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ORIGINAL ARTICLE

Prevalence of deep venous thrombosis detected by ultrasonography before surgery in patients with gastric cancer: a retrospective study of 1140 consecutive patients

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Abstract

Background The prevalence of deep venous thrombosis (DVT) in patients with gastric cancer before surgery is unknown. This study aimed to clarify the risk factors for DVT of the lower extremities in patients with gastric cancer before surgery and to evaluate the usefulness of ultrasonographic screening for prevention of postoperative pulmonary thromboembolism (PTE).

Methods Patients who had undergone lower-extremity venous ultrasonography before surgery for gastric cancer were retrospectively analyzed. Univariate and multivariate logistic regression analyses were performed to identify the predictors of DVT before surgery. Perioperative management of patients with DVTs and the incidence of postoperative PTE were investigated.

Results Of the total 1140 patients, 86 had DVT preoperatively. On univariate analysis, the incidence of DVT was significantly higher with: female sex; age $\geq$80 years; PS $\geq$ 1 (vs. PS = 0); stage IV (vs. stages I–III); history of preoperative chemotherapy; and the presence of a central venous catheter (CVC). Multivariate logistic regression analysis demonstrated that sex, age $\geq$80 years, PS $\geq$ 1, history of preoperative chemotherapy, and the presence of CVC were significantly correlated with DVT before surgery. Postoperative PTE occurred in 2 patients with proximal DVT. No patients in whom DVT was not detected developed PTE.

Conclusions Female sex, older age, worse PS, the presence of CVC, and a history of preoperative chemotherapy were the independent risk factors for DVT. Routine lower-extremity venous ultrasonographic screening is useful for prevention of PTE because it can identify patients at high or low risk for PTE.

Keywords Deep venous thrombosis · Gastric cancer · Pulmonary thromboembolism · Ultrasonography

Introduction

Pulmonary thromboembolism (PTE) is a serious postoperative complication [1], and about 80% of PTEs result from deep venous thrombosis (DVT) of the lower extremities [2]. Therefore, PTE and DVT have been regarded as sequential conditions, and they are grouped and generally called venous thromboembolism (VTE). Many studies have demonstrated the association between cancer and VTE [3–5].

However, only a few studies have focused on the prevalence and risk factors of DVT in patients with gastric cancer, although it is the most common risk factor for PTE. Kang et al. [6] reported the incidence in patients with inoperable advanced gastric cancer. However, their study was not intended for operable gastric cancer. Lee et al. [7] reported the prevalence, risk factors, and prognostic implications of VTE in patients with both operable and inoperable gastric cancer. In their study, the rate of concurrent diagnosis of gastric cancer and VTE was not reported. Furthermore, in these studies, the diagnostic tools

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for DVT and the process for identifying patients with DVT were unclear.

Contrast venography is still the gold standard for the diagnosis of DVT, although it is invasive. Recently, Doppler ultrasonography has been considered a useful tool in the diagnosis of DVT because it is easily accessible, non-invasive, and has high sensitivity and specificity [8, 9]. These reports showed that the sensitivity and specificity of ultrasonography of the leg were similar to those of computed tomography.

Larsen et al. [10] have demonstrated the prevalence and risk factors of DVT before treatment in patients with esophageal, gastroesophageal, and gastric cancer using lower-extremity venous ultrasonography to detect DVT. However, only 129 patients were enrolled in their study, and the covariates used to identify the independent risk factors were limited. In addition, the detailed anatomic distribution of DVTs was not reported.

We have carried out examinations for DVT using lower-extremity ultrasonography before surgery in 1140 consecutive patients, which is a sufficient number for analyzing the risk factors for DVT.

This study aimed to clarify the risk factors for DVT of the lower extremities in patients with gastric cancer before surgery and to evaluate the usefulness of ultrasonographic screening for prevention of postoperative PTE.

Therefore, the prevalence, anatomic distribution, and risk factors of DVT of the lower extremities before surgery were evaluated using lower-extremity ultrasonography in patients with gastric cancer. In addition, the clinical course of each patient was investigated to evaluate whether the presence of DVT was a predictive factor for postoperative PTE.

Materials and methods

This retrospective cohort study was conducted at Shizuoka Cancer Center, Shizuoka, Japan. This study was approved by the institutional ethics committee (27-J95-27-1-3). From May 2010 to December 2013, 1140 consecutive patients underwent lower-extremity venous ultrasonography before surgery for gastric cancer, and the results of these patients were analyzed. Lower-extremity venous ultrasonography was performed at the Ultrasound Unit by clinical technologists (K.N. and M.Y.) who were both trained in the performance of lower-extremity venous ultrasonography and certified as medical sonographers by the Japan Society of Ultrasonographics in Medicine. Neither contrast venography nor computed tomographic venography of the leg was performed.

According to the Japanese Guideline for Prevention of Venous Thromboembolism [11], most patients with gastric cancer are classified in the high-risk group for postoperative DVT. For high-risk group patients, physical treatments such as intermittent pneumatic compression or anticoagulant therapy are recommended in the guidelines. Therefore, in this study, for patients in whom DVT was not detected, graduated compression stockings and intermittent pneumatic compression were used from the morning of surgery until the patient was able to walk adequately. Patients with distal DVT were generally given anticoagulant therapy using low molecular weight heparin (LMWH) or fondaparinux. For patients in whom proximal DVT was detected, as a rule, a retrievable inferior vena cava filter (IVCF) was placed before surgery.

Clinicopathological data of the patients were retrieved by retrospective review of patient medical charts. The description of the cancer and the histological evaluation of the resected specimens were in accordance with the 7th TNM classification of malignant tumours [12]. Performance status (PS) was assessed using the scale of the Eastern Cooperative Oncology Group (ECOG) [13].

Statistical analysis was carried out using JMP version 8.0 for Windows (SAS Institute, Cary, NC, USA). The chi-square test was used to evaluate differences between demographic and categorical parameters. The Mann–Whitney U test was used to compare differences in quantitative parameters, and multivariate analysis was performed with multiple logistic analyses. A level of $p < 0.05$ was taken as significant. The probability of occurrence of postoperative PTE was estimated with 95% confidence intervals (95% CI) based on the Wilson score method.

Results

Patient characteristics

A total of 1140 patients (798 men, 342 women) were included in this study. The median time between the date of ultrasonography and surgery was 23 days (1–144 days). The patients ranged in age from 24 to 95 years, with a median age of 69 years. Patient characteristics are summarized in Table 1.

Prevalence and anatomic distribution of DVT

Of the 1140 patients, 86 (7.5%) were found to have DVT preoperatively, and all patients with DVT were asymptomatic. Six patients had only proximal DVT (thrombosis involving the popliteal vein and above), and 75 patients had only distal DVT; 5 patients had both proximal and distal DVTs. The anatomic distribution of DVT is shown in Table 2. The most common site of DVT was the soleal veins, followed by the peroneal veins, posterior tibial veins,

Table 1 Characteristics of the study population with gastric cancer

Clinicopathological factor	No. of patients (%)	
	($n = 1140$)	
Age (years)		
<60	236	(20.7)
60–69	369	(32.4)
70–79	416	(36.5)
≥80	119	(10.4)
Sex		
Male	798	(70.0)
Female	342	(30.0)
PS (ECOG)		
0	1001	(87.8)
1	118	(10.4)
≥2	21	(1.8)
Body mass index (kg/m^2)		
<25	895	(78.5)
≥25	245	(21.5)
Stage		
I	560	(49.1)
II	183	(16.1)
III	209	(18.3)
IV	188	(16.5)
Previous chemotherapy		
Present	50	(4.4)
Absent	1090	(95.6)
Hypertension		
Present	468	(41.1)
Absent	672	(58.9)
Hyperlipidemia		
Present	212	(18.6)
Absent	928	(81.4)
Chronic heart disease		
Present	91	(8.0)
Absent	1049	(92.0)
Smoking		
Smoker	285	(25.0)
Non-smoker	855	(75.0)
Administration of steroids		
Present	9	(0.8)
Absent	1131	(99.2)
Lower-extremity varicose veins		
Present	64	(5.6)
Absent	1076	(94.4)
Central venous catheter		
Present	23	(2.0)
Absent	1117	(98.0)
Leg paralysis		
Present	11	(1.0)
Absent	1129	(99.0)

PS performance status, *ECOG* Eastern Cooperative Oncology Group

Table 2 The anatomic distribution of deep venous thrombosis (DVT)

Distribution of DVT	Right	Left	Total	
Distal type			80	(7.0%)
Soleal vein	45	50		
Posterior tibial vein	7	0		
Peroneal vein	4	4		
Gastrocnemius vein	2	2		
Small saphenous vein	1	0		
Proximal type			11	(1.0%)
Popliteal vein	2	4		
Superficial femoral vein	3	1		
Deep femoral vein	0	1		
Common femoral vein	4	0		
External iliac vein	2	0		
Internal iliac vein	0	1		

DVT was found in 86 patients, and 5 patients had both distal and proximal types of DVT

and popliteal veins. In only 17 of 86 patients were the DVTs diagnosed as chronic by preoperative lower-extremity ultrasonography. Photographs of DVT detected by ultrasonography are shown in Fig. 1.

Risk factors of DVT

The clinicopathological factors and the presence or absence of DVT are summarized in Table 3. Of the 86 patients who were found to have DVTs, 43 were men and 43 were women. DVTs were found in 19.3% of elderly patients (aged ≥80 years) and 20.1% of patients with PS ≥ 1. Similarly, 12.3% of patients with stage IV gastric cancer, 20.0% of patients with a history of preoperative chemotherapy, and 30.4% of patients with a central venous catheter (CVC) were found to have DVTs. Conversely, the incidence of patients with DVT was low (4.5%) in patients whose body mass index (BMI) was ≥25 kg/m^2. Univariate analysis demonstrated that the incidence of DVT was significantly higher in

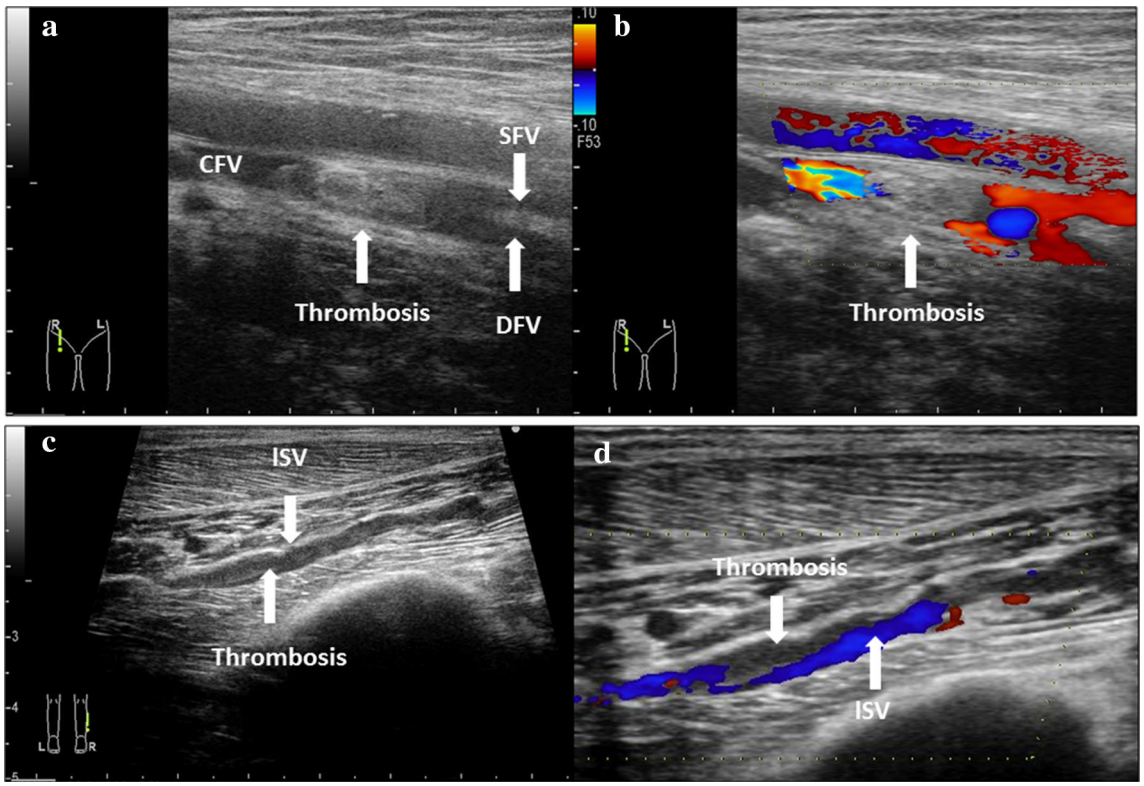

Fig. 1 Ultrasonographic images of patients with deep venous thrombosis. B-mode imaging shows the lateral soleal vein of the right side (**a**, **b**) and the right common femoral vein (**c**, **d**). *CFV* common femoral vein, *SFV* superficial femoral vein, *DFV* deep femoral vein, *LSV* lateral soleal vein

women, patients ≥80 years of age, PS ≥ 1 (vs. PS = 0), stage IV (vs. stages I–III), history of preoperative chemotherapy, and the presence of a CVC. To identify the predictors of DVT before surgery, the following indicators, which were identified as candidate predictors of DVT on univariate analysis, were evaluated: age, sex, PS, body mass index, tumor stage, history of preoperative chemotherapy, and CVC. Multivariate logistic regression analysis demonstrated that female sex, age ≥80 years, PS ≥ 1, history of preoperative chemotherapy, and the presence of a CVC were significantly correlated with DVT before surgery (Table 4).

The proximal type of DVT was significantly more common in patients with PS ≥ 1 (vs. PS = 0), history of preoperative chemotherapy, the presence of a CVC, and the presence of varicose veins of the lower extremity; all of these were found to be independent risk factors for the presence of proximal DVT.

In 1070 of 1140 patients, no supportive treatment such as chemotherapy or CVC for gastric cancer had been performed. Multivariate logistic regression analysis performed in these patients showed that female sex, age ≥80 years, and PS ≥ 1 were significantly correlated with DVT before surgery.

Incidence of postoperative PTE

In this series, postoperative symptomatic PTE occurred in 2 of 1140 patients (0.18%; 95% CI, 0.04–0.64%); both these patients were diagnosed as having proximal DVT preoperatively, for which a retrievable IVCF is usually placed. In 2 of 6 patients in whom an IVCF was not placed although they were diagnosed as having proximal DVT preoperatively, postoperative symptomatic PTE occurred. However, an IVCF was not placed in these patients, based on a cardiologist's decision. These patients were successfully treated by anticoagulant therapy.

In one patient, DVT was found preoperatively in the right popliteal vein and common femoral vein. However, an IVCF was not placed because the DVTs were considered to be old and organized. On the second postoperative day, the patient developed dyspnea, loss of consciousness, and hypotension after getting out of bed. Chest computed tomography showed shadow defects at the secondary bifurcation of the pulmonary artery. A retrievable IVCF was placed, anticoagulant therapy was performed, and the symptoms improved. It was confirmed that the DVTs were decreased on lower-extremity ultrasonography on the 14th postoperative day. The patient was discharged on the 15th

Table 3 Incidence of DVT according to patient characteristics

Clinicopathological factor	No. of patients (%)				*p* value
	DVT (−)		DVT (+)		
	n = 1054 (%)		*n* = 86 (%)		
Age (years)					
<80	958	(93.8)	63	(6.2)	<0.001
≥80	96	(80.7)	23	(19.3)	
Sex					
Male	755	(94.6)	43	(5.4)	<0.001
Female	299	(87.4)	43	(12.6)	
PS (ECOG)					
0	943	(94.2)	58	(5.8)	<0.001
≥1	111	(79.9)	28	(20.1)	
Body mass index (kg/m^2)					
<25	820	(91.6)	75	(8.4)	0.024
≥25	234	(95.5)	11	(4.5)	
Stage					
I–III	890	(93.5)	62	(6.5)	0.004
IV	164	(87.2)	24	(12.3)	
History of chemotherapy					
Absent	1014	(93.0)	76	(7.0)	0.003
Present	40	(80.0)	10	(20.0)	
Administration of steroids					
Absent	1045	(92.4)	86	(7.6)	1.000
Present	9	(100.0)	0		
Hypertension					
Absent	624	(92.9)	48	(7.1)	0.307
Present	430	(91.9)	38	(8.1)	
Chronic heart disease					
Absent	968	(92.3)	81	(7.7)	0.836
Present	86	(94.5)	5	(5.5)	
Smoking					
Non-smoker	785	(91.8)	70	(8.2)	0.154
Smoker	269	(94.4)	16	(5.6)	
Lower extremity varicose veins					
Absent	996	(92.6)	80	(7.4)	0.351
Present	58	(90.6)	6	(9.4)	
Central venous catheter					
Absent	1038	(92.9)	79	(7.1)	<0.001
Present	16	(69.6)	7	(30.4)	
Leg paralysis					
Absent	1044	(92.5)	85	(7.5)	0.580
Present	10	(90.9)	1	(9.1)	

DVT deep venous thrombosis, *PS* performance status, *ECOG* Eastern Cooperative Oncology Group

postoperative day while on anticoagulant therapy. Another patient had DVT in the right popliteal vein, and she was diagnosed as having asymptomatic PTE by chest computed tomography before surgery. However, she did not receive anticoagulant therapy because of tumor bleeding. She underwent gastrectomy without IVCF placement, and she developed dyspnea and loss of consciousness after leaving her bed on the second postoperative day. Anticoagulant therapy without IVCF placement was performed, and her symptoms improved. She was discharged on the 16th

Table 4 Multivariate analysis of risk factors for DVT

Variable	Odds ratio	95% CI	*p* value
Age			
≥80 vs. <80 years	2.904	1.611–5.091	<0.001
Sex			
Female vs. male	2.542	1.593–4.063	<0.001
PS (ECOG)			
≥1 vs. 0	3.023	1.724–5.191	<0.001
History of chemotherapy			
Presence vs. absence	3.479	1.462–7.642	0.006
Central venous catheter			
Presence vs. absence	3.928	1.260–11.122	0.020
Body mass index			
≥25 vs. <25 kg/m^2	0.650	0.310–1.246	0.203
Stage			
IV vs. I–III	1.240	0.682–2.169	0.469

DVT deep venous thrombosis, *CI* confidence interval, *PS* performance status, *ECOG* Eastern Cooperative Oncology Group

postoperative day on anticoagulant therapy. It was confirmed that the DVTs were decreased on lower-extremity ultrasonography 6 months after surgery.

Postoperative symptomatic PTE occurred in 2 of 11 patients with proximal DVT preoperatively (18.18%; 95% CI, 5.14–47.70%). On the other hand, postoperative symptomatic PTE did not occur in patients with distal DVT before surgery who were given anticoagulant therapy after surgery (95% CI, 0–4.87%), but 2 patients developed postoperative major bleeding. In both patients, fondaparinux was used, and the hemoglobin level was decreased on the 5th postoperative day. Computed tomography showed intraabdominal bleeding. Hemostasis was provided by stopping fondaparinux in 1 patient. However, re-operation for bleeding was needed in another patient. There was no mortality after postoperative bleeding. Because both patients received anticoagulant therapy with fondaparinux, we have subsequently selected LMWH for anticoagulant therapy after surgery. no postoperative major bleeding in 15 patients who underwent anticoagulant therapy with LMWH.

Of the 1054 patients in whom DVT was not detected preoperatively, none developed postoperative symptomatic PTE (95% CI, 0–0.36%) (Fig. 2).

Postoperative lower-extremity ultrasonography

Postoperative lower-extremity ultrasonography was not routinely performed. Only 36 of 86 patients who had DVT preoperatively underwent postoperative lower-extremity ultrasonography. The timing of the examination was not fixed, but most underwent lower-extremity ultrasonography 6 or 12 months after surgery. Median time from date of operation to postoperative lower-extremity ultrasonography was 251 days (2–1049 days). Of 36 patients, DVT disappeared in 11 and was decreased in 12. In contrast, DVTs increased in 3 patients, new DVT developed in 4 patients, and DVTs did not change in 6 patients. In 5 patients whose DVT was diagnosed as chronic DVT preoperatively, DVTs increased or developed.

Discussion

PTE, which results from DVT, is one of the potentially fatal postoperative complications. PTE and DVT are generally called VTE, and it is widely known that VTE is associated with cancer and is a predictor of decreased survival [3, 4, 14, 15]. However, there have been few reports of the incidence and clinicopathological characteristics of VTE in patients with gastric cancer. In the present study, the incidence and the risk factors of DVT before surgery were examined in all stages of gastric cancer. This is the first report of the rate of patients with DVT and the distribution and risk factors of DVT in patients with gastric cancer using preoperative screening lower-extremity venous ultrasonography.

In the present study, the incidence of DVT in patients with gastric cancer was 7.5%. Two large cohort studies that demonstrated the association between common cancers and VTE [3, 4] showed that the incidence of VTE in cases of gastric cancer was 3.0–4.9%. However, the clinicopathological characteristics of patients with gastric cancer were not reported in either of these studies. Kang et al. [6] reported that 3.3% of patients diagnosed with inoperable advanced gastric cancer were found to have VTE. However, their study was not intended for operable gastric cancer. Lee et al. [7] reported the incidence and risk factors of DVT in patients with both operable and inoperable gastric cancers. They reported that the 2-year cumulative incidence of VTE after diagnosis of gastric cancer was 3.8% in all patients, and 0.5%, 3.3%, 3.6%, 3.8%, and 24.4% in stages I, II, III, IV (M0), and IV (M1), respectively. However, the prevalence of DVT at the time of diagnosis of gastric cancer was not reported. They also reported that patients with stage IV (M1) had a higher incidence of VTE. Multivariate analysis demonstrated that the risk factors for the development of VTE were advanced stage, older age, and no major surgery, which is defined as surgery lasting more than 30 min. However, attention needs to be paid to the definition of no major surgery in this report. In their study, unresected patients with stage IV gastric cancer were included in the group of no major surgery. They also showed that DVTs and PTE were

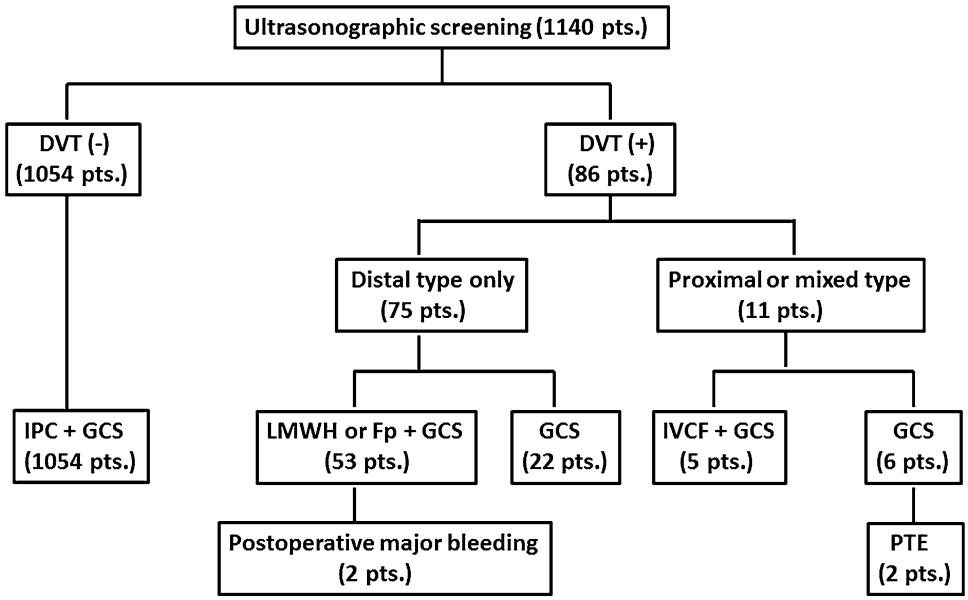

Fig. 2 Perioperative management and clinical course of patients with gastric cancer. *PTE* pulmonary thromboembolism, *DVT* deep venous thrombosis, *GCS* graduated compression stocking, *IPC* intermittent pneumatic compression, *LWMH* low molecular weight heparin, *Fp* fondaparinux

significant predictors of early death when compared with no occurrence of VTE. The rate of patients with DVT in the present study was higher than in these previous studies [6, 7]. In previous studies, the diagnostic tools for DVT and the process for the identification of patients with DVT were unclear [6, 7]. VTE was diagnosed using a variety of diagnostic tools, including lower-extremity ultrasonography, computed tomography (CT), CT angiography, or ventilation/perfusion scans, and the number of patients with asymptomatic VTE was not clear. In the present study, all patients with DVT were asymptomatic. Larsen et al. [10] reported the prevalence of DVT at diagnosis of upper gastrointestinal cancer using lower-extremity venous ultrasonography. They demonstrated that the prevalence of DVT in these patients was 16.2%. In their study, the prevalence of DVT was higher than in the present study. The high prevalence of DVT was likely caused by the high rate of patients with advanced-stage cancer, because 45% of patients were inoperable in their study.

In the present study, female sex, older age, worse PS, the presence of CVC, and a history of preoperative chemotherapy were the independent risk factors for DVT. However, there were no surrogate predictors that could be used to select patients who need attention and prophylaxis without lower-extremity ultrasonography. Several young male patients without CVC or preoperative chemotherapy had DVTs before surgery .

Previous reports demonstrated that female sex, older age, more advanced stage, higher American Society of Anesthesiologists (ASA) risk score, neo-adjuvant chemotherapy, and intrapelvic surgery were predictors for VTE in the perioperative period of abdominal surgery [7, 16–18]. In these studies, the presence or absence of CVC was not analyzed, although CVC-related venous thromboembolism was well known [19]. In the present study, stage IV was not an independent risk factor for DVT on multivariate analysis, although the rate of the presence of DVT in stage IV gastric cancer was higher than in stage I–III in a pairwise comparison by univariate analysis. Stage IV and the presence of CVC might be confounding variables. On the other hand, BMI < 25 kg/m^2 was a significant risk factor for DVT on univariate analysis in the present study. In this series, there were 18 patients with BMI ≥ 30 kg/m^2 and 136 patients with BMI < 18.5 kg/m^2. There is a possibility that poor nutritional status can affect the presence of DVT. Because of the high rate of patients with poor nutritional status, BMI < 25 kg/m^2 might be a significant risk factor for DVT.

In the present study, the proximal type of DVT was found in only 11 patients. When only these 11 patients were analyzed, the presence of varicose veins of the lower extremity was a risk factor for proximal DVT on univariate analysis. Königsbrügge et al. [20] demonstrated that the presence of varicose veins increased the VTE risk in cancer patients. However, it is difficult to explain why only proximal DVT was associated with varicose veins, because the population of patients with proximal DVT was very small. Genetic predisposition might be implicated in DVT, because older age was not a risk factor.

Recently, pharmacological thromboprophylaxis has been recommended for the prevention of VTE after major surgery, in addition to mechanical prophylaxis using intermittent pneumatic compression (IPC) [21]. However, it is possible that pharmacological prophylaxis may induce major bleeding complications as one of the adverse events of anticoagulant medication [22]. Garry et al. [23] showed

that the propagation rate to the popliteal vein or above from isolated distal DVT was 9% and the incidence of PTE was 1.5%. However, they concluded that it is controversial whether all isolated distal DVTs should be treated, because major bleeding occurred in 4.4% of patients with anticoagulant therapy. In the present study, the incidence of major bleeding was 3.8%. Postoperative bleeding could be minimized by the surgeon's efforts, but it is impossible to eliminate postoperative PTE without perioperative prevention. Actually, in 5 of 17 patients whose DVTs were chronic before surgery, DVTs increased or a new DVT was found. Therefore, anticoagulant therapy for all patients with preoperative DVT appears justified, although it increases bleeding risk.

On the other hand, in the present study, no patient developed postoperative symptomatic PTE among the 1054 patients in whom DVT was not detected preoperatively.

A previous report showed that IVCF placement reduced the risk of PTE for patients with proximal DVT over the short term. However, 2 years later, there was no significant benefit in terms of mortality or symptomatic pulmonary embolism, and an increase in recurrent DVT was noted in patients who received a filter [24]. Therefore, the American College of Chest Physicians (ACCP) guidelines recommend the use of IVCF only in patients with acute VTE who have a contraindication to anticoagulation, such as recent or planned major surgery or active bleeding [25].

In the present study, postoperative symptomatic PTE occurred in two patients with proximal DVT, and an IVCF was not placed in either patient. In two of six patients in whom an IVCF was not placed although they were diagnosed as having proximal DVTs preoperatively, postoperative symptomatic PTE occurred. Meignan et al. [26] reported that the frequency of silent PTE was 40–50% in patients with proximal DVT. Therefore, an IVCF should be placed in all patients with proximal DVT. The prevalence of proximal DVT was only 1.0%, but PTE is a life-threatening complication. Therefore, we consider that an IVCF should be placed for 1.0% of patients with gastric cancer. The results of this study support the idea that IVCF placement is not necessary for patients with distal DVT. Using lower-extremity ultrasonography, we could select which patients need IVCF placement.

In Japan, it costs about 50 USD per patient for lower-extremity ultrasonography and about 240 USD per patient for computed tomographic venography. Therefore, as a screening modality, ultrasonography is superior to computed tomography from the cost perspective. Then, it costs around 100 USD to administer LMWH for 5 days after surgery. Therefore, it costs around 57,000 USD for ultrasonographic screening for 1140 patients, but we can cut this back to around 105,400 USD for medication, if the 1054 patients without DVTs for whom anticoagulant therapy was recommended in the ACCP guidelines were not given LMWH after surgery. The expense of hospitalization for the 2 patients who developed PTE in the present study was 23,000 USD and 18,000 USD, respectively. The first patient underwent total gastrectomy, and the second patient underwent distal gastrectomy. In general, the cost of hospitalization of patients who undergo total gastrectomy and distal gastrectomy is around 17,000 USD and 15,000 USD, respectively, in Japan. Therefore, the cost of intensive care for these patients after developing PTE was 6000 and 3000 USD, respectively. Appropriate treatment after ultrasonographic screening can curtail the additional cost for PTEs.

This study had some limitations. First, it was a retrospective study in a single institution. As a rule, patients with distal DVT were given anticoagulant therapy, but approximately 30% of patients with distal DVT did not receive anticoagulant therapy by the surgeons' decision. Most patients with renal dysfunction or patients who underwent staging laparoscopy did not undergo anticoagulant therapy after surgery. Second, because neither contrast venography or computed tomographic venography was performed; therefore, the quality of ultrasonography could not be evaluated. However, the sensitivity and specificity of ultrasonography of the leg have been reported to be similar to those of computed tomography [9]. Furthermore, ultrasonography is easily accessible, noninvasive, and inexpensive. Therefore, preoperative screening for DVT by ultrasonography will become generally used in the future. Third, the incidence of postoperative asymptomatic DVT was unclear, because postoperative lower-extremity ultrasonography was not routinely performed; only patients who developed postoperative symptomatic PTE were identified. Fourth, patient food preferences such as garlic, ginseng, ginger, gingko, and vitamin E, which reduce the risk of DVT, were not evaluated [27]. Finally, most of the patients enrolled were Japanese. The high rate of DVT in Western countries is caused not only by advanced stage or high BMI, but also by genetic factors or a more sedentary culture. Therefore, the results of this study are considered to be generalizable in Japan because more than 1000 patients were analyzed, but generalizability to other countries, especially Western countries, is uncertain.

In conclusion, appropriate measures should be taken for patients with gastric cancer in the perioperative period, because 7.5% of them have asymptomatic DVTs, a risk factor for PTE. Female patients, age $\geq$80 years, patients with a history of preoperative chemotherapy, or patients with a CVC were at especially high risk for DVT.

This study showed that routine lower-extremity venous ultrasonographic screening is useful for identifying DVT in

not only potential high-risk patients for lethal PTE, most of which result from DVT, but also in low-risk patients for PTE, most of whom do not need anticoagulant therapy.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical standards 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 and later versions. Informed consent or a substitute for it was obtained from all patients before being included in the study.

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