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HIDDen: Hospice Inpatient Deep vein thrombosis Detection prospective longitudinal observational pilot study to explore the prevalence of venous thromboembolism in people with advanced non-malignant conditions

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DECLARATION OF INTERESTS

MW designed and teaches the Focussed Abdominal Ultrasound in Palliative Care training programme, running since 2007, which trained the research nurses for this study. SN has received speakers bureau fees from Pfizer, Daiichi Sankyo, Bayer and Advisory Board fees from Daiichi Sankyo. Other authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Concept: CW, MJJ, SN, MW; Design: CW, MJJ, SN, MW, AN, EN, VA; Data collection and management; FS, VA, MJJ, CW, SN, EN; Radiological review and training: EN, MW; Patient and public involvement leads: AN, SN; Data analysis: FS, VA; First draft of manuscript: CW; Critical revision of manuscript: CW, MJJ, VA, FS: Contribution to and approval of final manuscript: all authors

MJ, VA, and FS had access to all raw data. EN had access to all scan images.

DATA SHARING

Data can be accessed by contacting the corresponding author.

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ABSTRACT

Objectives

To gain preliminary data regarding the prevalence of proximal deep vein thrombosis (DVT) in those with non-malignant conditions admitted to specialist palliative care units (SPCUs).

Methods

Data were collected as part of a prospective longitudinal observational study in five SPCUs in England, Wales and Northern Ireland (Registration: ISRCTN97567719) to estimate the prevalence of proximal femoral vein DVT in people admitted to SPCUs. The primary outcome for this exploratory sub-study was the prevalence of DVT in patients with non-malignant palliative conditions. Consecutive consenting adults underwent bilateral femoral vein ultrasonography within 48 hours of admission. Data were collected on symptoms associated with venous thromboembolism. Patients were ineligible if estimated prognosis was less than five days. Cross-sectional descriptive analysis was conducted on baseline data and prevalence estimates presented with 95% confidence intervals.

Results

1390 patients were screened, 28 patients had non-malignant disease and all were recruited. Mean age 68·8 (SD 12·0), range 43 to 86 years; men 61%; survival mean 86 (SD 108.5) range 1 to 345 days. No patient had a history of venous thromboembolism. Four (14%) were receiving thromboprophylaxis. Of 22 evaluable scans, 8 (36%, 95% CI 17% to 59%) showed femoral vein DVT. Level of reported relevant symptoms (leg oedema, leg pain, chest pain, breathlessness) were high irrespective of the presence of DVT.

Conclusion

Our exploratory data indicate one in three people admitted to an SPCU with non-malignant disease had a femoral vein DVT. Although definitive conclusions cannot be drawn, these data justify a larger prospective survey.

Keywords venous thromboembolism, non-malignant, hospices, palliative care, thromboprophylaxis, DVT

INTRODUCTION

Venous thromboembolism (VTE); deep venous thrombosis (DVT) and pulmonary embolism (PE)) is the commonest preventable cause of hospital death(1), and prevention of hospital-acquired thrombosis is the number one hospital patient safety improvement strategy globally(2). Data on prevalence rates of VTE in different patient populations are scarce. In general medical units in non-critically ill patients, prevalence estimates are between 1.7% and 2.6% (3, 4) and higher (7.8%) in the critically ill (5). A prevalence of asymptomatic DVT of 5.5% (95% CI 3.1-9.5) in adults and 17.8% (95% CI 8.5-32.6) among patients over 80 years was found using compression ultrasound on hospital admission (6). We recently published data showing a prevalence of femoral DVT in patients with cancer admitted to a specialist palliative care unit (SPCU) of 34%, (CI 28% to 40%) (7) but there are no studies to our knowledge of the prevalence in patients with non-malignant disease admitted to this setting.

Current clinical guidelines for patients hospitalized with acute illness recommend pharmacological thromboprophylaxis (8). However, patients with a life expectancy of less than 3 months were excluded systematically from studies informing these guidelines. Most people with palliative conditions, particularly non-malignant ones, will be admitted to hospital where they will receive thromboprophylaxis routinely. Only a small proportion will be admitted to SPCUs where thromboprophylaxis is a matter of debate; the primary focus of palliative care being symptom control, not survival (9), and few prescribe thromboprophylaxis routinely (10-12).

The prevalence and clinical relevance of femoral vein DVT in people with advanced non-malignant disease, alongside the risks and benefits of anticoagulation in these patients is unknown. It is also unknown whether current practice in hospitals represents over-treatment and therefore the unnecessary risks of anticoagulation, or if current practice in SPCUs represents under-treatment with risk of symptomatic VTE.

Although SPCU services have traditionally been for people with cancer, services are extending to people with non-malignant disease. Therefore it is important to understand the relevance of thromboprophylaxis in this group of patients in this setting. We conducted this study to gain exploratory data regarding the prevalence of proximal DVT in those with non-malignant conditions admitted to SPCUs to determine whether a larger study was warranted.

METHODS

Study design and participants

Data were collected as part of a prospective multicentre longitudinal observational study to estimate the prevalence of proximal femoral vein DVT in people admitted to SPCUs. Methods are described in detail in the presentation of findings in people with cancer (7). This report presents the cross-sectional analysis of the baseline data and survival in the sub-group of patients with non-malignant disease.

Participants were enrolled to the parent study between 20/06/2016 and 16/10/2017. Eligible patients were consecutive adults, aged 18 and over, admitted to one of five SPCUs across England (n=1), Wales (n=1) and Northern Ireland (n=3), able to give fully informed written consent or with an appropriate consultee, and no physical impediment to femoral vein ultrasound examination. Patients with a clinician-estimated prognosis of five days or less, insufficient mental capacity and no appropriate consultee, or insufficient English/Welsh to provide consent were excluded.

In this sub-study, participants with non-malignant disease were included in the analysis.

Institutional and ethical (Yorkshire & the Humber - Leeds West Research Ethics Committee; 16/YH/0045) approvals were granted prior to recruitment and the study was registered (ISRCTN97567719).

Procedures

Participants had assessments performed by a research nurse within 48 hours of admission.

Study outcome measures included: i) bedside femoral and popliteal vein assessment by ultrasound, ii) clinical symptoms of venous thromboembolism (leg oedema, leg pain, chest pain and breathlessness).

Bilateral femoral and popliteal vein ultrasound scans were undertaken at the bedside by a research nurse within 48 hours of admission to a SPCU. All scans were digitally recorded and reviewed by the study radiologist (EN) who was the final arbiter of the presence of DVT or no DVT.

Survival was noted from the clinical record until the last participant had completed the three weeks follow up period of the parent study.

Outcomes

The primary outcome of the study was the prevalence of DVT. Secondary outcomes were symptoms attributable to DVT and survival.

Statistical analysis

Participant characteristics are summarised using descriptive analyses using mean (SD), minimum-maximum, or n (%), as appropriate. The prevalence (within 48 hours of SPCU admission) is expressed as a percentage with associated 95% confidence intervals (CI).

The study is reported in accordance with Strengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement (13).

Role of the funding source

The trial was funded by a competitive peer-reviewed grant from the National Institute Health Research (Research for Patient Benefit). The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The

corresponding author had full access to all the data in the study and has final responsibility for the decision to submit for publication.

RESULTS

Participant characteristics

1390 patients were screened between 20/06/2016 and 16/10/2017. All 28 patients with non-malignant disease were recruited (full flow chart available (7)), with a mean age 68·8 (SD 12·0), range 43 to 86 years. Other characteristics are shown in Table 1. All participants were admitted only once during the study period. No patient had a history of VTE (DVT or PE), and only 3 (10.7%) had a family history of VTE. None were taking anticoagulation for secondary prevention of VTE or were wearing anti-thromboembolic stockings. Documented risk factors for VTE included acute medical illness in the last 12 weeks (12, 42.9%), surgery in last 12 weeks (1, 3.6%), and bedbound during the last 12 weeks (3, 10.7%). The Well's deep vein thrombosis score was "likely" (≥ 2) for 7 (25%). Two-thirds (18, 64%) died during the study period and 10 (36%) were still alive at last follow up (mean survival 86 (SD 108.5) range 1 to 345 days).

Table 1 Demographic Data of Participants

		Number	%
Gender	Male	17	61%
	Female	11	39%
Diagnosis	Chronic Obstructive Pulmonary Disease	10	36%
	Interstitial Lung Disease	2	7%
	Congestive Cardiac Failure	3	11%
	Motor Neurone Disease	6	21%
	Parkinson's Disease	1	3.5%
	Renal Failure	1	3.5%
	Hepatic Failure	1	3.5%
	Other	4	14.5%

Ethnicity	White	28	100%
Smoking history	Current smoker	6	22%
	Ex-smoker	16	57%
	Never smoked	6	21%
Co-morbidities	Yes	24	86%
	No	4	14%
Anticoagulation thromboprophylaxis	Yes	4	14%
	No	24	86%

Prevalence of femoral vein deep vein thrombosis at admission

Doppler ultrasound scans were conducted on all 28 patients. The radiologist categorised them as "DVT present" (8, 29%), "no DVT" (14, 50%), "unable to evaluate" (4, 14%), data missing (2, 7%). Of the 22 evaluable scans, 8 (36%, 95% CI: 17% to 59%) showed femoral vein DVT. None of the patients with a family history of VTE had a positive DVT Doppler baseline scan. None of the patients with a DVT at baseline were receiving anticoagulation medication.

Associations with symptoms

10 (36%) reported lower limb oedema and 18 (64%) reported lower limb pain. Of the 8 patients with a DVT, 4 (50%) reported lower limb oedema and 3 (38%) reported lower limb pain.

10 (36%) reported chest pain and 25 (89%) reported breathlessness. Of the 8 patients with a DVT, 3 (38%) reported chest pain and all (100%) reported breathlessness.

Of the 8 patients with a DVT at baseline, 3 (38%) had had an acute medical illness in the last 12 weeks and 1 (12.5%) had been bedbound in the last 12 weeks.

Wells Score

When considering if a positive (or 'likely') Wells score predicted the likelihood of being diagnosed with a DVT, there was no significant difference (p=0.240) between the Wells score and those with or those without a DVT. In those who were diagnosed with a DVT only 2/8 (25%) had a Wells score 'likely', and in those with no DVT 1/14 (7%) had a Wells score 'likely.'

DISCUSSION

The number of patients in this study are relatively small but bedside conducted compression ultrasonography identified femoral DVT in approximately one in three patients, none of which had been identified as part of their clinical care. These figures are higher than estimates in the general medical population (3,4,6), and similar to those in the cancer population admitted to a SPCU reported in the parent study (7). This raises the question of whether prevalence of DVT in people with non-malignant disease increases at the end of life. The sample size was too small to explore the clinical relevance with regard to symptoms and survival. As the parent study failed to show a relationship between symptoms (other than leg oedema), survival or thromboprophylaxis and the presence of DVT in people with advanced cancer, these data justify a larger study. The larger study should aim to determine if VTE prevalence is greater in advanced non-malignant disease admitted to a SPCU compared with those in general medical wards, and if these are associated with greater symptom burden or reduced survival.

Strengths and limitations

The numbers of patients in this study were small allowing only preliminary data. However, this pragmatic multicentre study with broad entry criteria included a range of non-malignant conditions, representative of the non-malignant SPCU population. To optimize recruitment, compression ultrasonography was conducted at the bedside by trained research nurses and independently validated by a consultant

radiologist. Distal DVT and PE were not sought, so these results are likely to underrepresent the true incidence of VTE.

Clinical and research implications

Our preliminary data indicate a high prevalence of femoral DVT at the point of admission to SPCUs. Firm conclusions cannot be drawn, but these findings call for a larger prospective survey to be conducted.

CONCLUSION

Our exploratory data indicate that when patients with non-malignant disease as their primary palliative diagnosis were admitted to SPCUs, one in three had a femoral vein DVT. This is similar to the prevalence found in those with a malignant diagnosis. Although definitive conclusions cannot be drawn, these data justify a larger prospective survey to confirm or refute the figures, and explore whether the presence of DVT in this population has any impact on symptoms or survival.

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