Frequency and timing of clinical venous thromboembolism after major joint surgery

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Over a 13-year period we studied all patients who underwent major hip and knee surgery and were diagnosed with objectively confirmed symptomatic venous thromboembolism, either deep venous thrombosis or non-fatal pulmonary embolism, within six months after surgery. Low-molecular-weight heparin had been given while the patients were in hospital.

There were 5607 patients. The cumulative incidence of symptomatic venous thromboembolism was 2.7% (150 of 5607), of which 1.1% had developed pulmonary embolism, 1.5% had deep venous thrombosis and 0.6% had both. Patients presented with deep venous thrombosis at a median of 24 days and pulmonary embolism at 17 days after surgery for hip fracture. After total hip replacement, deep venous thrombosis and pulmonary embolism occurred at a median of 21 and 34 days respectively. After total knee replacement, the median time to the presentation of deep venous thrombosis and pulmonary embolism was 20 and 12 days respectively. The cumulative risk of venous thromboembolism lasted for up to three months after hip surgery and for one month after total knee replacement. Venous thromboembolism was diagnosed after discharge from hospital in 70% of patients who developed this complication.

Despite hospital-based thromboprophylaxis, most cases of clinical venous thromboembolism occur after discharge and at different times according to the operation performed.

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Venous thromboembolism, presenting as pulmonary embolism or deep venous thrombosis (DVT), is a recognised complication after major joint surgery.[1,2] In patients undergoing total hip (THR) or total knee replacement (TKR) or repair of a fracture of the hip, asymptomatic venographic DVT occurs in 40% to 60% of cases without prophylaxis, and symptomatic venous thromboembolism, including fatal pulmonary embolism, in up to 5%. With an ageing population and increasing use of THR and TKR the morbidity, mortality and cost of venous thromboembolism are likely to rise.

Numerous clinical trials have shown that asymptomatic DVT is significantly reduced after major joint surgery to around 20% to 40% with thromboprophylaxis such as low-molecular-weight heparin (LMWH).[2-4] The incidence of symptomatic venous thromboembolism, both during hospitalisation and up to several months afterwards is less well defined. Cessation of thromboprophylaxis exposes a substantial proportion of patients to a hypercoagulable state, which can persist for long periods after surgery. Data from epidemiological studies assessing the risk of venous thromboembolism after emergency surgery for hip fracture and THR and TKR have shown that these groups experience distinct periods of risk, lasting from about two weeks to three months.[5-7]

Two previous prospective studies from our hospital investigated the annual incidence of venous thromboembolism in patients undergoing major joint surgery, either emergency surgery for hip fracture or THR and TKR.[6,7] We continued to monitor such patients and now record the annual frequency and timing of clinically manifest venous thromboembolism over 13 years in 5607 patients.

Patients and Methods

The patients studied were all those discharged from Buskerud Hospital and University College after THR, TKR or surgery for hip fracture between 1989 and 2001. The hospital serves a mixed urban and rural population of approximately 250 000 and patients undergoing orthopaedic surgery at the hospital are almost always re-admitted there in the event of post-operative venous thromboembolism. Data

Table I. Annual incidence of pulmonary embolism (PE) and deep venous thrombosis (DVT) in patients undergoing major orthopaedic surgery by number and *percentage* where appropriate

Surgical group	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total	95% CI*
Hip fracture surgery															
Total operated	95	100	117	139	240	260	245	260	238	171	216	190	149	2420	
Confirmed PE	4	4	2	2	1	3	5	4	1	2	0	3	1	32	0.9 to 1.9
	(*4.2*)	(*4*)	(*1.7*)	(*1.4*)	(*0.4*)	(*1.2*)	(*2*)	(*1.5*)	(*0.4*)	(*1.2*)	(*0*)	(*1.6*)	(*0.7*)	(*1.3*)	
Confirmed DVT	2	5	0	4	4	3	5	3	4	0	1	4	1	36	1.0 to 2.1
	(*2.1*)	(*5*)	(*0*)	(*2.9*)	(*1.7*)	(*1.2*)	(*2*)	(*1.2*)	(*1.7*)	(*0*)	(*0.5*)	(*2.1*)	(*0.7*)	(*1.5*)	
THR†															
Total operated	153	114	136	189	175	140	184	160	215	232	254	253	307	2512	
Confirmed PE	5	0	1	4	2	2	2	3	0	0	2	3	4	28	0.7 to 1.6
	(*3.3*)	(*0*)	(*0.7*)	(*2.1*)	(*1.1*)	(*1.4*)	(*1.1*)	(*1.9*)	(*0*)	(*0*)	(*0.8*)	(*1.2*)	(*1.3*)	(*1.1*)	
Confirmed DVT	2	2	3	8	2	6	6	5	2	1	1	1	0	39	1.1 to 2.1
	(*1.3*)	(*1.8*)	(*2.2*)	(*4.2*)	(*1.1*)	(*4.3*)	(*3.3*)	(*3.1*)	(*0.9*)	(*0.4*)	(*0.4*)	(*6.4*)	(*0*)	(*1.6*)	
TKR‡															
Total operated	13	16	26	68	60	29	27	30	56	66	69	109	106	675	
Confirmed PE	0	0	0	0	1	0	1	0	1	0	0	0	1	4	0.2 to 1.5
	(*0*)	(*0*)	(*0*)	(*0*)	(*1.7*)	(*0*)	(*3.7*)	(*0*)	(*1.8*)	(*0*)	(*0*)	(*0*)	(*0.9*)	(*0.6*)	
Confirmed DVT	1	0	2	1	0	1	0	1	2	0	1	1	1	11	0.8 to 2.9
	(*7.7*)	(*0*)	(*7.7*)	(*1.5*)	(*0*)	(*3.4*)	(*0*)	(*3.3*)	(*3.6*)	(*0*)	(*1.5*)	(*0.9*)	(*0.9*)	(*1.6*)	

* exact binomial confidence interval ($\alpha = 0.05$)

† THR, total hip replacement

‡ TKR, total knee replacement

on those patients presenting with suspected venous thromboembolism which was subsequently confirmed up to six months after surgery were recorded. Patients were not routinely screened for venous thromboembolism on discharge, after which prophylaxis was also infrequent. Graduated compression stockings were not used routinely.

Thromboprophylaxis. All patients had received thromboprophylaxis with LMWH for approximately ten days or until discharge. Subcutaneous dalteparin (5000 IU) or enoxaparin (40 mg) had been administered 12 hours before surgery in elective cases and shortly after admission in emergencies and thereafter once daily.

Diagnosis of venous thromboembolism. Patients with suspected venous thromboembolism were investigated primarily by compression B-mode ultrasound with routine examination of deep, superficial and common femoral veins.[8] If no thrombosis was seen, venography was routinely performed using the technique of Rabinov and Paulin.[9]

Pulmonary embolism was confirmed either by ventilation/perfusion scintigraphy or CT. The criteria of Biello[10] and the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) investigators[11-14] were used for determining the probability of pulmonary embolism, with only high-probability scans being considered in our study.

Statistical analysis. The primary outcome was the incidence of objectively confirmed venous thromboembolism within six months of operation. Differences were compared using two-sided 95% confidence intervals (CI) estimated from the normal approximation to the binomial distribution. Descriptive statistics investigated the annual incidence and timing of venous thromboembolism in the three groups. The annual incidence of venous thromboembolism is given as the number of patients diagnosed each year along with the percentage of the total number of patients operated on in each surgical group. The time to diagnosis was presented as the median number of days after surgery. The procedure-specific cumulative incidence of thromboembolism was plotted and log-rank tests used to calculate the statistical significance of differences in the risk of developing venous thromboembolism among the groups and between hip and knee surgery. Using a regression analysis we tested the significance of a linear declining trend in the percentage of the total number of cases of venous thromboembolism from 1988 to 2001. A statistical database (SPSS 12 for Windows; SPSS Inc., Chicago, Illinois) and Microsoft Excel (Microsoft Corp., Redwood, Washington) were used for the descriptive analysis.

Results

A total of 5607 patients had major joint surgery. The mean age of patients with hip fracture and confirmed venous thromboembolism was 79 years compared with a mean of 69 and 73 years in those with THR and TKR respectively. There was no significant difference in the mean age of those with DVT and pulmonary embolism. The percentage of females in the three groups was 78%, 75% and 87%, respectively, and this is reflected in their higher frequency of venous thromboembolism.

A total of 2420 patients underwent surgery for hip fracture (including internal fixation and hemiarthroplasty but not THR), 2512 for THR and 675 for TKR. Symptomatic non-fatal venous thromboembolism was confirmed in 2.7% of patients (150 of 5607; 95% CI 2.2 to 3.1) with similar proportions of DVT (1.5%; 95% CI 1.2 to 1.9) and pulmonary embolism (1.1%; 95% CI 0.9 to 1.4). Seven patients developed concomitant DVT and pulmonary embolism (0.1%; 95% CI 0.03 to 0.2). Post-operatively, the proportion which developed DVT or pulmonary embolism was as follows: hip fracture, 1.5% and 1.3%; THR,

Table II. Length of hospitalisation and timing of deep venous thrombosis (DVT) after major hip and knee surgery, 1989 to 2001

	Number of patients (%)	Median (range) post-operative hospital stay (days)	Median (range) time to clinical DVT (days after surgery)
Hip fracture surgery			
DVT, all patients	36	12 (3 to 102)*	24 (3 to 150)
DVT diagnosed during initial hospitalisation	9/35 (*26*)	27 (9 to 102)	12 (3 to 27)
DVT diagnosed after discharge	26/35 (*74*)	11 (3 to 28)	29 (8 to 150)
Total hip replacement			
DVT, all patients	39	12 (4 to 48)*	21 (3 to 122)
DVT diagnosed during initial hospitalisation	9/38 (*24*)	17 (10 to 48)	10 (3 to 22)
DVT diagnosed after discharge	29/38 (*76*)	10 (4 to 30)	25 (6 to 122)
Total knee replacement			
DVT, all patients	11	15 (10 to 58)*	20 (6 to 150)
DVT diagnosed during initial hospitalisation	6/10 (*60*)	16 (11 to 58)	8 (6 to 20)
DVT diagnosed after discharge	4/10 (*40*)	13 (10 to 16)	27 (20 to 129)

* data not available for 1 patient

Table III. Length of hospitalisation and timing of pulmonary embolism (PE) after major hip and knee surgery, 1989 to 2001

	Number of patients (%)	Median (range) post-operative hospital stay (days)	Median (range) time to clinical PE (days after surgery)
Hip fracture surgery			
PE, all patients	32	16 (2 to 37)*	17 (1 to 173)
PE diagnosed during initial hospitalisation	14/31 (*45*)	20 (2 to 37)	9 (1 to 27)
PE diagnosed after discharge	17/31 (*55*)	12 (8 to 22)	29 (10 to 173)
Total hip replacement			
PE, all patients	28	10 (8 to 57)†	34 (3 to 150)
PE diagnosed during initial hospitalisation	5/21 (*24*)	17 (9 to 57)	7 (3 to 24)
PE diagnosed after discharge	16/21 (*76*)	10 (8 to 22)	41 (17 to 150)
Total knee replacement			
PE, all patients	4	14 (9 to 48)*	12 (2 to 150)
PE diagnosed during initial hospitalisation	2/3 (*67*)	29 (9 to 48)	5 (2 to 7)
PE diagnosed after discharge	1/3 (*33*)	14 (*14*)	17 (*17*)

* data not available for 1 patient
† data not available for 7 patients

1.3% and 1.2%; and TKR, 1.6% and 0.6% (Table I). Because of the low annual frequency of venous thromboembolism in each group, trends could not be calculated. The median time to presentation of venous thromboembolism varied among the groups. Patients presented with DVT at a median of 24 days and pulmonary embolism at 17 days after surgery for hip fracture. After THR, DVT and pulmonary embolism occurred at a median of 21 and 34 days respectively and after TKR at 20 and 12 days, respectively (Tables II and III).

In patients undergoing elective and emergency surgery of the hip, most cases of DVT were diagnosed after discharge (75%, 55 of 73). After TKR, DVT was less common after discharge and was found in four of ten patients (40%) (Table II). Similarly, pulmonary embolism was diagnosed after discharge in 33 of 52 (63%) patients undergoing THR and emergency hip surgery (Table III). After TKR, a similar number of cases of pulmonary embolism were diagnosed before (two) and after (one) discharge (Table III). Analysis of the cumulative rate of venous thromboembolism over time, according to the type of surgery showed an almost parallel increase in DVT and pulmonary embolism, reaching a plateau approximately three months after surgery. After TKR, a rapid rise in DVT and pulmonary embolism was noted, with the incidence stabilising after approximately one month (Fig. 1). The difference in temporal distribution of venous thromboembolism across the three groups was not statistically significant (log-rank test; $p = 0.71$). Similarly, no statistically significant differences were noted in the temporal distribution of those undergoing TKR and THR and emergency hip surgery (log-rank test, $p = 0.44$). Regression analysis indicated a statistically significant decline in the percentage of venous thromboembolism from 1989 to 2001 (slope = -0.0031; $p = 0.0013$; Fig. 2). Most of the decline was in patients undergoing TKR and THR between 1997 and 2001 (data not shown), compared with emergency hip surgery.

Discussion

Numerous orthopaedic studies using routine venography have shown a high frequency of silent DVT, despite pharmacological thromboprophylaxis.[2-4] The clinical relevance of such clots is controversial.[15,16] In our study, the overall incidence of clinical DVT was 1.3% to 1.6%. In patients undergoing either emergency surgery or elective THR, the incidence of clinical, non-fatal pulmonary embolism was

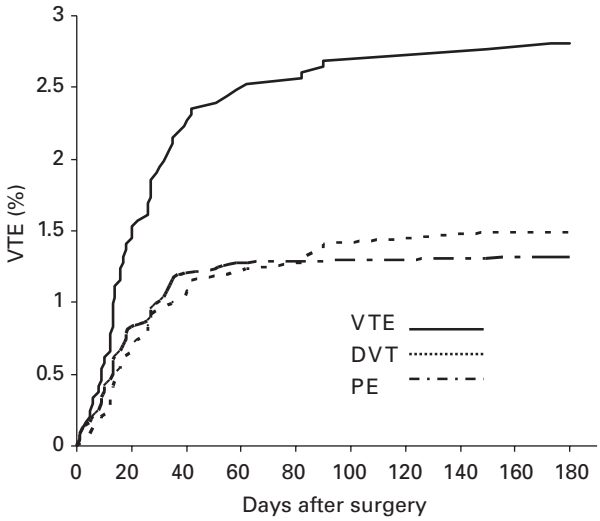

Fig. 1a

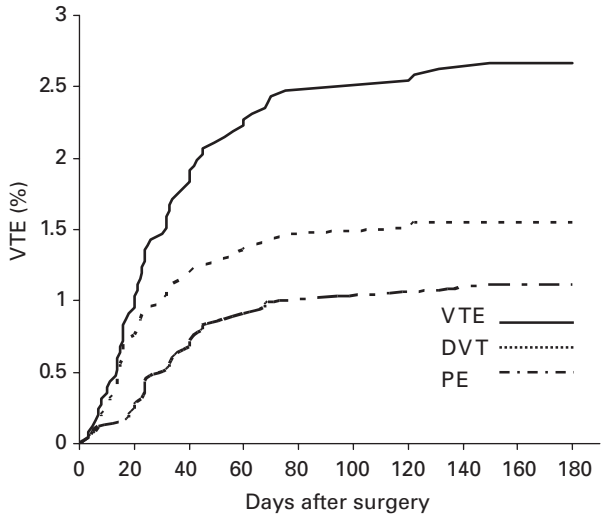

Fig. 1b

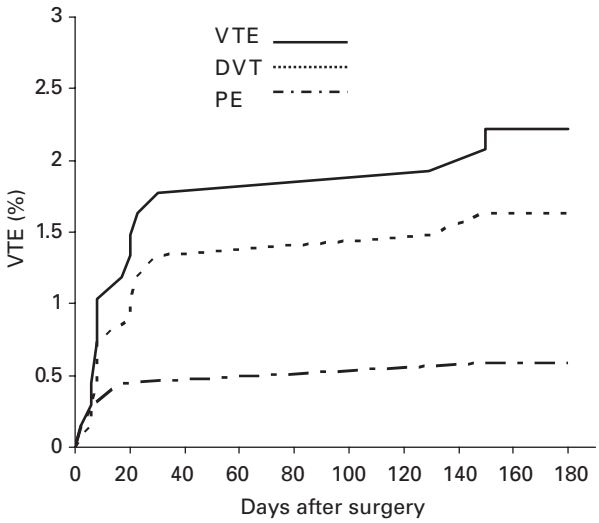

Fig. 1c

Group showing the cumulative incidence of venous thromboembolism *versus* time after a) surgery for fracture of the hip, b) total hip replacement and c) total knee replacement (VTE, venous thromboembolism; DVT, deep venous thrombosis; PE, pulmonary embolism).

similar (1.5% to 1.6%), with a lower incidence observed after TKR (0.6%). If the expected rate of fatal pulmonary embolism is included, based on outcome from a recent analysis (0.2% to 1%),[17] the overall rate of clinically manifest venous thromboembolism after major joint surgery is between 2.9% and 3.7% and therefore represents the most common post-surgical complication. Adverse thromboembolic outcomes would be expected in about one of 30 operated patients.

Our findings in patients undergoing THR or TKR are similar to those in other studies. Using pooled data from 6000 patients after elective THR and TKR, Douketis et al[3] reported an incidence of 3.2% of symptomatic venous thromboembolism at three months after operation with most cases (69%) occurring after discharge. O'Reilly, Burgess and Zicat,[18] reported an incidence of 1.2% of symptomatic pulmonary embolism on discharge in more than 6000 patients undergoing hip and knee surgery, similar to our findings. Two further reports noted an incidence at three months of non-fatal venous thromboembolism of between 2.1% and 5.3% in patients undergoing THR and TKR.[5,19] Finally, in a large study of nearly 7000 patients undergoing surgery for hip fracture,[20] 70% of whom received LMWH for at least four weeks, the incidence of venous thromboembolism of 1.3% up to three months after surgery was lower than that of our series.

Concomitant clinical DVT and pulmonary embolism was infrequent, indicating that symptoms of both are rare in the same patient. This suggests that although some DVTs may cause symptoms, others will embolise but remain symptomless. This contrasts with studies using mandatory radiological imaging techniques to screen both leg veins and pulmonary vessels in non-surgical patients with suspected DVT, when a high prevalence of concomitant DVT

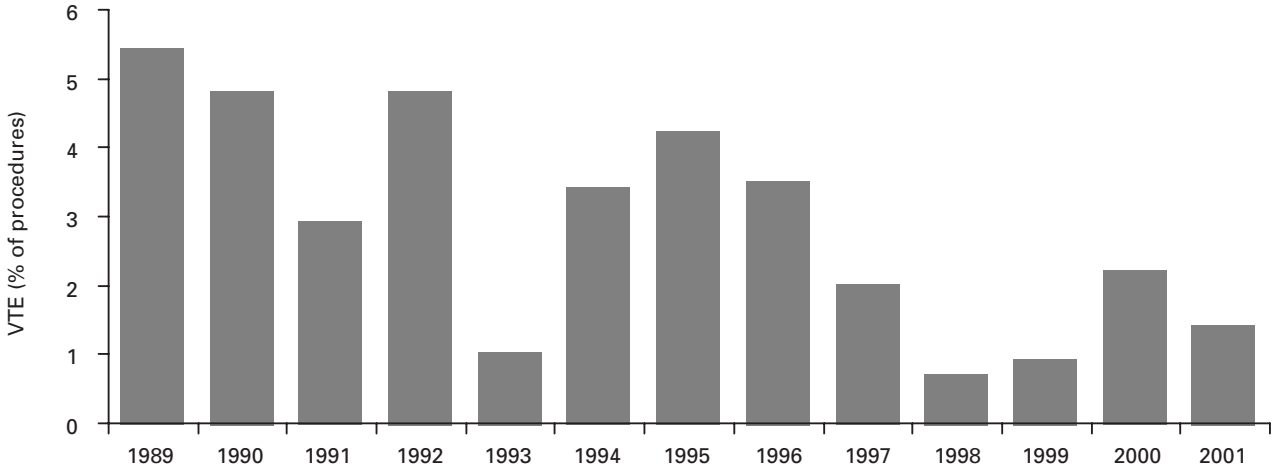

Fig. 2

Bar chart showing the cumulative incidence of venous thromboembolism (VTE) for the years 1989 to 2001 for all procedures.

and pulmonary embolism has been reported.[21] Our data further strengthens the notion that post-operative subclinical DVT remains the primary source of cases of clinical pulmonary embolism and that these mostly occur independently of overt DVT.

Regression analysis showed a significant decline in the cumulative incidence of venous thromboembolism over the study period. Since prophylaxis was generally standardised during this time the decline may be due to reasons such as improved surgical and anaesthetic care. However, because of the small number of cases occurring during the later part of the study, firm conclusions should be avoided and larger studies are required for confirmation.

We found that up to 70% of the emergency and elective hip surgery patients who developed symptoms of DVT or pulmonary embolism did so after discharge. For TKR, about half of the cases were diagnosed after discharge, indicating a shorter risk period for this group. This agrees with data which showed a reduced systemic blood flow for many weeks after hip surgery compared with that of a few days after TKR.[22] Also the benefit of prophylaxis after hospital discharge for TKR patients has not been demonstrated.[4]

The reason why surgeons seldom observe clinical venous thromboembolism may be due to the subclinical nature of the clotting masked by the post-operative inflammatory healing process and short hospitalisation of only a few days in most centres. With shorter hospital admissions after major joint surgery, an increasing proportion of patients will develop venous thromboembolism after discharge. This implies that patients and carers should be warned that venous thromboembolism is more likely to occur after discharge and informed of likely symptoms.

Throughout the study, LMWH prophylaxis was given routinely for a mean of ten days. Despite this, a persistent risk of clinical venous thromboembolism was noted. After elective and emergency hip surgery, the risk persisted for about three months, being higher in emergency cases. After TKR the risk period was about one month, in agreement with the findings of White et al.[5] This is slightly longer than we have previously reported[7] and is most likely to be due to the larger sample size obtained by extending our observation period to 13 years. The findings reaffirm previous observations and recommendations that, after hip surgery, prophylaxis should continue for longer and should not be stopped at discharge from hospital.

There are some limitations to our study. First, patients diagnosed with venous thromboembolism were restricted to those presenting to our radiology department. Those going elsewhere were not included, thereby underestimating the true rate of occurrence. Also, post-surgical fatal PE was not included and is likely to have occurred in and out of hospital. Information from the National Death Register would have allowed an estimation of the overall incidence of fatal pulmonary embolism. A recent analysis has indicated that between 10% and 40% of all deaths after major joint surgery are related to pulmonary embolism.[17] Estimates of fatal pulmonary embolism, however, remain elusive in most studies because of current autopsy rates of less than 10% of deaths. Secondly, pulmonary embolism was diagnosed only on the basis of high-probability imaging; patients with intermediate probability scans were excluded, resulting in a further underestimate of the actual rates. Taken together, we suspect that the rates here were probably an underestimation of the true frequency of venous thromboembolism.

This long observational study indicates that clinical venous thromboembolism remains a common problem after major joint surgery. The risk period is about three months after THR and hip fracture surgery, and about one month after TKR.

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