J R Coll Physicians Edinb 2020; 50: 19–24 | doi: 10.4997/JRCPE.2020.106 ORIGINAL RESEARCH PAPER

Long-term outcomes of patients investigated for suspected upper extremities deep venous thrombosis irrespective of imaging results

Daniel Tze Yee Ang[1], Tobias Walter Lombaert Haseler[2], Sidra Kosar[3], Katie Louise McCullough[4], Chibuzo Jemade[5], Caroline Gallacher[6], John Tallach Murchison[7], Khalida Ann Lockman[8]

Abstract

Background Outcome data are limited for upper extremity deep venous thrombosis (UEDVT). The outcomes of patients investigated for, but without UEDVT remain uncertain.

Methods Retrospective analysis of clinical records of adult patients undergoing Doppler ultrasound for potential UEDVT between 1 January 2007 and 31 December 2014 was undertaken. Primary outcome was all-cause mortality. Secondary outcomes were new cancer diagnosis and thromboembolic recurrence.

Results The final cohort (n = 528) comprised 25 primary UEDVT, 100 secondary UEDVT, 40 superficial-venous thrombosis and 363 without thrombus patients. There were 207 deaths. Survival was higher in primary than in secondary UEDVT (log-rank p < 0.0001) or those without thrombus (log-rank p = 0.001). Pre-existing cancer [hazard ratio 3.6 (95% confidence interval 1.5–8.9)] was the biggest independent predictor of mortality and leading cause of death. Developing UEDVT was a poor prognostic marker in cancer patients.

Conclusion There was high early mortality regardless of radiological findings, with the exception of primary UEDVT. Prospective studies evaluating aggressive treatment of underlying comorbidities in these patients are needed.

Keywords: deep venous thrombosis, survival, upper extremities deep venous thrombosis, venous thromboembolism

Financial and Competing Interests: No conflict of interests declared

Correspondence to:
Khalida Ann Lockman
Department of Acute and General Medicine
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh EH16 4SA
UK

Email:
ann.lockman@nhs.net

Introduction

Venous thromboembolism (VTE) continues to pose a significant challenge to global health, with an estimated 370,012 VTE-related deaths in the EU and between 25,000 and 32,000 deaths in the UK per annum.[1–3] Upper extremity deep venous thrombosis (UEDVT) are relatively rare, representing approximately 4% of all deep venous thrombosis (DVT).[4,5] This paucity is reflected in the volume of published data regarding UEDVT. Its incidence is on the rise due to increased use of indwelling central venous catheters, cardiac devices and peripherally inserted central catheter lines.[6]

A recent systematic review on UEDVT by Heil et al.[7] noted that data on UEDVT is still limited and heterogeneous. Many traditional treatment algorithms and long-term outcome studies for UEDVT were inferred from studies on lower limb DVT and pulmonary embolism (PE).[8–10] There is now growing evidence that UEDVT is associated with different risk factors, and incurs significant morbidity and mortality.[5,11,12] In the Malmo Thrombophilia Study, 24% UEDVT patients died at 62-month follow up.[13] In another study, Muñoz et al.[5] demonstrated higher 3-month overall mortality in patients with UEDVT than in those with lower limb DVT. Outcomes differ depending on patients' underlying comorbidities,[14] in particular cancer.[5] While mortality is high, there are a lack of published data on the documented causes of death for these patients.

Doppler ultrasound remains the first-line and most widely employed investigation for UEDVT.[7] From a clinical standpoint, there remains a gap in evidence regarding the outcomes of those investigated for, but with subsequent negative investigations for UEDVT. Many of these patients share the same comorbidities as patients with UEDVT and yet receive far less emphasis in today's pathway-driven ambulatory care setting. Often, a 'negative scan' is perceived as 'benign' and patients are not followed up owing to constraints on a healthcare system already under strain.

[1]Cardiology Registrar, Hairmyres University Hospital, East Kilbride, UK; [2,3,5,6]Clinical Fellow, Royal Infirmary of Edinburgh, Edinburgh, UK; [4]Foundation Doctor, Royal Infirmary of Edinburgh, Edinburgh, UK; [7]Professor of Radiology, Department of Radiology, Royal Infirmary of Edinburgh, Edinburgh, UK; [8]Consultant Endocrinologist and General Physician, Department of Acute and General Medicine, Royal Infirmary of Edinburgh, Edinburgh, UK

Table 1 Clinical characteristics of the study population

Characteristic	Primary DVT (n = 25)	Secondary DVT (n = 100)	Superficial VT (n = 40)	No thrombus (n = 363)	p-value
Age [median (IQR) years]	39 (26–51)	59 (41–74)	49 (39–63)	62 (46–76)	<0.001
Male	13 (52.0%)	46 (46.0%)	23 (57.5%)	153 (42.1%)	0.24
Inpatient Outpatient	5 (20.0%) 20 (80.0%)	65 (65.0%) 35 (35.0%)	25 (62.5%) 15 (37.5%)	234 (64.5%) 129 (35.5%)	<0.001
ITU	0 (0.0%)	5 (5.0%)	2 (5.0%)	37 (10.2%)	0.11
Laterality:					
Left	17 (68.0%)	51 (51.0%)	16 (40.0%)	167 (46.0%)	
Right	8 (32.0%)	43 (43.0%)	23 (57.5%)	182 (50.1%)	0.02
Bilateral	0 (0.0%)	3 (3.0%)	0 (0.0%)	9 (2.5%)	
Unspecified	0 (0.0%)	3 (3.0%)	1 (2.5%)	5 (1.4%)	
Confirmatory imaging:					
First Doppler	18 (72.0%)	84 (84.0%)	40 (100%)	N/A	–
Venogram	2 (8.0%)	9 (9.0%)	0 (0.0%)	N/A	–
Second Doppler*	4 (16.0%)	4 (4.0%)	0 (0.0%)	N/A	–
Others (e.g. CT)	1 (4.0%)	3 (3.0%)	0 (0.0%)	N/A	–
Risk factors:					
Previous/active cancer**	0 (0.0%)	47 (47.0%)	10 (25.0%)	118 (32.5%)	<0.001
Postoperative	0 (0.0%)	10 (10.0%)	4 (10.0%)	49 (13.5%)	0.19
Upper limb trauma/fracture	0 (0.0%)	4 (4.0%)	1 (2.5%)	17 (4.7%)	0.66
Instrumentation	0 (0.0%)	35 (35.0%)	12 (30.0%)	49 (13.5%)	<0.001
Infection/sepsis	1 (4.0%)	23 (23.0%)	18 (45.0%)	114 (31.4%)	0.002
IVDU	0 (0.0%)	6 (6.0%)	6 (15.0%)	13 (3.6%)	0.007
Previous VTE	1 (4.0%)	13 (13.0%)	8 (20.0%)	52 (14.3%)	0.34
Thrombophilic disorders	0 (0.0%)	14 (14.0%)	4 (10.0%)	13 (3.6%)	<0.001
Diabetes	1 (4.0%)	7 (7.0%)	3 (7.5%)	58 (16.0%)	0.03
Chronic kidney disease	0 (0.0%)	9 (9.0%)	6 (15.0%)	73 (20.1%)	0.006
Ischaemic heart disease	1 (4.0%)	15 (15.0%)	5 (12.5%)	73 (20.1%)	0.12
Ischaemic stroke	0 (0.0%)	5 (5.0%)	2 (5.0%)	47 (12.9%)	0.02
Congestive heart failure	0 (0.0%)	11 (11.0%)	2 (5.0%)	45 (12.4%)	0.15
Autoimmune/rheumatology	0 (0.0%)	10 (10.0%)	3 (7.5%)	33 (9.1%)	0.44
Hormonal therapy	0 (0.0%)	14 (14.0%)	1 (2.5%)	26 (7.2%)	0.03
Family history of VTE	2 (8.0%)	2 (2.0%)	1 (2.5%)	6 (1.7%)	0.20

Data are presented as median (IQR) or n and percentage from each group. $p < 0.05$ is considered significant.
*Second Doppler refers to Doppler ultrasound repeated at 7–10 days.
**Excluding non-melanomatous skin cancer
DVT: deep vein thrombosis; IQR: interquartile range; ITU: intensive treatment unit; IVDU: intravenous drug use; N/A: not applicable; VT: venous thrombosis; VTE: venous thromboembolism

In this study, we examined the demographics and long-term outcomes of all patients undergoing upper limb Doppler ultrasound for suspected UEDVT, regardless of subsequent imaging results. Documented causes of death during the follow-up period were also identified.

Methods

Study population

NHS Lothian provides acute hospital services for the city of Edinburgh and its surrounding residential areas (population ~860,000). All patients (n = 624) who underwent venous Doppler ultrasound of the upper extremities in the acute adult hospitals within NHS Lothian between 1 January 2007 and 31 December 2014 were included. Patients with postcodes outside the Edinburgh district were excluded owing to lack of follow-up data (n = 61). Other exclusion criteria were: incomplete clinical data including unavailable imaging reports (n = 7), venous ultrasound being performed for reasons other than DVT investigation (n = 28) and duplicate admissions or scans repeated in <7 days (n = 8). For those with multiple presentations (n = 99), the first presentation was considered the index presentation.

Definitions

UEDVT were classified into primary and secondary. Secondary UEDVT was defined as an event that occurred in the presence of one or more known risk factors: a previous history of VTE, pregnancy including up to 6 weeks postpartum; use of hormonal therapy, such as oral contraceptives/hormone replacement therapy/tamoxifen; recent (within 1 month of presentation) long-distance travel; prothrombotic coagulation disorders; surgery/trauma or fracture (within 3 months); immobilisation; the presence of indwelling venous catheters (central or peripheral); the presence of cardiac devices;

Table 2 Survival estimates of the study population

Time interval from index presentation	Survival estimates (%)			
	Primary DVT (n = 25)	Secondary DVT (n = 100)	Superficial VT (n = 40)	No thrombus (n = 363)
7 days	100	97	100	97
30 days	100	85	100	90
1 year	95	55	89	69
3 years	95	53	74	58
5 years	95	48	69	51
7 years	95	38	69	44

DVT: deep vein thrombosis; VT: venous thrombosis

intravenous drug use; previous diagnosis of cancer within 5 years (with the exception of non-melanomatous skin cancers); and, other medical conditions known to contribute to VTE (e.g. heart failure, sepsis and diabetes mellitus). Primary UEDVT was defined as an event without any of the known contributing risk factors above, or those thought to be caused by effort thrombosis (Paget–Schroetter syndrome) as determined by subsequent investigations. The outpatient cohort was defined as patients who were diagnosed and managed in an ambulatory care or outpatient clinic setting. The inpatient group included all patients who were diagnosed and managed during a hospital admission of any duration.

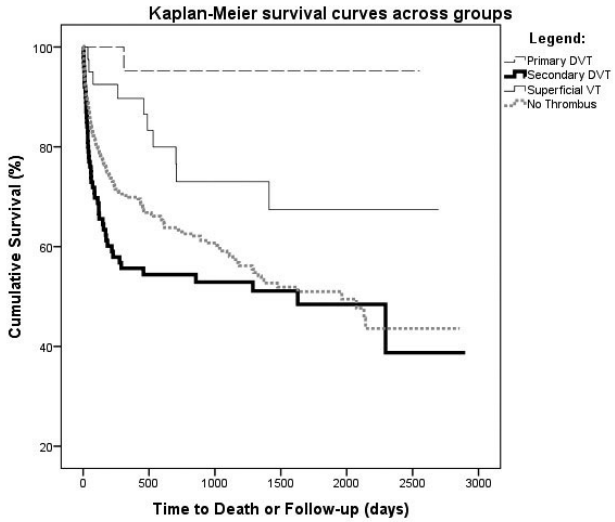
Outcomes

All cases were followed up from the date of index presentation until the date of death or 1 January 2015, whichever was earlier. Primary outcome for follow up was all-cause mortality. Secondary outcomes were the diagnosis of a new primary cancer and the subsequent diagnosis of VTE during follow up.

Data extraction and linkage

Demographic, clinical and imaging data were obtained from an integrated electronic clinical records system (TrakCare, InterSystems Corp., USA). For patients with UEDVT, the laterality (left, right or both arms), thrombus location and number of venous segments affected were recorded to establish the extent of thrombus burden. The Information Services Division (ISD) of NHS Scotland provided data linkage to the National Records Scotland database for accurate data on mortality and causes of death, as documented on death certificates. Secondary outcomes, clinical details on risk factors and underlying aetiology were obtained from the integrated electronic clinical records system.

Figure 1 Kaplan–Meier curves for primary upper extremities DVT, secondary upper extremities DVT, superficial VT and nonthrombus. DVT: deep vein thrombosis; VT: venous thrombosis



Ethical approval

This study received approval from the Caldicott Guardian of NHS Lothian and the Caldicott Guardian of ISD for NHS Scotland.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Macintosh, Version 21.0. (IBM Corp., USA). Data were presented as mean (standard deviation) or median [interquartile range (IQR)] for continuous variables, and as frequencies and percentages for categorical variables. Kaplan–Meier survival analysis was used to calculate the cumulative incidence of primary and secondary outcomes. Cox regression models were fitted to adjust for effects of the baseline characteristics and to determine their significance as predictors for each outcome. The risk of the outcomes was presented as hazard ratios (95% confidence intervals). The proportional hazard assumptions were determined using log minus log plots for each variable. A p-value of <0.05 was deemed significant.

Results

Baseline clinical characteristics

The final cohort comprised 528 patients. The median age was 59 (IQR 43–75) years. Men accounted for 44.5% of the study population. UEDVT was confirmed in 125 patients (23.7%). Of these, 20% (25 out of 125) were classified as primary UEDVT and 80% (100 out of 125) as secondary UEDVT. A total of 40 (7.6%) patients had isolated superficial venous thrombosis (SVT). The remaining 363 patients (68.8%) did not have thrombus detected. Investigation and management of UEDVT were undertaken in the outpatient setting in 199 (37.7%)

Table 3 Predictors of mortality across the groups

Predictor	Univariate		Multivariate	
	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age	1.05 (1.04–1.06)	<0.001	1.04 (1.03–1.05)	<0.001
Male	0.98 (0.74–1.29)	0.87	1.08 (0.81–1.44)	0.60
Inpatient	4.04 (2.81–5.82)	<0.001	3.00 (2.07–4.37)	<0.001
Cancer	3.25 (2.47–4.28)	<0.001	2.67 (1.98–3.60)	<0.001
Renal disease	1.96 (1.43–2.70)	<0.001	0.87 (0.60–1.25)	0.44
Ischaemic heart disease	2.12 (1.56–2.89)	<0.001	1.33 (0.93–1.89)	0.12
Heart failure	2.86 (2.04–4.02)	<0.001	1.40 (0.94–2.06)	0.10
Stroke	1.65 (1.12–2.41)	0.01	1.12 (0.75–1.66)	0.58
Infection/sepsis	1.33 (1.00–1.77)	0.05	–	–
Instrumentation	1.17 (0.84–1.64)	0.36	–	–
Chemotherapy	2.48 (1.77–3.49)	<0.001	–	–
Previous VTE	0.80 (0.53–1.21)	0.30	–	–

CI: confidence interval; HR: hazard ratio; VTE: venous thromboembolism

patients. The remaining 329 (62.3%) were hospitalised at the time of diagnosis, of which 44 (13.4%) were in the context of intensive care admissions.

DVTs were diagnosed on the basis of first Doppler ultrasound in 81.6% (102 out of 125), the second Doppler ultrasound in 6.4% (8 out of 125), venogram in 8.8% (11 out of 125) and CT imaging in 3.2% (4 out of 125) of cases. Venogram or CT imaging was employed in addition to Doppler ultrasonography in 4.8% of the study population. Further baseline characteristics of the study population are summarised in Table 1.

The majority of primary DVT (80%) were diagnosed in an outpatient setting. In contrast, more than half of the patients with secondary DVT, SVT or without thrombus were investigated during an inpatient stay ($p < 0.001$). Subclavian, axillary and internal jugular veins were affected by UEDVT in 63.2% (79 out of 125), 58.4% (73 out of 125) and 26.4% (33 out of 125) of cases, respectively. In 38.4% (48 out of 125) of cases, a single venous segment was affected and in 36.0% (45 out of 125) of cases, two venous segments were involved.

Overall survival

During the follow-up period, there were 207 deaths (39.2%). Median follow up for the 321 (60.8%) patients who were alive at the time of censoring was 2.7 (95% CI 1.2–4.6) years. Death occurred in 48% (48 out of 100) of patients with secondary UEDVT. There were 10 deaths (25.0%) among patients with isolated SVT. For those without thrombus, 40.8% (148 out of 363) died during the follow-up period. There was one death recorded for primary UEDVT. Survival estimates for each group are summarised in Table 2.

As shown by the Kaplan–Meier curves (Figure 1), the long-term survival for primary UEDVT was the most favourable, followed by patients with isolated SVT. Outcomes were worst for patients with secondary DVT (log rank $p < 0.0001$) and those without thrombus (log rank $p = 0.001$). There was not a statistically significant difference (log rank $p = 0.14$) in the unadjusted risk of death for secondary UEDVT compared with those without thrombus [HR 1.3 (95% CI 0.9–1.8)].

Predictors of mortality

The main unadjusted predictors of mortality across groups were age [HR 1.05 (95% CI 1.0–1.1)], hospitalisation at time of diagnosis [HR 4.0 (95% CI 2.8–5.8)], diagnosis of cancer [HR 3.3 (95% CI 2.5–4.3)], chronic kidney disease [HR 2.0 (95% CI 1.4–2.7)], ischaemic heart disease [HR 2.1 (95% CI 1.6–2.9)] and heart failure [HR 2.9 (95% CI 2.0–4.0)] (Table 3). However, after multivariate adjustment, the only significant predictors of mortality were age, hospitalisation and cancer. Age was an independent risk factor for mortality, with a 4% rise in the adjusted risk of death with each advancing year. There was 52.3% (172 out of 329) mortality among those hospitalised at time of presentation, vs 17.6% (35 out of 199) of outpatients. The diagnosis of UEDVT itself was not found to be a significant predictor of death after adjusting for the above variables [HR 1.09 (95% CI 0.78–1.54); $p = 0.61$].

Cancer and mortality

Cancer was a significant predictor of mortality [adjusted HR 2.7 (95% CI 2.0–3.6)]. Among those with secondary UEDVT, cancer was associated with a threefold increase in mortality [HR 3.6 (95% CI 1.5–8.9)] after adjusting for age, sex, inpatient stay, recent instrumentation, ischaemic heart disease, heart failure and renal disease. Of the 175 patients with a known diagnosis of cancer at the time of index presentation, 111 (63.4%) died during the follow-up period, with a short median time to death of 82 (IQR 30–268) days. UEDVT in patients with cancer was associated with worse outcomes, with only 29% alive at 1 year, vs 53% in cancer patients without thrombus (log rank $p = 0.013$).

Cancer remained a significant predictor of mortality for those without thrombus [HR 2.5 (95% CI 1.7–3.5)] after adjusting for age, sex, inpatient stay, recent instrumentation,

Table 4 Contributory causes of death in the study population

Cause of death	Primary DVT (n = 25)	Secondary DVT (n = 100)	Superficial VT (n = 40)	No thrombus (n = 363)	p-value
VTE-related deaths	0 (0.0%)	4 (4.0%)	0 (0.0%)	3 (0.8%)	0.07
Non VTE-related deaths					
Cancer	0 (0.0%)	35 (35.0%)	5 (12.5%)	67 (18.5%)	<0.001
Breast	0 (0.0%)	4 (4.0%)	0 (0.0%)	16 (4.4%)	
Lung	0 (0.0%)	13 (13.0%)	2 (5.0%)	18 (5.0%)	
Gynaecology	0 (0.0%)	2 (2.0%)	1 (2.5%)	3 (0.8%)	
Haematology	0 (0.0%)	3 (3.0%)	0 (0.0%)	16 (4.4%)	
Cardiovascular disease	1 (4.0%)	10 (10.0%)	2 (5.0%)	64 (17.6%)	0.02
Respiratory disease	0 (0.0%)	13 (13.0%)	2 (5.0%)	59 (16.3%)	0.04
Renal	0 (0.0%)	4 (4.0%)	0 (0.0%)	29 (8.0%)	0.07
Infection/sepsis	0 (0.0%)	4 (4.0%)	1 (2.5%)	17 (4.7%)	0.66
Other chronic illness	0 (0.0%)	3 (3.0%)	4 (10.0%)	22 (6.1%)	0.22

Data were obtained through record linkage from the Information Service Division NHS Scotland, with up to 10 causes per case.
DVT: deep vein thrombosis; VT: venous thrombosis; VTE: venous thromboembolism

ischaemic heart disease, heart failure and renal disease. Other independent predictors of death in this group were: inpatient stay [adjusted HR 2.9 (95% CI 1.9–4.5)], recent instrumentation [adjusted HR 1.9 (95% CI 1.2–3.1)] and older age [adjusted HR 1.06 (95% CI 1.04–1.07)].

Causes of death

Of the 207 deaths that occurred during the follow-up period, 107 (51.7%) were from cancer. The most common primaries were lung (29.9%), breast (18.7%) and haematological (17.8%). Cancer was the leading cause of death in secondary UEDVT, accounting for 72.9% (35 out of 48) of deaths in this group. The median time from diagnosis of UEDVT to cancer-related death was 1.7 (IQR 0.9–4.1) months. Cancer was also the leading cause of death in patients without thrombus (45.3%; 67 out of 148), with a median time from index investigation to cancer-related death of 4.2 (IQR 0.9–15.3) months.

Other significant causes of death in patients without thrombus include cardiovascular disease (ischaemic heart disease, peripheral vascular disease or aortic aneurysm) (43.2%; 64 out of 148), respiratory disease (39.9%; 59 out of 148) and renal disease (19.6%; 29 out of 148). Causes of death for all groups are summarised in Table 4.

New primary cancer and VTE events during follow up

There were 19 (3.6%) new primary cancers diagnosed during the follow-up period. Of these, 14 cases occurred in patients without thrombus, three were diagnosed in the secondary UEDVT group and one occurred in the SVT group.

New or recurrent VTE events were recorded in 33 (6.3%) patients. Of these, 21.2% (7 out of 33) were fatal. New or recurrent VTE occurred in 12.0% (3 out of 25) of primary UEDVT, 11.0% (11 out of 100) of secondary UEDVT, 10.0% (4 out of 40) of SVT and 4.1% (15 out of 363) of those without thrombus. Patients with secondary UEDVT were three-times more likely to develop a recurrent episode of VTE during follow up than patients without thrombus at index presentation [unadjusted HR 3.0 (95% CI 1.4–6.4); log rank p = 0.005].

Discussion

Our study supports the current use of Doppler ultrasound as the initial investigation of choice for UEDVT, with 81.6% of diagnoses being made on first scan. The demonstrated predilection for left-sided UEDVT is in keeping with previous publications and is probably a result of anatomical reasons as elegantly explained by Prescott et al., in 1979.[15]

It is worth recognising that many patients in this study were significantly unwell, as demonstrated by over 60% inpatients at presentation. Nonetheless, a striking finding in this study is the high mortality among patients undergoing investigation for potential UEDVT regardless of the subsequent radiological results. The outcomes were particularly poor for secondary UEDVT with 70% of deaths occurring within 3 months of index presentation. Of concern, the mortality among patients without thrombus was similar to that seen in secondary UEDVT, with 50% of deaths observed within 3 months of follow up. Few studies have demonstrated poor outcomes in the former group.[16]

Given that there were significant comorbidities (malignancy, hospitalisation and advanced age) at baseline among patients without thrombus, we accept there is an element of confounding from these prognostically significant risk factors. However, as previously mentioned, these patients are often overlooked by algorithms focused on detecting thrombus. They are heterogeneous and far too diverse to be managed using a single algorithm. Greater clinical emphasis should be placed on this group of ‘scan negative’ patients, with treatment directed at optimising any underlying pathology.

The outcomes for patients with cancer were poor with only 53% survival at 1 year. This is comparable to the quoted 47% survival in a recent studies.[4,17] A possible confounder is the high proportion (62.3%) of cancer patients presenting as inpatients for our study. DVT status was not shown to be a significant predictor of mortality in the cohort as a whole, but its presence was associated with worse outcomes among patients with cancer. The short lag time between presentation and subsequent death in patients with cancer suggests that

arm swelling and DVT are late signs of advanced malignancy and are poor prognostic indicators. While patients were treated in the standard fashion with anticoagulation, the high early mortality makes it challenging to propose an intervention strategy that might improve outcomes. Cancer being the documented leading cause of death further illustrates the point, as VTE treatment with anticoagulation will not alter the underlying malignant process.

The incidence of recurrent VTE after UEDVT of 11.2% in our cohort is similar to figures published in recent metanalyses.[4,18] The majority of UEDVT recurrence occurred as expected in the cohort with secondary UEDVT. However, in contrast to a previous study we did not find a significant association between UEDVT and new primary cancer.[19] A potential reason for this is the smaller size and inadequate power of our study.

There are limitations to our study that must be acknowledged. We were unable to obtain adequate clinical data to fully account for confounding factors likely to affect mortality. For example, data on obesity, tobacco consumption, cancer staging and treatment at time of Doppler ultrasound were not consistently available. Whilst the size of our UEDVT cohort is limited, this reflects the relative rarity of the condition particularly in direct comparison to lower limb DVT.[11] Our findings are reflective of real-world experience and are geared towards identifying opportunities to improve patient care.

There was significant mortality among patients presenting with suspected UEDVT irrespective of imaging outcomes. Outcomes were particularly poor for inpatients, the elderly and the comorbid, particularly patients with cancer. The presence of UEDVT was a poor prognostic indicator among patients with cancer, with a high early mortality. Focus should be shifted towards identifying high-risk patients based on underlying comorbidities, regardless of UEDVT status. Prospective multicentre studies are needed to discern if aggressive treatment of underlying pathologies at this stage will yield any survival benefit.

Acknowledgements

The authors are grateful to the administrative staff of the Radiology department at the Royal Infirmary of Edinburgh for their assistance with IT support for data extraction. We are also immensely grateful to Mr Doug Kidd and his team from Information Services Division (ISD), NHS Scotland for his assistance in data linkage.

References

1 Raskob GE, Angchaisuksiri P, Blanco AN et al. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol* 2014; 34: 2363–71.
2 Cohen AT, Agnelli G, Anderson FA et al. Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost* 2007; 98: 756–64.
3 Hill J, Treasure T, National Clinical Guideline Centre for Acute and Chronic Conditions. Reducing the risk of venous thromboembolism in patients admitted to hospital: summary of NICE guidance. *BMJ* 2010; 340: c95.
4 Bleker SM, van Es N, van Gils L et al. Clinical course of upper extremity deep vein thrombosis in patients with or without cancer: a systematic review. *Thromb Res* 2016; 140: S81–8.
5 Munoz FJ, Mismetti P, Poggio R et al. Clinical outcome of patients with upper-extremity deep vein thrombosis: results from the RIETE Registry. *Chest* 2008; 133: 143–8.
6 Lamontagne F, McIntyre L, Dodek P et al. Nonleg venous thrombosis in critically ill adults: a nested prospective cohort study. *JAMA Intern Med* 2014; 174: 689–96.
7 Heil J, Miesbach W, Vogl T et al. Deep vein thrombosis of the upper extremity. Dtsch Arztebl Int 2017; 114: 244–9.
8 Kobberoe Sogaard K, Schmidt M, Pedersen L et al. 30-Year mortality following venous thromboembolism: a population-based cohort study. *Circulation* 2014; 130: 829–36.
9 Spencer FA, Gore JM, Lessard D et al. Patient outcomes after deep vein thrombosis and pulmonary embolism: the Worcester Venous Thromboembolism Study. *Arch Intern Med* 2008; 168: 425–30.
10 Heit JA, Silverstein MD, Mohr DN et al. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. *Arch Intern Med* 1999; 159: 445–53.
11 Schleyer AM, Jarman KM, Calver P et al. Upper extremity deep vein thrombosis in hospitalized patients: a descriptive study. *J Hosp Med* 2014; 9: 48–53.
12 Kahn SR, Elman EA, Bornais C et al. Post-thrombotic syndrome, functional disability and quality of life after upper extremity deep venous thrombosis in adults. *Thromb Haemost* 2005; 93: 499–502.
13 Isma N, Svensson PJ, Gottsater A et al. Upper extremity deep venous thrombosis in the population-based Malmo thrombophilia study (MATS). Epidemiology, risk factors, recurrence risk, and mortality. *Thromb Res* 2010; 125: e335–8.
14 Grigorian A, Nahmias JT. *Deep Venous Thrombosis (DVT), Upper Extremity.* Treasure Island: StatPearls Publishing; 2019.
15 Prescott SM, Tikoff G. Deep vein thrombosis of the upper extremity: a reappraisal. *Circulation* 1979; 59: 350–5.
16 Baarslag HJ, Koopman MM, Hutten BA et al. Long-term follow-up of patients with suspected deep vein thrombosis of the upper extremity: survival, risk factors and post-thrombotic syndrome. *Eur J Intern Med* 2004; 15: 503–7.
17 Bleker SM, Es N, Kleinjan A et al. Current management strategies and long-term clinical outcomes of upper extremity venous thrombosis. *J Thromb Haemost* 2016; 14: 973–81.
18 Monreal M, Munoz FJ, Rosa V et al. Upper extremity DVT in oncological patients: analysis of risk factors. Data from the RIETE registry. *Exp Oncol* 2006; 28: 245–7.
19 Adelborg K, Horvath-Puho E, Sundboll J et al. Risk and prognosis of cancer after upper-extremity deep venous thrombosis: a population-based cohort study. *Thromb Res* 2018; 161: 106–10.