There are some limitations to the present study. It had a retrospective design, and the study was based on a small sample size with limited medical records. As leg-US was performed to diagnose DVT, the measurement of thrombus size was challenging, and evaluation of remission, whether thrombus was decreased on the follow-up test, was subjective.

5. Conclusion

In conclusion, this analysis showed that routine DVT screening for all surgical patients might not be necessary, and asymptomatic DVT might not always require medical treatment such as anticoagulant agents, although careful management including anticoagulant use is needed for patients following orthopedic surgery, those with a high D-dimer level, and those who occasionally show non-organized thrombus.

Ethical approval

This retrospective study was approved by the Institutional Review Board (R201604-02) and conducted in accordance with the Declaration of Helsinki.

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Authors' contributions

HE, KS, MH, HW, YY: study conception, design, data analysis, and drafting of the manuscript. DU, TT, TS, KF, HI: data collection. HE, KS, MH, YY: interpretation, critical revision of the manuscript. All authors contributed to the article and approved the submitted version.

Trail registry number

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Consent

Not applicable.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

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