Incidence of Venous Thromboembolism in the Wake of the Clots in Legs Or sTockings after Stroke (CLOTS) Study

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Background and Purpose—In the United Kingdom, compressive stockings were standard care in all stroke units until the publication of the Clots in Legs Or sTockings after Stroke (CLOTS) trial results in May 2009, which concluded that stockings were ineffective. The aim of this audit was to assess whether this change in practice was associated with any change in venous thromboembolism incidence in routine clinical practice.

Method—All stroke register entries at the University Hospital of North Staffordshire from 2 years before the publication of the CLOTS trial results to 2 years after were identified and included in this audit. The hospital radiology reporting system was then cross-checked for evidence of venous thromboembolism on computed tomography pulmonary angiogram, ventilation/perfusion lung scan, and leg Doppler reports.

Results—There were 773 patients in the before cohort and 861 in the after cohort (mean age, 74/74 years; men, 47%/45%; and ischemic stroke, 87%/85%, respectively). Symptomatic venous thromboembolism incidence was the same in both cohorts, 21 (2.7%) in the before cohort and 26 (3.0%) in the after cohort (P=0.8). There was a trend toward more deep vein thrombosis (9 [1.2%] versus 19 [2.2%]; P=0.1) and fewer pulmonary embolisms (12 [1.6%] versus 6 [0.7%]; P=0.2) in the after cohort.

Conclusions—Discontinuation of compressive stockings did not increase venous thromboembolism incidence. There was a trend toward more deep vein thrombosis and fewer PEs after CLOTS, which might be because of increased clinical vigilance in the diagnosis of deep vein thrombosis, but a chance variation cannot be excluded. **(*Stroke*. 2013;44:2910-2912.)**

Key Words: pulmonary embolism ■ venous thromboembolism ■ venous thrombosis

Venous thromboembolism (VTE; eg, deep venous thrombosis [DVT] and pulmonary embolism [PE]) is a common complication of acute stroke. Its incidence varies between studies.[1–7] In 2009, the Clots in Legs Or sTockings after Stroke (CLOTS) 1 trial reported an incidence of 10% for DVT diagnosed by Doppler, of which 7% were asymptomatic and 3% were symptomatic, and there was a 1% incidence of symptomatic PE.[1]

In the Chinese Acute Stroke Trial (CAST) and in a study of in-hospital deaths after stroke in Germany, half of the reported PEs were fatal,[2,3] but it is conceivable that not all PEs were diagnosed because the observed rates were very low, at 0.1% and 0.4%, respectively. In addition to the risk of PE, DVT may lead to chronic venous stasis and ulceration, with considerable burden on the patient and long-term costs for the National Health Service. Prophylactic anticoagulation lowers the risk of DVT and PE after stroke, but reduction of symptomatic PE is balanced by an equal increase in symptomatic intracerebral hemorrhage. United Kingdom stroke guidelines do not support routine prophylactic anticoagulation (Royal College of Physicians guidelines 2008 and 2012).[8,9]

Compressive stockings effectively reduce DVT in inpatients[10] and have been used as the main method of thrombosis prevention in most stroke units in the United Kingdom until May 26, 2009, when the CLOTS 1 trial showed that stockings were ineffective in this patient group.[1] There was concern among clinicians that the change in practice may lead to an increase in VTE. This audit was performed to establish

Table 1. Baseline Demographic Characteristics and Details of the Stroke

	Before CLOTS, n=773	After CLOTS, n=861
Age, mean (SD), y	74 (14)	74 (14)
Sex, men, n (%)	365 (47)	386 (45)
Intracerebral hemorrhage, n (%)	96 (12)	121 (14)
Stroke pathology not known, n (%)	8 (1)	7 (1)
Cerebral infarct, n (%)	669 (87)	732 (85)
Infarct classification		
Total anterior circulation infarct, n (%)	151 (20)	154 (18)
Partial anterior circulation infarct, n (%)	126 (16)	119 (14)
Lacunar infarct, n (%)	198 (26)	256 (30)
Posterior circulation infarct, n (%)	63 (8)	99 (12)
Infarct type not defined, n (%)	140 (18)	115 (13)
Using antiplatelet medication, n (%)	585 (76)	624 (73)
Time from admission to first therapy session, median (IQR), d	1 (1–2)	1 (0–1)

CLOTS indicates Clots in Legs Or sTockings after Stroke trial; and IQR, interquartile range.

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Table 2. Incidence Venous Thromboembolism in the Before and After Clots in Legs Or sTockings after Stroke Cohorts

	Before, n=773	After, n=861	Total, N=1634
Deep vein thrombosis, n (%)	9 (1.2)	19 (2.2)	28 (1.7)
Pulmonary embolism, n (%)	12 (1.6)	6 (0.7)	18 (1.1)
Total, N (%)	21 (2.7)	26 (3.0)	47 (2.9)

whether the incidence of VTE has changed since stopping the use of compressive stockings after the publication of the CLOTS 1 trial.

Materials and Methods

In this standards-based retrospective clinical audit, data of 1638 stroke patients were collected from the Stroke Register at the University Hospital of North Staffordshire for the 2 cohorts: before cohort (between May 27, 2007 and May 25, 2009) and after cohort (May 27, 2009 and May 25, 2011). The admission date was defined as the date when the patient was admitted to University Hospital of North Staffordshire after presenting with a stroke.

In the before cohort, full-length graduated compression stockings were used from the day of admission for every stroke patient unless there were definite contraindications or if they were participating in the CLOTS study. Patients in the after cohort were not treated with compression stockings. Prophylactic anticoagulation was not used routinely on the unit during the before and after phases, but it was considered in patients with a history of VTE or with known thrombophilia. Stocking use before and cessation of use after CLOTS was supported by local guidelines and followed consistently. Because the unit took part in the CLOTS trial and followed the results live, change in practice was immediate and comprehensive, especially because neither patients nor nurses liked the stockings. For the audit, each stroke patient's records were accessed using CRIS radiology software to determine the following:

1. Whether and when they had been diagnosed as having either a DVT or PE, or both, in the time period of 14 days before and 90 days after the admission date.
2. Whether an ultrasound Doppler of the lower limb veins, ventilation/perfusion scan scan, or computed tomography (CT) pulmonary angiogram had been performed and, if so, whether a diagnosis of PE had been made or not.

For each scan, it was recorded whether the scan was positive or negative for DVT, which leg was affected, and whether the DVT was

Table 3. Incidence of Symptomatic Venous Thromboembolism in Observational Studies, Registries, and Randomized Clinical Trials

	Type of Study/ Clinical Trial	Centers	Intervention	Number of Patients	Incidence of Symptomatic DVT		Incidence of Symptomatic PE	
This audit	Retrospective notes survey	Single		1668	1.7%		1.1%	
Tong, 2010[13]	Retrospective health care cost survey	Multi		28 985	0.8%		0.3%	
Heuschmann, 2004[3]	Stroke register	Multi		10 800			0.4%	
Langhorne, 2000[14]	Prospective survey	3 sites		311	2%		1%	
Davenport, 1996[15]	Retrospective notes survey	Single		607	3%		1%	
Dromerick, 1994[16]	Retrospective notes survey	Single		100			0%	
					Active	Control	Active	Control
EXCLAIM, 2012[17]	RCT		Enoxaparin 14 d vs enoxaparin 28 d	389	0.0%	1.3%*	0.0%	0.7%*
CLOTS 1, 2009[1]	RCT		Full-length CS vs no CS	2518	2.9%	3.4%	1.0%	1.6%
PREVAIL, 2007[12]	RCT		Enoxaparin vs UFH	1762	0.2%	0.6%*	0.2%	0.9%*
TOAST, 1998[11]	RCT		Danaparoid vs placebo	1281	0.3%	1.6%	0.3%	0.6%
IST, 1997[7]	RCT 2×2		Aspirin vs no aspirin UFH vs no UFH	19 435			0.5% 0.6%	0.8% 0.8%
CAST, 1997[2]	RCT		Aspirin 150 mg/d vs placebo*	21 106			0.1%	0.2%

CAST indicates Chinese Acute Stroke Trial; CLOTS, Clots in Legs Or sTockings after Stroke; CS, compressive stockings; DVT, deep venous thrombosis; EXCLAIM, EXtended CLinical prophylaxis in Acutely Ill Medical patients; IST, International Stroke Trial; PE, pulmonary embolism; PREVAIL, Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy; RCT, randomized controlled trial; TOAST, Trial of ORG 10172 in Acute Stroke Treatment; and UFH, unfractionated heparin.

*Active controls rather than placebo or standard care.

proximal or distal. Proximal DVTs were defined as located in the knee and thigh (ie, in the femoral vein) and distal DVTs were defined as located below the knee (ie, in the popliteal vein). Both occlusive and nonocclusive thromboses were included.

Baseline clinical data for each cohort were summarized using means, medians, and percentages. Differences in DVT and PE incidence between the before and after cohorts were tested for statistical significance using 2-tailed Fisher exact tests.

Results

One thousand six hundred sixty-eight patients were included in the audit. Thirty-four patients were recruited to CLOTS and, therefore, were excluded from the audit, leaving 773 patients in the before cohort and 861 in the after cohort. Patients were well-matched for age, sex, stroke diagnosis (infarct or hemorrhage), infarct subtype, and treatment with antiplatelet agents (Table 1).

The incidence of symptomatic VTE was the same for both cohorts, with 21 (2.7%) events in the before cohort and 26 (3.0%) in the after cohort (P=0.8). However, there was a trend toward more DVTs (9 [1.2%] versus 19 [2.2%]; P=0.1) and fewer PEs (12 [1.5%] versus 7 [0.8%]; P=0.2) in the after cohort (Table 2). All diagnoses of VTE were confirmed by leg Doppler, ventilation/perfusion scan, or pulmonary angiogram. None of the VTE events was diagnosed by postmortem examination.

Discussion

The results of this audit show that there was no increase in VTE after the routine use of compressive stockings was stopped in acute stroke patients at University Hospital of North Staffordshire. Our findings confirm the results of the CLOTS 1 trial and extend the findings from the trial population to day-to-day routine clinical practice.[1]

The incidence rates of DVTs and PEs in our audit cohort were 1.7% and 1.1%, respectively, which is similar to previous United Kingdom–based surveys, as shown in Table 3. The incidence of symptomatic PE and DVT in our cohort is also comparable with that of the control groups of large, randomized, controlled studies, which range between 0.2% (CAST) and 1.6% (CLOTS 1) for PE and between 1.6% (Trial of ORG 10172 in Acute Stroke Treatment) and 3.4% (CLOTS 1) when compared against placebo or usual care (Table 3).[1–7,11–17] Our results, the results of previous surveys, and results from the control groups of randomized controlled trials suggest that symptomatic PE is a rare complication of stroke and that symptomatic DVT is slightly more common but <4%.

Although we showed no overall change in VTE, the trend toward higher rates of DVT and lower rates of PE in the after cohort could be because of random variation; however, because the change in practice caused great anxiety on our unit and prompted the team to examine calves on a daily basis, it could have been because of greater vigilance in diagnosis of DVT. This could explain the trend and also point toward an effective method of prevention of PE. Because the incidence of PE is low, a study to test this hypothesis would have to be very large.

Disclosures

None.

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