

Dilemmas in the management of venous thromboembolism in older patients

ABSTRACT

Venous thromboembolism most commonly affects older patients. Despite the high incidence in this population, challenges remain in terms of the understanding of its presentation, diagnosis and management. Old age is associated with multi-morbidities which may complicate the diagnosis of venous thromboembolism as signs or symptoms may be attributed to underlying medical conditions. The presence of certain comorbidities (such as congestive cardiac failure and chronic obstructive pulmonary disease) also increases the risk of venous thromboembolism, but could mimic the clinical features of pulmonary embolism. In addition, the physiological processes associated with ageing and factors such as immobility and malignancy, which are more common in older people, will further increase the thrombotic risk. Dilemmas also exist with treatment decisions because of the concomitant increased risk of bleeding, comorbidities, polypharmacy, frailty and the risk of falls.

Venous thromboembolism is predominantly a disease of older patients. Owing to its multi-causal aetiology and the presence of multiple morbidities in this population, uncertainties remain in its presentation, diagnosis and management.

Venous thromboembolism is a disorder encompassing deep vein thrombosis and pulmonary embolism. It is the third most common cardiovascular disease with an annual incidence of 1–2 per 1000 of the population (approximately two-thirds of cases are deep vein thrombosis and one-third are pulmonary embolism) (Cushman, 2007). An increase in the incidence of venous thromboembolism has been observed from 2001–2009 (Heit et al, 2016). This may, in part, be attributed to the use of advanced medical diagnostic tools such as computed tomography, pulmonary angiography and magnetic resonance imaging (Heit et al, 2016).

The incidence of venous thromboembolism increases with age and is predominantly a disease of older patients (approximately 1 in 100 000 in childhood *vs* 1 in 100 in people over the age of 80 years per year) (Engbers et al, 2010). The older population includes people aged 65 years and above. The difference in incidence between the young and the older population suggests that age is a

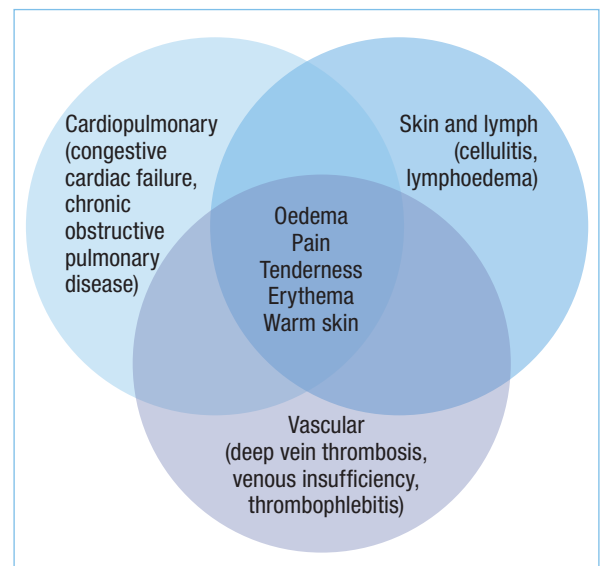
non-modifiable risk factor of venous thromboembolism. However, in this population it may be difficult to make a diagnosis because of the overlapping presentation (signs and symptoms) of venous thromboembolism with other medical conditions.

Presentation of venous thromboembolism in older patients

Deep vein thrombosis classically presents as leg swelling, tenderness and erythema. However, other pathologies can cause these symptoms in older patients in whom comorbidities may either present with or increase the risk of these symptoms, e.g. increased risk of cellulitis in diabetes, venous insufficiency or peripheral arterial disease (Figure 1).

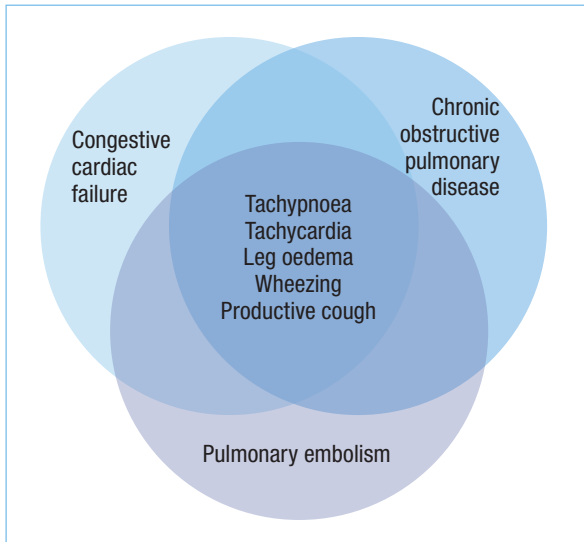
Pulmonary embolism can present with a wide range of symptoms including dyspnoea, tachypnoea, tachycardia, haemoptysis, pleuritic chest pain and syncope. In older patients, pulmonary embolism may present with non-specific symptoms such as confusion and fever (Gosney et al, 2012). A study analysing the symptoms of pulmonary embolism in older patients and the young population found that collapse as a symptom was more common than chest pain in older patients compared to the young ($P < 0.02$) (Timmons et al, 2003). However, this was a small sample study (sample size 60) at a district general hospital and selected patients on the basis of a positive

Figure 1. Symptoms of deep vein thrombosis. One or more of these may also be seen in other diseases, for example cardiopulmonary, vascular, and skin and lymph pathologies.



Miss Musfira Shakeel, Medical Student, University of Manchester, Manchester M13 9WL
Dr Jecko Thachil, Consultant Haematologist, Department of Haematology, Manchester Royal Infirmary, Manchester
 Correspondence to: Miss M Shakeel
 (musfira.shakeel@student.manchester.ac.uk)

Figure 2. Overlapping signs and symptoms of cardiopulmonary diseases.



spiral computed tomography result, hence generalization to the wider population of older patients may be difficult. Nevertheless, in older patients with multiple comorbidities the symptoms of venous thromboembolism lack specificity.

In addition, because of the multiple morbidities commonly seen in older patients, the symptoms may be attributed to underlying medical conditions, most commonly cardiopulmonary pathologies (Figure 2). Approximately one in four atypical exacerbations of chronic obstructive pulmonary disease are misdiagnosed as pulmonary embolism as the cause of acute shortness of breath (Moua and Wood, 2008). This can make it quite challenging to diagnose or rule out venous thromboembolism. However, there are certain factors that may support a diagnosis. Cardiopulmonary pathologies commonly present with hypoxaemia and dyspnoea. Correcting hypoxaemia by oxygen or positive pressure flow may point towards a diagnosis of chronic obstructive pulmonary disease whereas massive pulmonary embolism involving intrapulmonary or intracardiac shunt may be resistant to this (Moua and Wood, 2008). Severe dyspnoea out of proportion to the pulmonary vascular congestion may suggest heart failure rather than pulmonary embolism (Piazza and Goldhaber, 2008).

Risk factors for venous thromboembolism in older patients

Once venous thromboembolism is suspected, the next step is to determine the risk factors. Several factors can contribute to the process of venous thrombosis in older patients. It is important to have a good understanding of these so that the right measures can be taken to prevent or appropriately treat venous thromboembolism. Ageing in itself is a risk factor for venous thromboembolism. The likely mechanism may be decreased levels of anticoagulant factors, for example protein C and protein S, and increased

Figure 3. Risk factors for venous thromboembolism in older patients. Arrows indicate the multicausal nature of the disease in older patients.

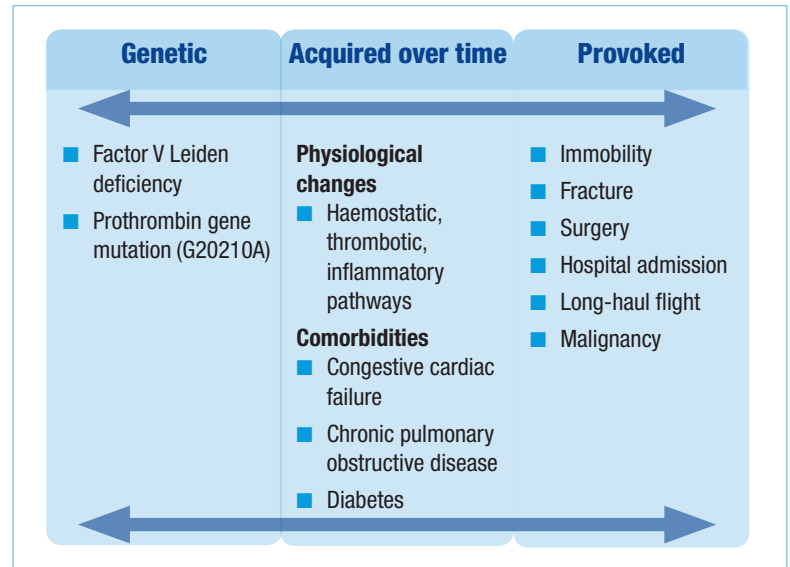


Table 1. Risk factors for venous thromboembolism, associated prevalence and attributed risk in the elderly population

Risk factor	Prevalence (%)	Attributed risk (%)
Immobilization	25	66–83
Malignancy	10	86
Congestive cardiac failure	22	33–60
Chronic obstructive pulmonary disease	11	33
Diabetes mellitus	16	0–50
Genetic factors	7	50–80

Adapted with permission from Engbers et al (2010)

levels of procoagulants (Corrigan et al, 2016). This prothrombotic state and venous stasis as a result of reduced lower limb strength and mobility in older patients puts them at a higher risk of venous thromboembolism. Age-specific changes in haemostatic and inflammatory pathways may further contribute to the risk (Johnson et al, 2016).

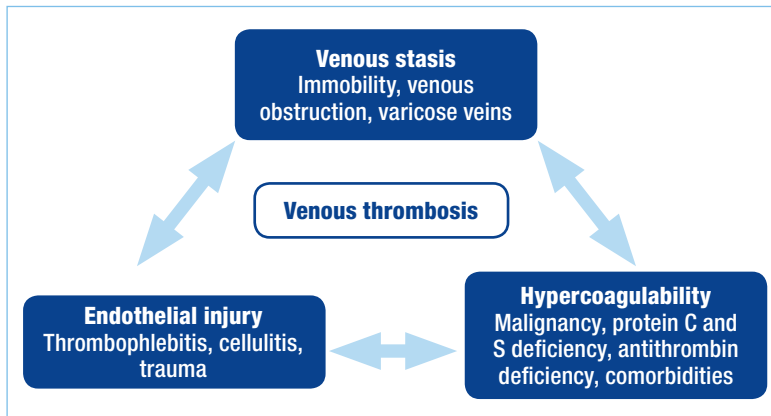
In addition to these physiological changes several other factors predispose this population group to a higher risk of thrombosis. The risk factors can be divided into provoking or genetic factors or those acquired over time (Figure 3).

Table 1 outlines the risk factors for venous thromboembolism, their prevalence and attributed risk in older patients. Generally these risk factors increase the risk of thrombosis by predisposing to one or more of the pathological processes of Virchow's triad (Figure 4).

Immobility and venous thromboembolism

Immobility, leading to stasis and venous pooling, increases the risk of venous thromboembolism. It can occur as a result of general hospitalization, surgery, fractures and long

Figure 4. Virchow's triad (endothelial injury, hypercoagulable state and venous stasis) – these factors in combination describe the pathogenesis of thrombosis.



haul flights (more than 4 hours). Having different causes of immobility, underlying pathologies and time period of immobility used by different studies makes it difficult to pinpoint the factors that link immobility with the risk of deep vein thrombosis. Nevertheless, in older patients thrombosis is associated with surgery, fractures, plaster cast, minor leg injuries and transient immobility at home (Engbers et al, 2014). Although not age-specific, a meta-analysis analysing the risk of venous thromboembolism in medical bedridden patients found an overall risk ratio of 1.86 (confidence interval 1.61–2.14, $P < 0.001$) in terms of thrombotic burden of immobilization (Pottier et al, 2009). However, the impact of the underlying condition cannot be excluded. A case-control multicentre study analysing independent risk factors for deep vein thrombosis in hospitalized patients (aged 65 years and over) found an odds ratio of 6.67 (confidence interval 2.97–14.99, $P < 0.0001$) in those bedridden for up to 14 days (Weill-Engerer et al, 2004). Immobility in any form increases the risk of venous thrombosis. The most likely causative factor is venous stasis while additional risk factors (such as multi-morbidities) further increase the risk.

Malignancy and venous thromboembolism

Malignancy is a hypercoagulable state and increases the risk of venous thromboembolism by 7-fold (Engbers et al, 2010). The incidence of most cancers increases with age; hence there is an increased risk of cancer and cancer-associated thrombosis in older patients. Certain cancers are associated with a greater risk (for example, pancreas, brain, lung and ovarian) and the greater the spread of cancer (stage 4) the higher the risk (Chee et al, 2014). In addition to cancer-related factors, treatment-related factors are also associated with venous thromboembolism, for example, central venous catheters, chemotherapy and anti-angiogenic and hormonal agents. Venous thromboembolism has a poor prognosis in cancer patients and tends to recur. Hence it is essential to provide prophylaxis and effectively manage venous thromboembolism in cancer patients in order to reduce morbidity, mortality and improve the quality of life.

Multi-morbidities and venous thromboembolism

With increasing age the incidence of multi-morbidities (having more than one disease) increases. Over the age of 85 years, the prevalence of multi-morbidity is reported to be as high as 95.1% (Formiga et al, 2013). Several medical conditions are associated with the risk of venous thromboembolism, most commonly cardiopulmonary disease such as congestive cardiac failure, chronic obstructive pulmonary disease and pneumonia. Despite the high prevalence of these conditions in older patients, not much research has been done specifically investigating their role in this population.

Congestive cardiac failure

Congestive cardiac failure is an independent risk factor for venous thromboembolism both in inpatients and outpatients. Venous thromboembolism is more likely to develop in those with congestive cardiac failure than in those without congestive cardiac failure, with odds ratio of 0.97 (95% confidence interval 0.97–0.97, $P < 0.04$) and 1.06 (95% confidence interval 1.06–1.07, $P < 0.04$) in those aged 60–79 and ≥ 80 years respectively (Beemath et al, 2006; Dean and Abraham, 2010). In such patients pulmonary embolism is more common than deep vein thrombosis.

Chronic obstructive pulmonary disease

Another risk factor for venous thromboembolism, especially pulmonary embolism, is chronic obstructive pulmonary disease. The prevalence of pulmonary embolism ranges from 20% (in outpatient chronic obstructive pulmonary disease exacerbations) to 25% (in those requiring hospital admission) (Rizkallah et al, 2009; Piazza et al, 2012). In addition, pulmonary embolism in hospitalized patients with chronic obstructive pulmonary disease increases mortality, with immobility an additional poor prognostic factor (Piazza et al, 2012).

Pneumonia

Pneumonia is associated with an increased risk of venous thromboembolism. This may be caused by the underlying inflammatory process initiating coagulation. Although not directly studied in older patients, a large scale patient sample using self-report found a 5-fold increase in venous thromboembolism with pneumonia, with pulmonary embolism more prominent than deep vein thrombosis (Ribeiro et al, 2012). Although the accuracy of self-report is questionable, retrospective cohort studies have also found an increased risk of acute venous thromboembolism with pneumonia (Samama, 2000; Smeeth et al, 2006).

Others

In addition to the cardiopulmonary conditions mentioned above, other risk factors are associated with increased risk of venous thromboembolism. A meta-analysis of 33 case-control and cohort studies found a significantly higher prevalence of venous thromboembolism in patients

with body mass index ≥ 30 kg/m² (odds ratio=2.45, 95% confidence interval 1.78–3.35), hypertension (odds ratio=1.40, 95% confidence interval 1.06–1.84) and hypercholesterolaemia (weighted mean differences=8.94mg/dl, 95% confidence interval 3.52–14.35mg/dl) (Ageno et al, 2008). However, the prevalence of venous thromboembolism was similar in people with diabetes and those without diabetes. Contradictory results have been found with diabetics and risk of venous thromboembolism – some studies indicate an increased risk of venous thromboembolism, but others show no effect. Overall, the risk is known to be higher in younger compared to older patients with diabetes (Engbers et al, 2010). Because the prevalence of diabetes is much higher in older patients compared to the young (16% *vs* 6%), this may suggest an equal risk of venous thromboembolism in the two populations (Engbers et al, 2010).

Genetic conditions and venous thromboembolism

Although inherited conditions mainly present in young patients, conditions such as factor V Leiden deficiency are often found in older patients presenting with venous thromboembolism. The hypercoagulability in factor V Leiden deficiency results from failure of inactivation of factor V by protein C. It is found in approximately 20% of individuals with their first presentation of venous thromboembolism, which also includes a minority of people over the age of 70 years (Johnson et al, 2016). In addition to factor V Leiden deficiency, prothrombin G20210A mutation and non-O blood group are also risk factors for venous thromboembolism in older patients (Karasu et al, 2016). Hence, it is important to elicit any past medical history as well as exploring other potential provoking factors. In older patients, acquired forms of thrombophilia such as hyperhomocysteinaemia, myeloproliferative disorders and heparin-induced thrombocytopenia are more common (Johnson et al, 2016).

The effect of an isolated risk factor is difficult to study in older patients as they commonly present with multiple morbidities. Hence, in this population venous thromboembolism is a multicausal disease. Additionally, venous thromboembolism is associated with high rates of mortality. There is a 6% mortality rate associated with deep vein thrombosis within 1 month of the episode and 10% for pulmonary embolism (Cushman et al, 2004). Hence, a better understanding of the presentation and risk factors for venous thromboembolism in older patients is required so that a prompt diagnosis is made and treatment initiated.

Diagnostic challenges of venous thromboembolism in older patients

Pulmonary embolism remains underdiagnosed in older patients. As high as 40% of cases of pulmonary embolism found at post-mortem were not clinically suspected (Gosney et al, 2012). In terms of diagnosis of venous

thromboembolism, determining the pre-test probability remains the first step. Commonly used criteria for pulmonary embolism include the Well's score and the revised Geneva score. Dependent on clinical probability, the next step involves either D-dimers or more specific investigations if there is a high level of suspicion. D-dimer is a non-specific marker (specificity of 40–56%) and normally increases with age (Righini et al, 2000). This is mainly attributed to multiple morbidities in this population. Hence, only a lower than normal D-dimer value is useful, but this does not exclude venous thromboembolism if the clinical suspicion remains. This questions the cost-effectiveness of non-invasive diagnosis in older patients population. The use of age-adjusted D-dimer (age of the patient x10) as a cut-off in comparison to the standard value of 500 µg/litre may be more applicable (Righini et al, 2014). Although this can be easily calculated by physicians, this is not yet implemented in clinical practice and requires further validation.

Imaging deep vein thrombosis and pulmonary embolism can also be problematic. The gold standard for deep vein thrombosis diagnosis is venous ultrasonography and for pulmonary embolism is computed tomography pulmonary angiography. While in those with long-standing oedema it can be challenging to completely rule out deep vein thrombosis, the risk of radiation and contrast dye exposure associated with computed tomography pulmonary angiography cannot be ignored.

Treatment challenges of venous thromboembolism in older patients

The basis of venous thromboembolism treatment is anticoagulation. The most common risk of anticoagulation is bleeding, and increasing age is associated with a greater risk of anticoagulation-associated bleeding (Johnson et al, 2016). With every 10-year increase in age, the risk of bleeding increases by 40% (Barco et al, 2013). Ultimately the physician must balance the risk of haemorrhage *vs* the benefit of anticoagulation, and these factors should be discussed in detail with the patient and the family. Some of the most challenging aspects of venous thromboembolism management in older patients involve extended prophylaxis in patients with unprovoked venous thromboembolism who might benefit from lifelong anticoagulation. Decision tools, such as DASH and HERDOO2, may help balance risks of thrombosis and bleeding. All anticoagulants increase the risk of bleeding.

Along with this, important considerations in older patients include renal function, frailty, comorbidities, risk of falls and current medications and their interactions (Robert-Ebadi et al, 2009). For example, in those with a high risk of falls, anticoagulant agents that can be easily reversed, such as warfarin, may be preferred in the absence of any contraindications. However, this needs to be balanced with the requirement for regular monitoring and interactions with other medications, especially in a frail older patient on polypharmacy.

KEY POINTS

- Venous thromboembolism is predominantly a disease of older patients.
- Presentation of pulmonary embolism may be atypical or can be attributed to co-existing medical conditions, such as cardiopulmonary disease, congestive cardiac failure and chronic obstructive pulmonary disease.
- Venous thromboembolism has multi-causal aetiology in older patients.
- Comorbidities, such as congestive cardiac failure, chronic obstructive pulmonary disease, pneumonia, diabetes, hypertension and hypercholesterolaemia, increase the risk of venous thromboembolism.
- Malignancy is a strong risk factor of venous thromboembolism, incidence of which increases with age.
- Despite the high incidence of venous thromboembolism in older patients, not much research on its risk factors has been done specifically in this age group.
- The choice of anticoagulation in older patients is determined by the risk of bleeding and falls, presence of comorbidities, polypharmacy and drug interactions, frailty, patient circumstances and preferences.

Several different anticoagulants are currently used in practice, but each has its own challenges (Table 2). The direct oral anticoagulants have mainly replaced the vitamin K antagonist warfarin which was the cornerstone of venous thromboembolism treatment. Meta-analysis of randomized trials concluded that direct oral anticoagulants having equal efficacy to conventional anticoagulants in older patients, with a reduced risk of intracranial bleeding (Sardar et al, 2014). Currently licenced direct oral anticoagulants in the UK include dabigatran (direct thrombin inhibitor) and apixaban, edoxaban and rivaroxaban (factor Xa inhibitors). Owing to the lack of evidence directly comparing the different direct oral anticoagulants and differences in study populations, it is difficult to choose the most appropriate one for different indications (National Institute for Health and Care Excellence, 2017). This decision is directed by the patient's preferences and clinical circumstances. It should also be highlighted that the pivotal trials using direct oral anticoagulants included very few patients over the age of 90 years and, as such, the efficacy and safety in this group is not known. Additionally, frailty and multi-morbidities may not have been represented in these trials. Although many physicians consider the ease of using direct oral anticoagulants an advantage, a reversal agent is only

currently available for dabigatran. However, antidotes for factor Xa inhibitors, e.g. andexanet, have shown efficacy in clinical trials.

Conclusions

Venous thromboembolism in older patients has a high prevalence and disease burden. Several factors can contribute to venous thromboembolism, so a high index of suspicion should remain when considering the diagnosis. However, this can be challenging as a result of multiple morbidities and overlapping symptoms which may delay the diagnosis. Careful management planning is required in this age group because of the polypharmacy, drug interactions and increased risk of bleeding. **BJHM**

Conflict of interest: Miss M Shakeel: none; Dr J Thachil has been paid honoraria by Bayer, BMS-Pfizer and Boehringer Ingelheim.

- Agno W, Becattini C, Brighton T, Selby R, Kamphuisen PW (2008) Cardiovascular risk factors and venous thromboembolism: a meta-analysis. *Circulation* **117**(1): 93–102. <https://doi.org/10.1161/CIRCULATIONAHA.107.709204>
- Barco S, Cheung YW, Eikelboom JW, Coppens M (2013) New oral anticoagulants in elderly patients. *Best Pract Res Clin Haematol* **26**(2): 215–224. <https://doi.org/10.1016/j.beha.2013.07.011>
- Beemath A, Stein PD, Skaf E, Al Sibae MR, Alesh I (2006) Risk of venous thromboembolism in patients hospitalized with heart failure. *Am J Cardiol* **98**(6): 793–795. <https://doi.org/10.1016/j.amjcard.2006.03.064>
- Chee CE, Ashrani AA, Marks RS, Petterson TM, Bailey KR, Melton LJ 3rd, Heit JA (2014) Predictors of venous thromboembolism recurrence and bleeding among active cancer patients: a population-based cohort study. *Blood* **123**(25): 3972–3978. <https://doi.org/10.1182/blood-2014-01-549733>
- Corrigan D, Prucnal C, Kabrhel C (2016) Pulmonary embolism: the diagnosis, risk-stratification, treatment and disposition of emergency department patients. *Clin Exp Emerg Med* **3**(3): 117–125. <https://doi.org/10.15441/ceem.16.146>
- Cushman M (2007) Epidemiology and risk factors for venous thrombosis. *Semin Hematol* **44**(2): 62–69. <https://doi.org/10.1053/j.seminhematol.2007.02.004>
- Cushman M, Tsai AW, White RH, Heckbert SR, Rosamond WD, Enright P, Folsom AR (2004) Deep vein thrombosis and pulmonary embolism in two cohorts: the longitudinal investigation of thromboembolism etiology. *Am J Med* **117**(1): 19–25. <https://doi.org/10.1016/j.amjmed.2004.01.018>
- Dean SM, Abraham W (2010) Venous thromboembolic disease in congestive heart failure. *Congest Heart Fail* **16**(4): 164–169. <https://doi.org/10.1111/j.1751-7133.2010.00148.x>
- Engbers MJ, Van Hylckama Vlieg A, Rosendaal FR (2010) Venous thrombosis in the elderly: incidence, risk factors and risk groups. *J Thromb Haemost* **8**(10): 2105–2112. <https://doi.org/10.1111/>

Table 2. Anticoagulants, their indication and associated challenges when treating older patients

Anticoagulant	Indication	Challenges
Unfractionated heparin	Renal insufficiency, high bleeding risk	Increased risk of heparin induced thrombocytopenia, and osteoporosis, and poor pharmacokinetics compared to low molecular weight heparin. Requires monitoring
Low molecular weight heparin	First-line treatment usually for venous thromboembolism, continued treatment in cancer patients	Caution required in those with renal impairment
Warfarin	Commonest anticoagulant until recently after initial treatment with low molecular weight heparin	Narrow therapeutic range, food and drug interactions, international normalized ratio monitoring needed, patient adherence important
New oral anticoagulants	Alternative to warfarin, patient choice	No data in very old patients. Only dabigatran has reversal agent

- j.1538-7836.2010.03986.x
- Engbers MJ, Blom JW, Cushman M, Rosendaal FR, van Hylckama Vlieg A (2014) The contribution of immobility risk factors to the incidence of venous thrombosis in an older population. *J Thromb Haemost* **12**(3): 290–296.
- Formiga F, Ferrer A, Sanz H, Marengoni A, Albuquerque J, Pujol R; Octabaix study members (2013) Patterns of comorbidity and multimorbidity in the oldest old: the Octabaix study. *Eur J Intern Med* **24**(1): 40–44. <https://doi.org/10.1016/j.ejim.2012.11.003>
- Gosney M, Harper A, Conroy S (2012) *Geriatric Medicine*. Oxford University Press, Oxford
- Heit JA, Spencer FA, White RH (2016) The epidemiology of venous thromboembolism. *J Thromb Thrombolysis* **41**(1): 3–14. <https://doi.org/10.1007/s11239-015-1311-6>
- Johnson SA, Eleazer GP, Rondina MT (2016) Pathogenesis, diagnosis, and treatment of venous thromboembolism in older adults. *J Am Geriatr Soc* **64**(9): 1869–1878. <https://doi.org/10.1111/jgs.14279>
- Karasu A, Engbers MJ, Cushman M, Rosendaal FR, van Hylckama Vlieg A (2016) Genetic risk factors for venous thrombosis in the elderly in a case-control study. *J Thromb Haemost* **14**(9): 1759–1764. <https://doi.org/10.1111/jth.13409>
- Moua T, Wood K (2008) COPD and PE: a clinical dilemma. *Int J Chron Obstruct Pulmon Dis* **3**(2): 277–284.
- National Institute for Health and Care Excellence (2017) Anticoagulants, including non-vitamin K antagonist oral anticoagulants (NOACs). www.nice.org.uk/advice/ktt16 (accessed 3 June 2017)
- Piazza G, Goldhaber SZ (2008) Pulmonary embolism in heart failure. *Circulation* **118**(15): 1598–1601. <https://doi.org/10.1161/CIRCULATIONAHA.108.803965>
- Piazza G, Goldhaber SZ, Kroll A, Goldberg RJ, Emery C, Spencer FA (2012) Venous thromboembolism in patients with chronic obstructive pulmonary disease. *Am J Med* **125**(10): 1010–1018. <https://doi.org/10.1016/j.amjmed.2012.03.007>
- Pottier P, Hardouin JB, Lejeune S, Jolliet P, Gillet B, Planchon B (2009) Immobilization and the risk of venous thromboembolism. A meta-analysis on epidemiological studies. *Thromb Res* **124**(4): 468–476. <https://doi.org/10.1016/j.thromres.2009.05.006>
- Ribeiro DD, Lijfering WM, Van Hylckama Vlieg A, Rosendaal FR, Cannegieter SC (2012) Pneumonia and risk of venous thrombosis: results from the MEGA study. *J Thromb Haemost* **10**(6): 1179–1182. <https://doi.org/10.1111/j.1538-7836.2012.04732.x>
- Righini M, Goehring C, Bounameaux H, Perrier A (2000) Effects of age on the performance of common diagnostic tests for pulmonary embolism. *Am J Med* **109**(5): 357–361. [https://doi.org/10.1016/S0002-9343\(00\)00493-9](https://doi.org/10.1016/S0002-9343(00)00493-9)
- Righini M, Van Es J, Den Exter PL et al (2014) Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA* **311**(11): 1117–1124. <https://doi.org/10.1001/jama.2014.2135>
- Rizkallah J, Man SFP, Sin DD (2009) Prevalence of pulmonary embolism in acute exacerbations of COPD: a systematic review and meta-analysis. *Chest* **135**(3): 786–793. <https://doi.org/10.1378/chest.08-1516>
- Robert-Ebadi H, Le Gal G, Righini M (2009) Use of anticoagulants in elderly patients: practical recommendations. *Clin Interv Aging* **4**: 165–177.
- Samama MM (2000) An epidemiologic study of risk factors for deep vein thrombosis in medical outpatients: the Sirius study. *Arch Intern Med* **160**(22): 3415–3420. <https://doi.org/10.1001/archinte.160.22.3415>
- Sardar P, Chatterjee S, Chaudhari S, Lip GYH (2014) New oral anticoagulants in elderly adults: evidence from a meta-analysis of randomized trials. *J Am Geriatr Soc* **62**(5): 857–864. <https://doi.org/10.1111/jgs.12799>
- Smeth L, Cook C, Thomas S, Hall AJ, Hubbard R, Vallance P (2006) Risk of deep vein thrombosis and pulmonary embolism after acute infection in a community setting. *Lancet* **367**(9516): 1075–1079. [https://doi.org/10.1016/S0140-6736\(06\)68474-2](https://doi.org/10.1016/S0140-6736(06)68474-2)
- Timmons S, Kingston M, Hussain M, Kelly H, Liston R (2003) Pulmonary embolism: differences in presentation between older and younger patients. *Age Ageing* **32**(6): 601–605. <https://doi.org/10.1093/ageing/afg098>
- Weill-Engerer SA, Meaume S, Lahlou A et al (2004) Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case-control multicenter study. *J Am Geriatr Soc* **52**(8): 1299–1304. <https://doi.org/10.1111/j.1532-5415.2004.52359.x>

Organised by
BRITISH JOURNAL OF
**HOSPITAL
MEDICINE**

In association with
 THE UK
SEPSIS
TRUST

4th national conference

Sepsis: improving recognition and management 2017

America Square Conference Centre, London 10th November 2017

Highlights will include:

- The changing face of sepsis: operational solutions and global picture **Dr Ron Daniels, Dr Andrew Brent, Jacqui Jones, Dr Edwin Borman**
- When is it safe to stop antibiotics for sepsis: sooner or later? **Professor Paul Dark**
- Bridging the gap: the handover between primary care, acute and ICU setting **Tracy Nichols, Dr Gail Hayward, Dr Simon Nadel**
- Antimicrobial resistance: can we continue with the current treatment model? **Emma Cramp**

For more information: Call us on +44(0)20 7501 6796
www.mahealthcareevents.co.uk/Sepsis2017

