

2017

VENOUS THROMBOSIS IN THE ELDERLY

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- Not made use of the work of any other student(s) past or present without acknowledgement.
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Abbreviations

Acronym	Meaning
CCF	Congestive Cardiac Failure
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CTPA	Computerised Tomography Pulmonary Angiography
CVA	Cerebrovascular Accidents
DOAC	Dual Oral Anticoagulants
DVT	Deep Vein Thrombosis
HTN	Hypertension
IHD	Ischaemic Heart Disease
MI	Myocardial Infarction
PE	Pulmonary Embolism
TIA	Transient Ischaemic Attack
V/Q	Ventilation/Perfusion
VTE	Venous Thromboembolism

Abstract:

Despite the high incidence of venous thromboembolism (VTE) in the elderly population, not much literature, specifically in this high-risk group is present. Hence its presentation, risk factors and management remains a challenge. We analysed clinical notes of 200 patients (100 DVT and 100 PE) aged 75-100 years who presented with suspicion of VTE to the Manchester Royal Infirmary over a time-period of 6 months (August 2016-January 2017). Those with confirmed DVT in contrast to suspected-only DVT more frequently presented with symptoms such as unilateral leg swelling and warm skin. PE presented with similar signs and symptoms in both suspected-only and confirmed cases. Chronic conditions, such as chronic kidney disease, cardiovascular accidents and previous DVT/PE were more common in cases of confirmed VTE. Provoked factors, such as cancer, reduced/restricted mobility and travel history were associated with VTE. Confirmed cases of VTE were most commonly treated with direct oral anticoagulants. Non-DVT cases had cellulitis as the most frequent alternative diagnosis and for PE it was infection. Although this study provides a better understanding of the clinical picture of VTE in elderly population, more research is required to replicate and validate the findings so they can be applied to the clinical practice.

1. Introduction

Venous thromboembolism (VTE) is a vascular disorder consisting of deep vein thrombosis (DVT) and pulmonary embolism (PE). It is the third commonest vascular disease with an annual incidence of 1-2 per 1,000 of the population (DVT 45-117 and PE 29-78 per 100,000 person years, respectively) (1–3). Due to increased utilisation of the advanced medical diagnostic tools such as the computed tomography, pulmonary angiography and magnetic resonance imaging there has been an increase in the incidence of PE± DVT from 2001-2009 (4).

The incidence of VTE increases with age and is predominantly a disease of older people (**Figure 1**). The incidence is 3 times greater in those over the age of 75 compared to adults aged 55 or less (5). The difference in incidence in young and older population suggests that age is a non-modifiable risk factor of VTE. However, in this population it may be difficult to make a diagnosis because of the overlapping, non-specific presentation (signs and symptoms) of VTE with other medical conditions. In addition, the presence of certain medical conditions, such as congestive cardiac failure and chronic pulmonary disease, may increase the risk of VTE. Because the rate of comorbidities increases with an increase in age, elderly people with non-specific symptoms are commonly admitted to the hospital, thus increasing the burden to the healthcare services. However in this population not many studies are carried out looking into the signs, symptoms and risk factor of VTE and hence it remains incompletely understood. Furthermore, due to the presence of comorbidities, polypharmacy, risk of falls and frailty in elderly population management of VTE remains a challenge.

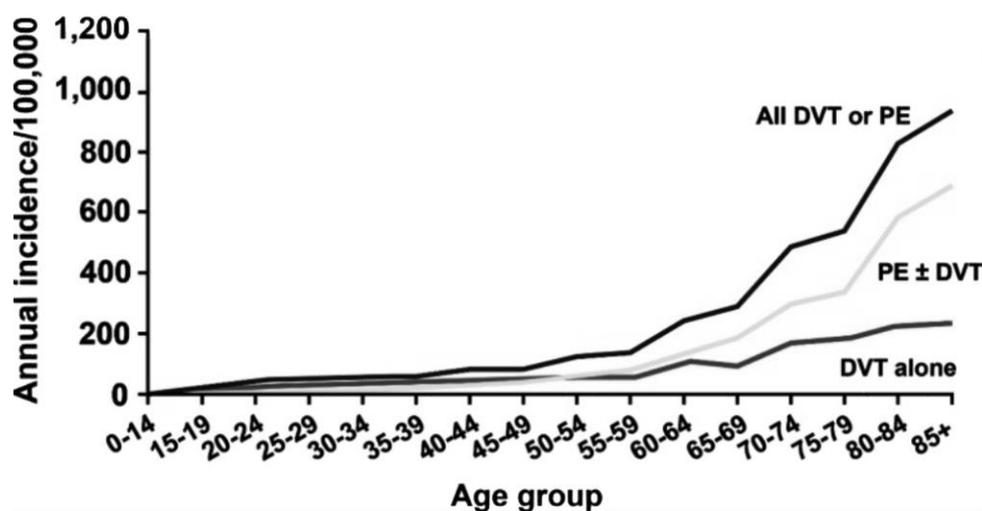


Figure 1. Annual incidence (per 100,000) of deep vein thrombosis (DVT) and pulmonary embolism (PE) in different age groups. The incidence of DVT and PE increases with age, with a greater increase in PE±DVT than DVT alone. PE= pulmonary embolism; DVT= deep vein thrombosis. Taken from (5).

Aim: The aim of this study is to analyse the presentation, risk factors and management of VTE in the elderly population. This will allow a better understanding of VTE in this high-risk group of patients, so that a prompt diagnosis can be made and the most appropriate treatment initiated which may help reduce hospital admissions or hospital stay.

Objective: Analyse online case notes (using Chameleon) of patients aged 75-100 years with suspected DVT and PE for the signs and symptoms, comorbidities, provoking factors, treatment and treatment-associated complications.

2. Methodology:

A retrospective analysis of the signs, symptoms, risk factors, comorbidities and treatment in patients aged 75-100 years who had presented with a suspicion of VTE during the time-period of 6 months (beginning of August 2016 till the end of January 2017) was carried out. The list of patients who had a Doppler ultrasound scan for suspected DVT and a computer tomography pulmonary angiography (CTPA) for suspected PE at Manchester Royal Infirmary was obtained. In total 100 patients for

suspected DVT and 100 patients for suspected PE aged 75-100 years were randomly selected using the RAND function in Excel. The electronic medical record system Chameleon was used to access clinical notes and gather information on signs and symptoms, comorbidities and provoked factors of VTE, scan results, treatment and treatment-associated complications. The signs and symptoms, comorbidities and potential provoked factors were gathered from the indication posted on the scan report or on A&E admission sheet. The imaging report was used to obtain the diagnosis. For information on treatment and treatment related complications discharge notes were used. Any missing or incomplete information was gathered by going through other clinical notes which included any follow ups, GP letters and further hospital admissions. These were followed up till the most recent information available on Chameleon. The data was collected into an Excel spreadsheet to minimise the risk of patient identification. Data was analysed quantitatively as suspected (patient in whom VTE was suspected, but no evidence on imaging was found) and confirmed (presence of DVT or PE on imaging) cases of VTE.

3. Results

We analysed data of 100 patients with suspected DVT and 100 patients with suspected PE. In total, 17 of the suspected DVT cases and 20 of the suspected PE cases had confirmed DVT and PE on the scan (**Figure 3.1**). Out of the 17 patients with DVT, 3 had chronic and 14 had acute DVT. From the 14 acute cases two patients had a confirmed PE either by a CTPA or V/Q scan. In 21 cases of suspected DVT, calf DVT was not 100% excluded. Of the 20 confirmed PE cases, 4 had a confirmed DVT while for the rest of the cases it could not be established from the notes, hence it is not known.

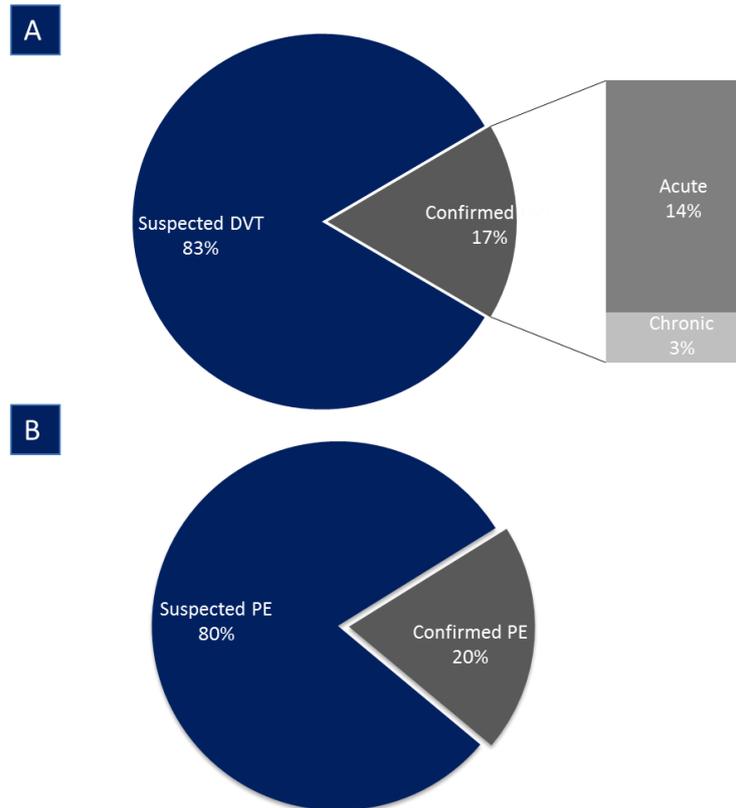


Figure 3.1. Total number of suspected and confirmed cases of VTE. **A.** The number of suspected and confirmed cases of deep vein thrombosis (DVT). There were 100 cases of DVT of which only 17% had a confirmed DVT on the scan. In confirmed cases 14% were acute while 3% were chronic. **B.** The number of suspected and confirmed cases of pulmonary embolism (PE). There were 100 cases of suspected pulmonary embolism (PE) of which only 20% had a PE on the scan.

Age and VTE:

To make the analysis easier we divided the patient ages into groups (**Figure 3.2**). These included ages 75-80, 81-85; 86-90; 91-95 and 96-100 years. The majority of the patient who presented with suspicion of DVT or PE were aged 75-80 years (42% DVT, 41% PE). As the age increased the number of patients presenting with suspected VTE decreased. The majority of the patients (8%) with confirmed DVT scan were aged 81-85 years while for PE 75-80 years (11%). None of patients aged 91-100 had a confirmed DVT, while for PE this was the case with the age range 96-100 years. To

conclude the most common age of presentation of VTE was 75-80 years, for confirmed DVT 81-85 years and PE 75-80 years.

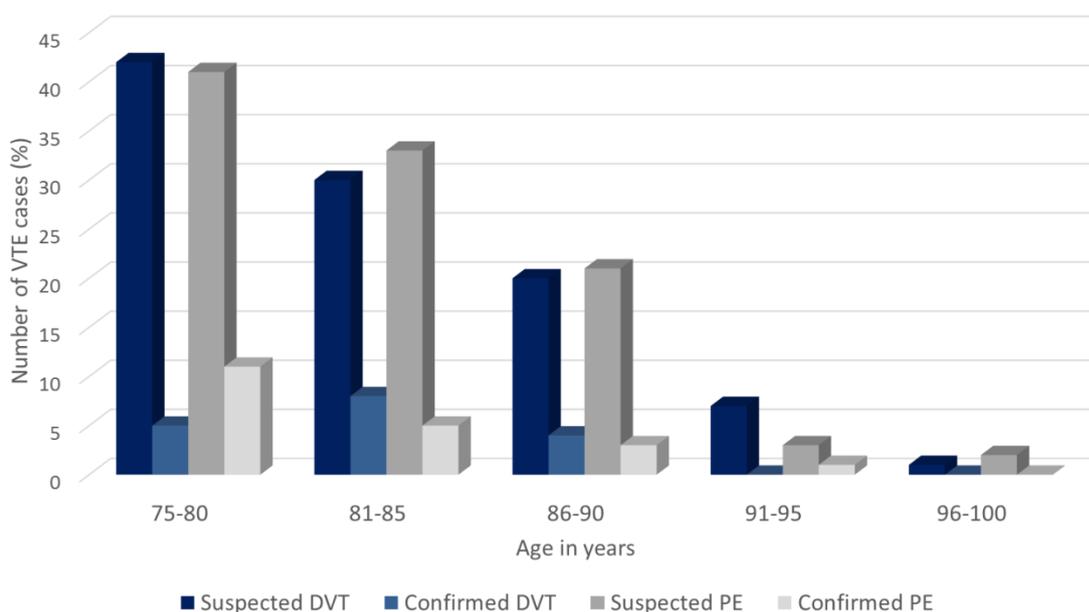


Figure 3.2. Different age range in years and the number of suspected and confirmed deep vein thrombosis (DVT) and pulmonary embolism (PE) cases.

Presentation of VTE:

The presenting signs and symptoms of those with suspected and those with confirmed DVT or PE were analysed.

Presentation of DVT:

In 99% of the DVT cases there was involvement of the lower limbs while only 1% presented with symptomatic upper limb. In suspected cases of DVT the most common presenting symptom was leg oedema with 56.6% presenting with unilateral and 21.7% with bilateral swelling (**Figure 3.3A**). The second commonest sign and symptom was pain/tenderness (49.4%), followed by erythema (21.7%) and warm skin (10.8%). A few patients presented with symptoms suggestive of PE. These included chest pain 1.2%, breathlessness 7.2% and cough 1.2%. Atypical or non-specific symptoms were also

found: dizziness 1.2%, confusion 1.2%, abdominal pain 1.2%, itching 1.2%, weeping leg 2.4%, unable to weight bear 2.4% and leg hardening 1.2%.

In those with confirmed DVT on the scan, unilateral leg swelling was the most common symptom, accounting for 76.5% of the cases (**Figure 3.3B**). Other signs and symptoms included: tenderness/pain (11.7%), erythema (23.1%), and warm skin (23.1%). Symptoms of PE were also seen in 35.3%: cough 1.2%, chest pain 11.8% and dyspnoea 17.6%. Out of the 17 positive DVT cases, 11.8% also had a positive CTPA suggestive of a PE. To summarise, unilateral leg swelling was the most frequent symptom observed in both suspected and confirmed cases of DVT. In confirmed cases of DVT warm skin and PE symptoms were more common and pain/tenderness less common compared to the suspected cases.

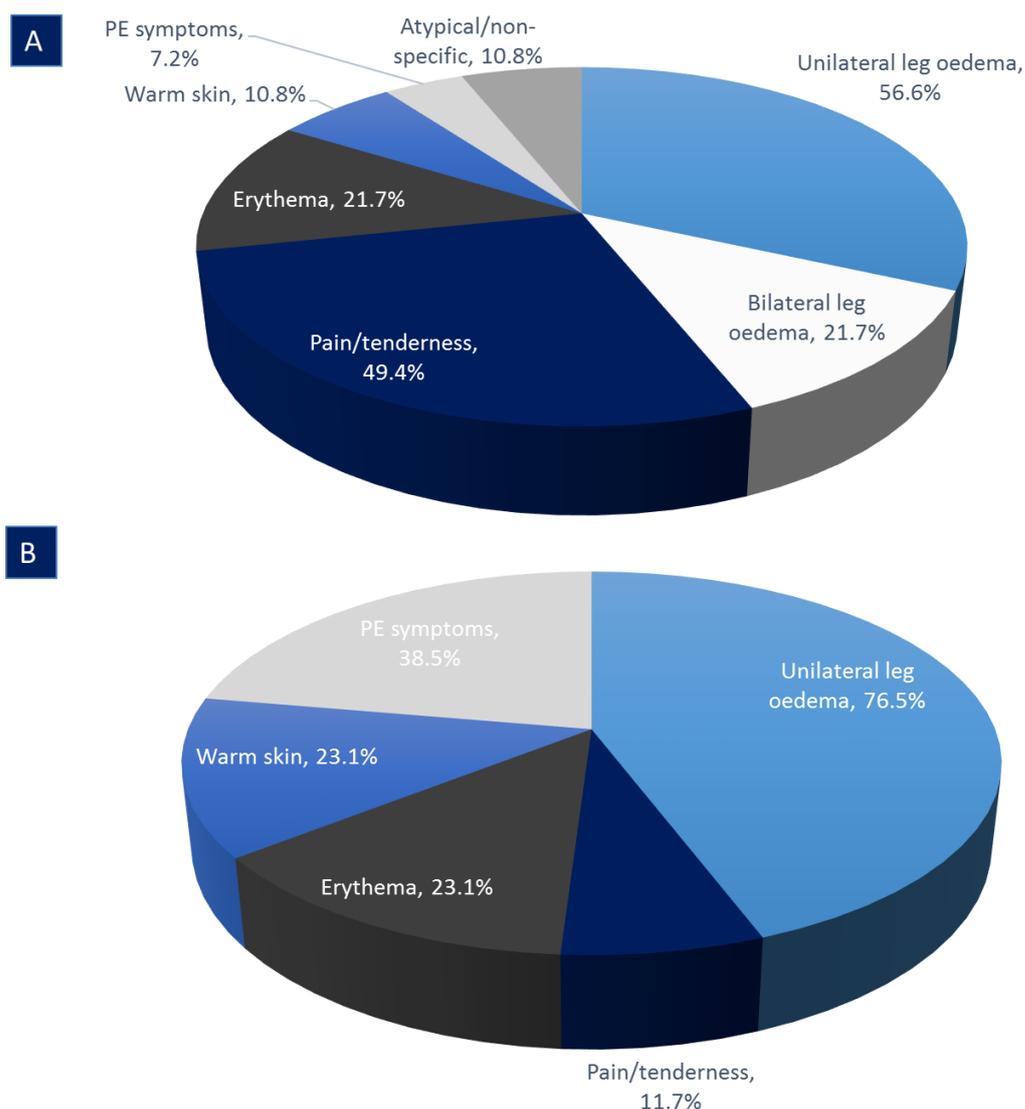


Figure 3.3. Signs and symptoms of deep vein thrombosis. **A.** Signs and symptoms in suspected cases of DVT. **B.** Signs and symptoms in confirmed cases of DVT.

Presentation of PE:

In suspected cases of PE, but a negative CTPA, the most common presenting complaint was dyspnoea (45%), followed by desaturation (30%), pleuritic chest pain (23.8%), tachycardia (15%), tachypnoea (12.5%) and haemoptysis (5%) (**Figure 3.4A**). Five percent presented with collapse, 2.5% with ECG changes suggestive of PE and 3.8% with DVT symptoms. Atypical and non-specific symptoms were also noted: non-specific chest pain (13.8%), abdominal pain (1.3%), dizziness (1.3%), confusion (1.3%), non-productive cough (3.75%), fever (1.3%) and palpitations (1.3%). In CTPA

confirmed cases of PE common signs and symptoms included dyspnoea (40%), desaturation (40%), pleuritic chest pain (20%) and tachycardia (20%) (Figure 3.4B). Five percent symptoms were of collapse and 10% non-specific chest pain. To summarise, the presenting signs and symptoms of PE were quite similar in both suspected and confirmed cases of PE.

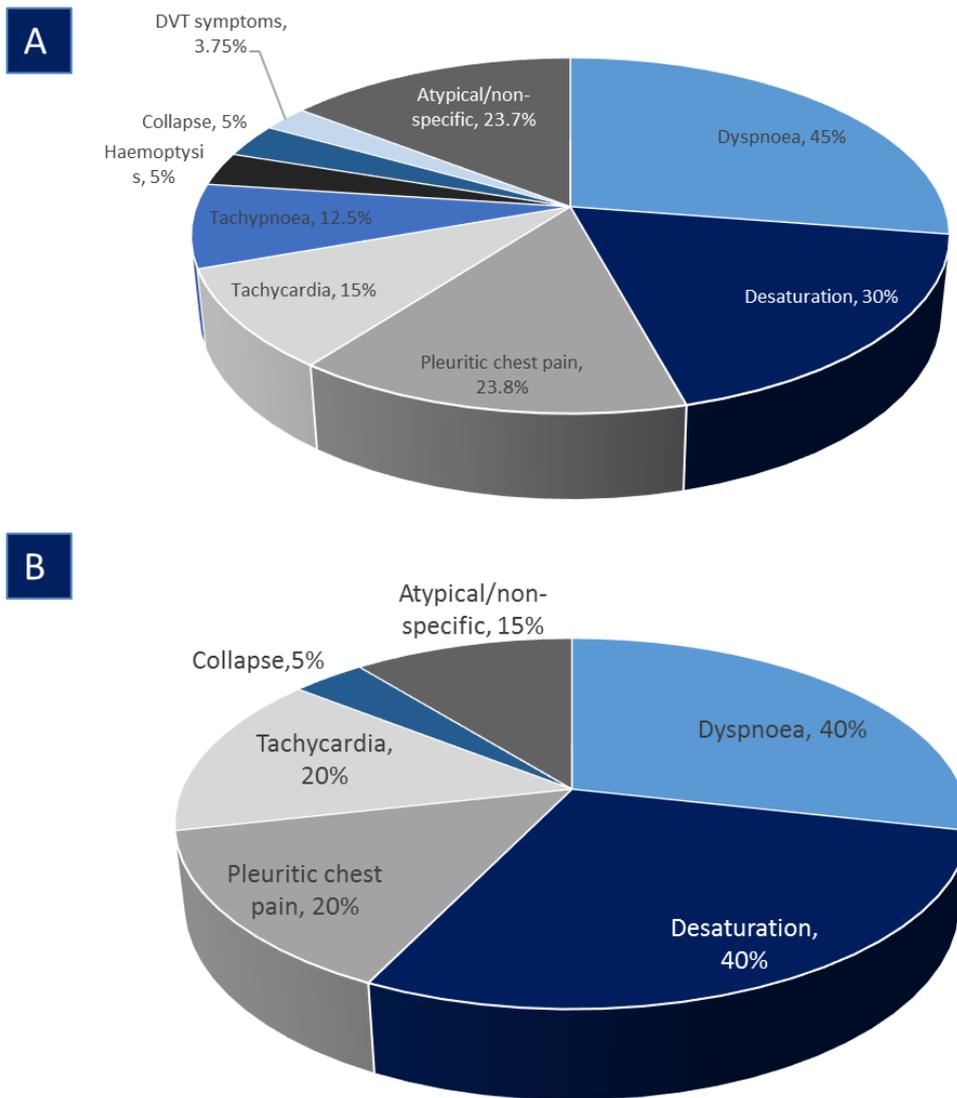


Figure 3.4. Signs and symptoms of pulmonary embolism (PE). **A.** Signs and symptoms of PE in suspected cases of PE. **B.** Signs and symptoms of PE in confirmed cases of PE.

Risk factors of DVT:

Multiple-morbidities:

Of the 200 patient notes analysed, only 3 did not have any comorbidity or any risk factor of VTE (unprovoked VTE). The risk factors were divided into co-morbidities, provoked and genetic. Several medical conditions as comorbidities were identified. For the purpose of analysis 12 most common and relevant ones were chosen (**Table 1**). For suspected cases of DVT, hypertension was the most prevalent medical condition (33.7%), followed by diabetes (22.8%), ischaemic heart disease and myocardial infarction (16.9%), atrial fibrillation (16.9%), previous PE/DVT (15.7%), COPD (12.0%), heart failure (10.8%), chronic kidney disease (8.43%), cerebrovascular disease or transient ischaemic attack (6.02%), and venous problems (7.22%). In confirmed DVT cases comorbidities included diabetes (11.8%), IHD/MI (11.8%), previous DVT (29.4%), chronic kidney disease (17.6%), atrial fibrillation (11.8%), HTN (11.8%), COPD (5.9%) and high cholesterol (5.9%). In suspected cases of PE, hypertension was seen in 32.5% cases, COPD/bronchiectasis in 20% patients while IHD/MI and diabetes in 17.5% patients. For those with confirmed PE, common comorbidities included HTN (40%), IHD/MI (35%), high cholesterol (15%), CVD/TIA (15%) and previous PE/DVT (15%). In short, higher rates of chronic kidney disease, cerebrovascular disease and a history of VTE was seen in those with confirmed DVT compared to suspected DVT cases. For confirmed PE cases medical conditions such as hypertension, ischemic heart disease, high cholesterol, chronic kidney disease, cerebrovascular diseases and previous DVT/PE were more common than in suspected cases of PE.

Comorbidities	Suspected DVT	Confirmed DVT	Suspected PE	Confirmed PE
Diabetes	22.8%	11.8%	17.5%	10.0%
HTN	33.7%	11.8%	32.5%	40.0%
Atrial fibrillation	16.9%	11.8%	11.3%	10.0%
IHD/MI	16.9%	11.8%	17.5%	35.0%
Heart failure	10.8%	0.0%	6.3%	5.0%
High cholesterol	7.2%	5.8%	2.5%	15.0%
COPD/bronchiectasis	12.0%	5.8%	20.0%	5.0%
CKD	8.4%	17.6%	2.5%	5.0%
CVD/TIA	6.0%	29.4%	1.3%	15.0%

Venous problems	7.2%	5.8%	0.0%	0.0%
Previous DVT/PE	15.7%	29.4%	5.0%	15.0%
Infection	8.4%	0.0%	11.3%	5.0%

Table 1. Comorbidities and the associated frequency in suspected and confirmed deep vein thrombosis (DVT) and pulmonary embolism (PE) cases. Venous problems include varicose veins, venous eczema and venous insufficiency). HTN=hypertension; IHD= ischaemic heart disease; MI= myocardial infarction; COPD=chronic obstructive pulmonary disease; CKD= chronic kidney disease; DVT=deep vein thrombosis; PE= pulmonary embolism

Provoked factors:

Provoked factors were divided into reduced/restricted mobility, cancer, recent surgery, and recent travel or unprovoked. Reduced and restricted mobility included factors such as bed-bound, fracture and falls. Such group consisted of 28.9% cases in suspected DVT, 23.5% cases of confirmed DVT, 21.3% suspected PE and 30% confirmed PE cases (**Figure 3.5**). In provoked cases, malignancy was seen in 15.7% suspected DVT, 23.5% confirmed DVT, 33.8% suspected PE and 40% with confirmed PE. Surgery was found in 18.1% cases of DVT suspicion, 11.8% for confirmed DVT, 13.8% suspected PE and 5% with confirmed PE. Recent travel was found in 1.2% of suspected DVT, 11.8% in confirmed DVT and none of the cases of suspected or confirmed PE. Fifteen percent of PE cases had no provoked factors.

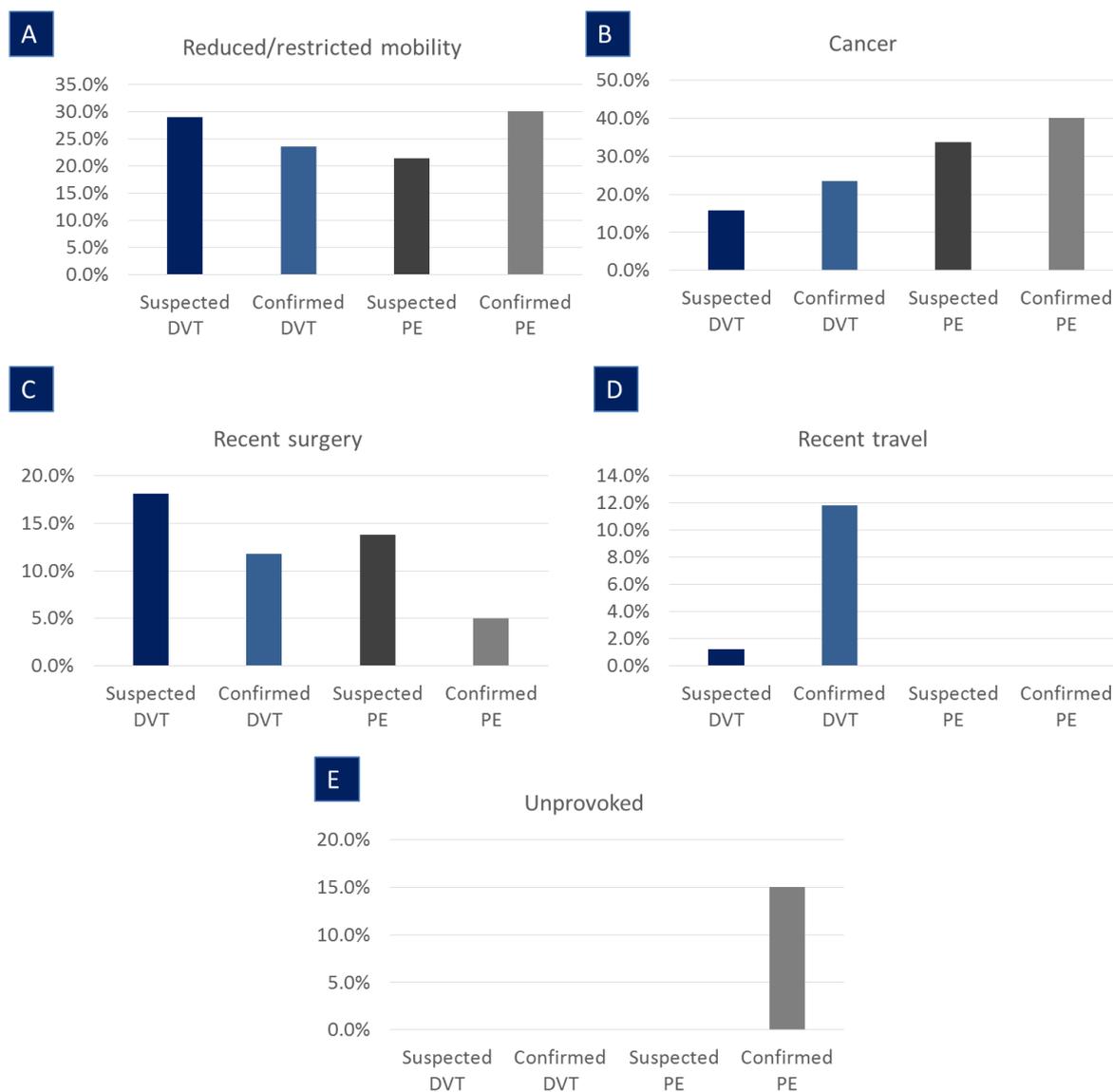


Figure 3.5. Provoked risk factors of venous thromboembolism (VTE). **A.** The percentage of cases with reduced/restricted mobility in suspected and confirmed cases of deep vein thrombosis (DVT) and pulmonary embolism (PE). **B.** The percentage of cases with cancer in suspected and confirmed cases of DVT and PE. **C.** The percentage of cases with recent surgery in suspected and confirmed cases of DVT and PE. **D.** The percentage of cases with the history of recent travel in suspected and confirmed cases of DVT and PE. **E.** The percentage of cases with unprovoked VTE.

Genetic factors:

Genetic factor was found in only one person with suspected DVT. The patient had a history of haemophilia.

D-dimers:

Although not the primary aim of the study, the levels of d-dimers were also noted for suspected and confirmed cases of VTE only where mentioned in the notes. D-dimer levels above 500 µg/L are considered high. D-dimers were raised for 12% with suspected DVT and 11.8% with confirmed DVT. In terms of PE, 43.8% with suspected PE and 45% patients with confirmed PE had elevated d-dimers.

Management:

Most of the patients with confirmed DVT were managed by one of the direct oral anticoagulants (DOACs) (47%). Of the DOACs 23.5% (4 patients) were treated with apixaban and 23.5% with rivaroxaban. Three patients (17.6%) were given dalteparin while 17.6% were managed on warfarin. Two of the patients (11.8%) on warfarin had inferior vena cava filters inserted. The treatment is not known for 3 cases (17.6%). In terms of the management of PE, 4 patients (20%) were treated with dalteparin, 5 with warfarin (25%), 6 (30%) with DAOCs (4 Apixaban, 1 rivaroxiban and 1 dabigatran) and 2 (10%) had IVC filters inserted.

Complications were reported for with warfarin (recurrent bleeding, significant blood loss, requiring blood transfusions), apixaban (haematuria), rivaroxaban (neutropenia). One person developed tinnitus from rivaroxaban and apixaban. Despite been on dalteparin, one patient developed PE.

Alternative diagnosis:

For 83 cases of unconfirmed DVT, the actual diagnosis was not known for 53.0% of the patients. The most frequent alternative diagnosis was cellulitis which accounted for 16.9% of the cases (**Figure 3.6A**). Other diagnoses included heart failure (3.6%), Baker's cyst (3.6%), haematoma (3.6% cases), septic arthritis (2.4%), drug reaction (2.4%), varicose veins/venous insufficiency (3.6%), septic wound (2.4%) and lymphedema (2.4%), mechanical fall (1.2%), pseudogout (1.2%) and postoperative oedema (1.2%).

Eighty unconfirmed PE cases had infection/inflammation± effusion as the most common diagnosis (23.8%) (Figure 3.5B). Heart failure was the second commonest alternative diagnosis (15%). Other included lung cancer/metastasis (8.6%), COPD (7.5%), atelectasis (3.8%), TB (2.5%), fat embolus (1.25%), sarcoidosis (1.25%), acute bronchitis (1.25%), gastro-oesophageal disease (1.25%), hyponatremia (1.25%), severe aortic stenosis (1.25%) and respiratory failure (1.25%). The diagnosis was inconclusive or unknown for 30% of the cases. The results indicate that the most common pathology attributed to DVT in the elderly is cellulitis while for PE it is infection.

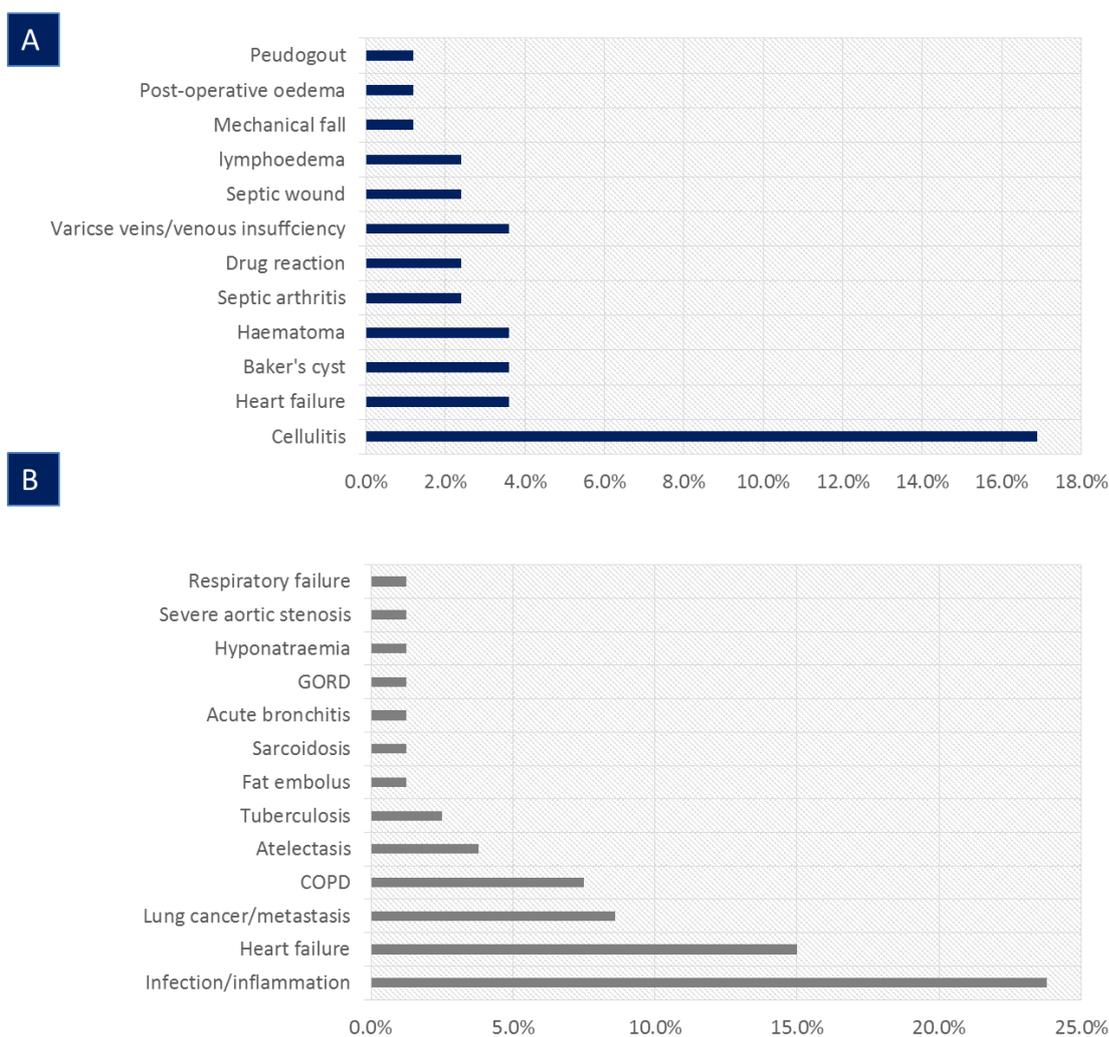


Figure 3.6. The definitive diagnosis in those suspected with DVT. **A.** Definitive diagnosis in patients suspected with deep vein thrombosis (DVT). **B.** Definitive diagnosis in patients presenting with suspicion of pulmonary embolism (PE).

4. Discussion

The incidence of VTE increases with age. However, with an increase in age the presentation and diagnosis becomes a challenge. This is because with an increase in age the rate of multi-morbidities increases (6). The presentation may be atypical or can mimic other medical conditions. Due to the diagnostic dilemmas elderly patients presenting with signs and symptoms of VTE are frequently hospitalised.

We found that the majority of the suspected VTE cases did not have the disease. Out of the 200 suspected cases of VTE only 18.5% (37 cases) had confirmed VTE. Additionally, in 2 of the confirmed DVT cases PE was also present which was the main indication for a scan for DVT. DVT acutely presented in only 14% of the cases. This suggest that there were more cases of confirmed PE than DVT. Previously, an increase in the incidence of PE is seen relative to the incidence of DVT with an increase in age (1,7). Hence our study's finding is in line with those previously reported.

We found that in 21 cases calf DVT was not 100 excluded. This was mainly due to oedematous lower limbs which made it difficult to examine the deep veins. From the results it is evident that 7.2% of the patients had venous problems. This in addition to other co-morbidities commonly causing peripheral oedema, such as heart failure, kidney failure or lymphoedema, not only makes the initial presentation, but also the diagnosis difficult in elderly population who generally have higher prevalence of these conditions.

In our study, 20% patients with PE had a confirmed DVT on the scan. For the rest of the cases it could not be established from the notes. The reported rate of identification of a simultaneous DVT with confirmed PE is up to 40% (8). The lower percentage in this study could be solely attributed to the incomplete/missing clinical notes.

Age and VTE:

Our results indicate that the age range of 75-85 years had the highest number of confirmed VTE cases, 75-80 years for PE and 81-85 years of age for DVT. Although VTE was suspected in all age

ranges, a decreased was observed with the increase in age. Hence our findings are not consistent with the previously reported prevalence of VTE which is known to increase with an increase in age. Several factors can be attributed to this inconsistency in results. Firstly, the majority of the patients in our sample were aged 75-85 years (146 out of 200) and our findings may solely be due to a lower number of patients with age range 95-100 years. Other studies have not stratified patient age in such groups, especially with a separate group for ages 85-100 years. Secondly, we only focussed on patient's presenting to the Manchester Royal Infirmary which is a part of Central Manchester University hospitals. At the trust patients over the age of 90 only account of 1.44% of the patient population and generally there is an increased prevalence of long-term conditions (9). This may have accounted for the lower number of patients aged 95-100 years. Thirdly, VTE is underdiagnosed in most of the cases, with figures up to 40% been reported based on post-mortem studies for PE (10). These underdiagnoses of PE may become more common with the increase in age due to atypical presentation, such as syncope/collapse. Hence these factors may have attributed to the discrepancy in the results observed in this study.

Presentation of VTE:

In our study the majority of the cases of DVT involved lower limbs with only 1% presenting with upper limb DVT. The lower extremity is known to be the commonest site for DVT (11,12).

We found that the most common symptom of DVT was unilateral oedema. Bilateral oedema was seen in suspected cases; however, this was not the case in confirmed DVT cases. This suggests that unilateral swelling is highly suggestive of DVT while bilateral oedema excludes the diagnosis of DVT. To date none of studies have specifically looked at the signs and symptoms of DVT in the elderly population, though in the literature unilateral limb swelling is considered to be the most specific symptom of DVT (13). This may be particularly useful in elderly population with comorbidities which can also present with oedema, or most commonly bilateral oedema, for example, heart failure, COPD, liver and kidney failure. Other symptoms of DVT, such as pain/tenderness was less common

and warmth was more common in those with confirmed DVT. Hence, these in combination of unilateral limb swelling may be highly suggestive of DVT in the elderly population. In confirmed cases of DVT, PE symptoms was seen in 38.5% of the people in contrast to 7.2% with no DVT. This may be explained for the finding that in the elderly PE is more common than DVT (1).

Having compared the cases of confirmed PE and suspected cases of PE it is evident that the common presenting signs and symptoms of PE in the elderly include desaturation, dyspnoea, pleuritic chest pain and tachycardia. However, because a similar percentage was seen in the two groups, these signs and symptoms remain non-specific in the elderly population. An analysis of studies involving patient aged 65 or above with PE found similar results: dyspnoea (range 59%–91.5%), tachypnoea (46%–74%), tachycardia (29%–76%), and chest pain (26%–57%). However, in our study tachypnoea was not seen, though desaturation was a key sign (14). The discrepancy in the results can be explained due to this non-systematic review analysing different studies which had different number of patients and different methodologies used in each study which may explain the wide ranges of percentages. Nevertheless, it is clear that such symptoms in this population can be attributed to other cardiopulmonary conditions presenting in a similar way, for example, atrial fibrillation for tachycardia, COPD and heart failure for desaturations and dyspnoea, pleuritic chest pain for pneumonia or pleural effusion. Hence, a low index of suspicion should remain.

In addition to the above symptoms, collapse was seen in 5% of patients with suspected and confirmed PE. Collapse is another non-specific sign which may indicate a more severe PE. Though this study was not a comparison of VTE presentation in the young and older population, it is known that syncope presents more commonly in elderly compared to the young (15). Not many studies have investigated the signs and symptoms of VTE in the elderly population which makes it problematic to check the consistency of results and hence the reliability of the study.

Risk factor of VTE:

We divided the risk factors into comorbidities, provoked risk factor and genetic factors. In this study 99% of patients had one or more risk factor of VTE. Although not specific to the elderly, one or more risk factors are found in 96% of the patients treated for VTE (16). From our results it can be seen that a prior VTE is associated with increased VTE compared to those with only suspicion of VTE. Having a past medical history of VTE increases the chance of recurrence, especially in the presence of additional risk factors (17). This specially implies to the elderly population in whom age and the presence of chronic condition can further increase the risk. In terms of comorbidities several medical conditions were seen in suspected and confirmed cases of VTE (**Table 1**). In confirmed cases of DVT, cardiovascular accident/ transient ischaemic attack and chronic kidney disease appeared to be more common than in cases with no confirmed DVT. For confirmed cases of PE, greater number of certain diseases were seen than in suspected PE cases. These included hypertension, ischaemic heart disease/myocardial infarction, high cholesterol, chronic kidney disease, cerebrovascular accident/ transient ischemia attack and previous DVT/PE. Previously studies have looked at the risk factors of DVT in the elderly population. Having a severe medial disorder is a risk factor for VTE (18). Medical conditions associated with an increased risk of VTE include heart failure, COPD, hypertension, high cholesterol, diabetes and venous problems (19–21). Although this study's result do not indicate an increased incidence of COPD, heart failure, venous problems and diabetes in those with confirmed DVT or PE, it does reflect the dilemmas and diagnostic uncertainties as the signs and symptoms of some of these conditions may be mistaken for VTE or vice versa. In this study there were 21 cases of DVT which were inconclusive of calf DVT commonly as a result of peripheral oedema. The underlying cause of peripheral oedema is not known. Some of the medical condition mentioned may have been contributing to this, however, it remains uncertain. Nonetheless, our findings suggest that cardiovascular diseases and a previous VTE may increase the risk of VTE.

In terms of provoked risk factors we found an increased prevalence of cancer in those with confirmed VTE. Reduced or restricted mobility was seen in confirmed PE cases and recent travel in confirmed DVT cases, more so than in those suspected of PE and DVT cases, respectively. Malignancy in any age is associated with increased risk of VTE (22). Recent travel and reduced and restricted mobility, although a separate group in this study, increase the risk of VTE by the same mechanism which is venous stasis. Immobilisation has been associated with 40% of VTE (19). This can substantially increase the risk of VTE in the elderly who are prone to falls and are frail. In our study the confirmed VTE cases did not have an increased prevalence of recent surgery compared to suspected VTE cases. Surgery is a known risk factor of DVT and in those over the age of 65 has shown to develop despite being on prophylactic treatment (23). A reason might be that we did not specify recent surgery and it is difficult to determine this from the notes, unless specified clearly when referring for a scan.

In our study genetic risk factors accounted for a very small percentage. Only one person with suspected DVT had a history of haemophilia. Hence it may suggest that the prevalence of genetic conditions is not increased in the elderly population. A case control study analysing genetic risk factors in the elderly population found an increased risk of venous thrombosis in those aged 70 or over (24). Our study did not find any genetic factors contributing to VTE, which may be due only a small percentage (18.5%) of patients with confirmed VTE.

We also noted the d-dimer levels in these with suspected and confirmed cases of VTE. Twelve percent of suspected DVT cases and 44% of suspected PE cases had raised levels of d-dimers. This indicates that d-dimers are not a specific marker of VTE. The specificity is known to be only 40-56% in general population (25). In the elderly its diagnostic implications are further questioned as there is normally an increase in levels of d-dimers with age and the presence of comorbidities can further make the diagnosis difficult (25). Hence in elderly population the use of age-adjusted d-dimers may play a better role in diagnostic work-up for VTE (26).

Management of VTE:

It was difficult to establish from the online notes the treatment and its associated complications for all the patients treated for VTE. For the cases with known management plan DOACs was the most popular treatment strategy for both DVT and PE (altogether 38% of the VTE cases). DOACs have mostly replaced warfarin due to the lower bleeding risk and equal efficacy compared to other form of anticoagulation in the elderly (55). However, warfarin was the treatment of choice in 22% of patients. Though it was not the primary aim of the study it would have good to analyse the indication for the choice of anticoagulation used.

Different complications were reported with different forms of anticoagulation. With warfarin bleeding was report, which can be mainly attributed to its narrow therapeutic window, interactions with food and medications. Warfarin requires regular monitoring of the INR which can be difficult in the frail elderly population.

The two DOACs commonly prescribed include apixaban and rivaroxaban. Side effects associated with these included haematuria, tinnitus and neutropenia (with rivaroxaban alone). While bleeding is a known side effect on all the anticoagulation, other side effects (tinnitus and neutropenia) have been reported previously and are more common in those over the age of 60 (27–29).

One person developed DVT despite being treated with dalteparin. Dalteparin, a low molecular weight heparin, has shown to be effectively prevent VTE and is considered safe in elderly (30). To fully conclude the efficacy of dalteparin as an anticoagulant it would be more appropriate to take other factors in considerations such as other risk factors, timing and dosing of dalteparin.

Though from this study we are not fully able to evaluate the treatment modalities for VTE, from the results we have gathered DOACs are at an increase use in elderly population which may be due to their superiority in terms of lower bleeding risk. However, despite the advantages of DOACs for the

elderly patients warfarin is still used in certain cases. One reason may be the rapid reversibility option available for warfarin in cases of high risk of falls. Additionally, some of the side effects of anticoagulants are more common or pronounced in the elderly population; hence, precaution is required in this population (8).

Alternative diagnoses to VTE:

DVT:

From this study the most common diagnosis in suspected DVT cases was cellulitis which accounted for 17% of the cases. Cellulitis presents in a similar way to DVT with warmth, erythema and oedema. Secondary cellulitis can develop in those presenting with DVT (31). Hence those presenting with such symptoms should be evaluated for both. Other common ones observed in this study included heart failure, Baker's cyst, haematoma and venous insufficiency or varicose veins. Baker's cyst and calf haematoma have been previously reported as presenting as pseudo-DVT (32). In the elderly population due to the presence of multi-morbidities medical conditions such as heart failure and venous insufficiency can be mistaken for DVT or vice versa and hence these patients frequently require hospital admission, which increases the burden for the health services.

PE:

The most frequent diagnosis made in suspected PE cases was lung infection/inflammation. Heart failure, lung cancer, COPD and atelectasis were other common diagnoses. PE can present with a wide range of non-specific signs and symptoms which are in common with many other conditions, most commonly cardiopulmonary conditions. A study analysing the diagnosis of patients presenting to the emergency department with cardiopulmonary symptoms reported PE as the actual diagnosis in less than 4%. Most of the symptoms were due to other cardiopulmonary conditions, such as dyspnoea due to acute heart failure, COPD and pneumonia and chest pain due to myocardial infarction (33). Additionally, in the elderly population these conditions can coexist or can be a complication of an underlying condition. For example, pneumonia and pulmonary embolism can co-

exist while a complication of COPD is PE (34,35). Hence, in the elderly population the diagnosis is not always straightforward and a complete clinical picture, including past medical history needs to be taken into account.

Limitations of the study:

Our study has several limitations. Firstly, we analysed retrospective data using the online system Chameleon to assess patients' clinical notes. Retrospective analysis as opposed to prospective analysis has inferior level of evidence. Additionally, the use of online clinical notes has its own limitations. It is difficult to gather all the information and the missing information may lead to confounding of the results, for example, some of the risk factors, may have been missing. We were only able to identify one person with genetic risk factor which may be due to this reason. In majority of the cases the complete management plan was not clear and the complications related to the anticoagulants were difficult to establish.

Another limitation of our study is that the signs and symptoms were not quantified. Although we gathered the reported signs and symptoms of tachycardia, tachypnoea and desaturations, we did not know the actual values. Nonetheless the signs and symptoms we observed in our study are those typical of a VTE. For future studies this can be further improved on so that the signs and symptoms in elderly population are objectively measured and any differences observed in the suspected and confirmed cases of VTE can be analysed.

Our patient sample may have been another source of bias. Our patient sample consisted of patients who have had CTPA in suspicion of PE. This excluded the patients who may have had ventilation/perfusion (V/Q) scan for suspected PE. V/Q scan is normally indicated in those with no lung pathology that can affect the result of the scan. Hence the sample in this study may have a higher rate of lung problems which may have confounded the result of comorbidities and alternative diagnoses. However, CTPA is considered the gold standard for investigating PE and is recommended over V/Q scan, depending on the availability.

Furthermore, we only analysed patients presenting to the Manchester Royal Infirmary at a given time point (August 2016-January 2017). The patient population presenting to the hospital generally has a high rate of long-term conditions (9). Hence it affects the generalisability of the findings. Additionally, the prevalence of some conditions may be higher during the time-period was used to analyse the results. For example, community acquired pneumonia is most frequent in winter which may explain why this was the most common alternative diagnosis in suspected cases of VTE (36). However other studies have produced replicative results thus increasing the reliability of our study.

5. Conclusion:

VTE is predominantly a disease of elderly population, yet not much research has been done specifically in this population and hence it remains incompletely understood. Our analysis of the signs and symptoms suggest that DVT in the elderly population may commonly present with unilateral limb oedema, warmth and PE symptoms while PE can present with low oxygen saturations, dyspnoea, tachycardia, pleuritic chest pain or collapse. These signs and symptoms overlap with several other medical conditions and in elderly population this can be particularly problematic as there is a high rate of multi-morbidity. In the elderly VTE is a multi-causal disease with increasing age and several chronic conditions being a non-modifiable risk factor developed over-time while provoked factors such as immobility or malignancy further aggravating the risk of VTE. Active cancer, chronic conditions, such as CCF, respiratory insufficiency and age over 75 years is associated with proximal vein thrombosis which can more likely result in fatal PE (37). Hence a high index of suspicion should remain in this population and a thorough history and examination should be carried out to elicit any provoked factors or identify any comorbid conditions associated with VTE. More research is required to fully grasp the nature of VTE in elderly population with the aim to reduce hospital admissions and disease burden on the healthcare services.

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