MyelomaAcademy™

NURSING BEST PRACTICE GUIDE

Venous Thromboembolic Events (VTEs)

This document is one of the Myeloma Academy Nursing Best Practice Guides for the Management of Myeloma series. The purpose of this Guide is to enhance knowledge and inform nursing practice of Venous Thromboembolic Events (VTEs) in the care of myeloma patients.

After reading this, you should be able to:

- Define VTEs
- Understand the factors, symptoms and consequences of VTEs in myeloma patients
- Be aware of clinical testing and assessment tools for VTEs
- Understand the treatment for VTEs
- Understand the nurse's role in assessment, intervention and management of VTEs and in patient education about this complication

The information contained within this Guide should be used in conjunction with local policies, protocols and best practice guidelines in oncology.

Background

A venous thromboembolic event (VTE) is the term used to describe the formation of a blood clot (thrombus) within a vein. The most common location for a VTE is the veins of the legs, known as deep vein thrombosis (DVT). VTEs pose serious health problems affecting nearly 2 in 1,000 people in the UK each year[1].

The clinical consequences of a VTE are varied and may include:

- Post-thrombotic chronic venous insufficiency
- Skin changes and ulcerations
- Pulmonary embolism
- Ischaemic stroke

KEY FACTS

- Myeloma patients are at risk of a VTE because of the combination of the myeloma, its treatments and individual risk factors
- This risk increases significantly with thalidomide or Revlimid® treatment combinations
- Assessment of risk and appropriate prophylactic treatment is a priority in the prevention and management of a VTE

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A VTE can affect anyone and they can occur for no apparent reason. However, a number of factors increase an individual's risk of a VTE. These include: age; family history; long periods of immobility; obesity; recent injury or surgery; use of oral contraceptives, other comorbidities and presence of varicose veins in cancer patients[2].

Compared to the general population, myeloma patients are at a higher risk of a VTE. This is thought to be due to the cumulative combination of individual risk factors associated with the patient, the myeloma itself and the treatment the patient is receiving[3].

Of the various risk factors for a VTE in myeloma patients anti-myeloma treatment carries the greatest risk, especially with the introduction of immunomodulatory drugs (IMiDs), such as thalidomide and Revlimid (lenalidomide). Although these treatments have improved survival[4], they have also significantly increased the incidence of a VTE in myeloma patients[3] particularly when used in combination with high-dose dexamethasone[5-7]. Typically this risk is greatest during initial treatment[8], due to the high tumour burden. Rates of VTE are also influenced by the use of erythropoiesis-stimulating agents[9].

In contrast, Velcade® (bortezomib) does not appear to increase the risk of a VTE but instead may exert anti-thrombotic activity[10, 11].

Without doubt, a VTE can cause life-changing complications and permanently affect the lives of patients and their families. Impairment resulting from a VTE can interfere with the course of treatment and complicate decisions regarding future treatment options and possible drug combinations. Therefore, primary prevention and optimum management of a VTE plays a major role in the overall treatment and care of myeloma patients. Indeed, mortality in cancer patients with VTE is higher than in other VTE patients[12].

The following describes the medical approach to the treatment of a VTE and provides guidance on nursing interventions and nursing management of myeloma patients at risk of a VTE.

GENERAL RECOMMENDATIONS:

- ★ The risk of a VTE should be identified and managed through rigorous documented assessment
- ★ The decision to commence prophylaxis should be carefully considered and made only after performing a full assessment of all the underlying risk factors including individual, disease-related, treatment-related and bleeding-related risks
- ★ Thromboprophylaxis, such as aspirin, LMWH or warfarin, is recommended for patients receiving Revlimid or thalidomide who have additional risk factors for thrombosis
- ★ Anticoagulant treatment should be started immediately if there is clinical evidence that a patient is developing a VTE

NURSING RECOMMENDATIONS:

- ★ The patient's risk of a VTE should be ascertained not only at diagnosis but throughout their care pathway
- ★ Prophylactic measures should be implemented once a patient has been identified to be at risk
- ★ Provision should be made for monitoring bleeding complications
- ★ Signs and symptoms of a VTE should be closely monitored so that an early diagnosis can be made and anticoagulant treatment instigated
- ★ Patients and their families should be educated on all aspects of a VTE and its prevention, treatment and potential complications

Medical Approach

For myeloma patients, primary prevention of a VTE is a priority. For patients who have had a VTE, early treatment and effective management is crucial to prevent serious complications from arising.

The following provides best practice guidance for nursing interventions related to the assessment, prevention, treatment and monitoring of a VTE, and for nursing management involving a more holistic approach to care and in providing education and support for myeloma patients at risk of, or who have had, a VTE.

Assessment

Assessment of myeloma patients for their risk of a VTE should be performed at:

- Diagnosis
- Before the start of treatment, particularly thalidomide or Revlimid
- Relapse
- On admission electively or for emergency care

The risk assessment must take into account patient factors (e.g. previous VTEs, obesity, comorbidities, other medications, in-dwelling catheter), myeloma factors (e.g. stage of myeloma, hyperviscosity) and treatment factors (e.g. concurrent use of steroids, chemotherapy).

Formal documentation of this process is recommended, for example, using a risk assessment proforma (see Table 1). Completion of the assessment should identify those patients who are at low risk of a VTE and do not require intervention from those with additional risk factors making them at risk of a VTE and requiring thromboprophylaxis.

Before starting prophylactic treatment, the risks of VTE should be balanced against the risks of bleeding. Patients who are, or are likely to become, thrombocytopenic because of an inherited or acquired haemostatic disorder which interrupts the normal production of blood and/or blood flow, may present challenges when given thromboprophylaxis. Therefore, assessment of bleeding risk is necessary.

It is crucial to obtain baseline platelet counts before deciding on thromboprophylaxis and to consider checking further platelet counts every two to four days during the first two weeks for some treatments.

Patients with platelet counts <100 x 10^9/L need to be monitored closely. If the counts fall below 50 x 10^9/L, it is recommended that thromboprophylaxis is stopped except in very high-risk cases. For these patients, consultation with a haemostasis expert may be necessary to decide the best approach on a case by case basis.

Other assessments to make include any contraindications such as: hypersensitivity to a particular drug; bacterial endocarditis; or current or recent history of peptic ulcer disease.

Thromboprophylaxis

The most appropriate thromboprophylactic treatment plan for each individual patient will be given based on the risk assessment performed. In general, prophylactic measures can be categorised as:

- Pharmacological
  - Aspirin
  - Low molecular weight heparin (LMWH)
  - Warfarin
- Mechanical
  - Sequential compression devices
  - Antithrombotic stockings
  - Exercise

- Myeloma treatment-related
  - Reduce thalidomide dose
  - Reduce Revlimid dose
  - Change dexamethasone schedule

Thromboprophylaxis must be tailored to the individual and although pharmacological anticoagulant treatment is the mainstay, additional mechanical intervention and/or changes to myeloma-related treatment may also be included. Since no head-to-head studies comparing the efficacies of different pharmacological thromboprophylactic treatments have been conducted, most practitioners are guided by the following recommendations[13]:

- Patients not on thalidomide or Revlimid with no risk factors – no thromboprophylaxis required
- Patients not receiving thalidomide or Revlimid but at risk of a VTE because of admission to hospital for the management of acute episodes of, for example, dehydration or infection – consider thromboprophylaxis on a case-by-case basis
- Patients receiving thalidomide or Revlimid with 0 – 1 additional risk factor – consider prophylactic dose of aspirin 75mg od. po
- Patients receiving thalidomide or Revlimid with 1 – 2 additional risk factors – consider prophylactic dose of low molecular weight heparin (LMWH) e.g. dalteparin 5000 IU od. SC or enoxaparin 4000 IU od. SC
- Patients receiving thalidomide or Revlimid with 3 or more additional risk factors – require full anti-coagulation e.g. dalteparin 200 IU/kg od. SC or warfarin (target INR 2.5)

Patients with renal impairment (creatinine clearance < 30ml/min) may have unpredictable responses to LMWH so doses may need to be reduced. Anti-factor Xa assay is sometimes used to monitor for LMWH clearance[14].

It is important also to be aware of the possibility of heparin-induced thrombocytopenia (HIT). Although a rare condition, it can occur within two weeks of starting LMWH and is characterised by a sudden fall in platelet counts of >50% from baseline. LMWH should be stopped and an alternative sought.

The duration of thromboprophylaxis remains a contentious issue. The risk of a VTE is highest at diagnosis and reduces as the patient responds to anti-myeloma treatment, however the risk often increases at times of progression and relapse.

Thromboprophylaxis is therefore recommended for the first four to six months and then should be de-escalated or discontinued unless there are ongoing significant risk factors, or signs of disease progression.

Recently published guidelines from the IMWG, EMN, ASCO and BCSH all include recommendations on prevention of VTE[15-18].

Treatment

Despite best efforts, thromboprophylaxis cannot completely prevent a VTE and proper diagnosis and management should one occur is crucial.

For myeloma patients with a suspected VTE, a diagnosis should be made with the appropriate imaging techniques. Full anticoagulant treatment with a LMWH or warfarin should be started with the regular follow-up platelet count checks.

If the patient is on thalidomide or Revlimid, it may be necessary to temporarily halt treatment until a fully anti-coagulated state is established.

Nursing interventions and management

Nurses play a pivotal role in the overall management of myeloma patients at risk of or who require treatment for a VTE.

The following provides best practice recommendations for nursing interventions related to the assessment, treatment and monitoring of patients at risk of, or who have had, a VTE and for nursing management involving a more holistic approach to care and in providing education and support for this group of patients.

Interventions

- Make sure that a VTE risk assessment has been performed and made available to the medical team during the consultation
- Be vigilant and alert the medical team to any contraindications patients may have to prophylactic treatment
- Advocate on behalf of the patient if they have a particular preference for taking thromboprophylaxis orally or by injection
- Educate patients and their families on the correct technique/safe disposal of self-administered subcutaneous Heparin or ensure that you have referred the patient to a community district nurse for administration at home
- Make sure patients understand the significance of, and comply with, using mechanical devices as prescribed
- Do not offer anti-embolism stockings to patients with peripheral neuropathy
- Be vigilant for signs of a VTE or side-effects of treatment or prophylaxis and alert the medical team as soon as possible

Management

- Educate patients and their families about a VTE, what the risk factors are, how they can be prevented, what signs and symptoms to look out for and the importance of reporting these as soon as possible. These include:
  - Deep vein thrombosis – fever, tachycardia, swelling/heat, dull ache or pain
  - Pulmonary embolism – anxiety, sudden breathlessness, chest pain
- Inform the patient and their family about each anticoagulant treatment, its actions, possible side-effects and the importance of reporting them:

  These include:
  - Unusual bruising
  - Nosebleeds and/or bleeding from the gums
  - Coughing or vomiting blood or clots
  - Passing pink, red or brown urine
  - Passing red or black tarry stools
  - Headaches, dizziness or weakness
- Provide patients with written information to help to understand about a VTE
- Provide patients with a 24-hour contact number and encourage them to seek help at any time if they develop symptoms of a VTE or are concerned about any side-effects of anticoagulant treatment
- Discuss with and advise patients and their families of the benefits of lifestyle changes such as diet, exercise, lowering cholesterol, losing weight, smoking, in reducing preventable risk factors

- Recognise that for some patients who have previously had a VTE, psychological effects may be apparent and offer support or referral to a counsellor
- Promote interdisciplinary communication between colleagues about patients to ensure successful prevention of a VTE
- Be advocates for patients in creating and implementing a care plan that adheres to cultural/individual beliefs e.g. the use of porcine-derived heparin
- Stay current with new developments in the thrombosis field

Summary

Myeloma patients are at a significantly greater risk of a VTE than the general population. The consequences of a VTE are serious and potentially life-threatening. Therefore, prevention through thromboprophylaxis is crucial to its management.

Nurses are at the forefront of coordinating measures to prevent a VTE and/or its complication. Their role in risk assessment, implementing timely prophylaxis and providing vital education and support for patients and their families is crucial in improving quality of life and prioritising positive outcomes for patients.

Abbreviations

- **CrCl** Creatinine clearance
- **HIT** Heparin-induced thrombocytopenia
- **IMiD** Immunomodulatory drug
- **INR** International normalised ratio
- **IU** International units
- **LMWH** Low molecular weight heparin
- **od.** Once daily
- **po** Orally (per os)
- **pt** Prothrombin time
- **SC** Subcutaneous
- **VTE** Venous thromboembolic event

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ABOUT THE NURSING BEST PRACTICE GUIDES

The Nursing Best Practice Guides have been developed by Myeloma UK and an expert nursing advisory group, with input from relevant specialist healthcare professionals. They have been developed to enhance nurse knowledge, inform nursing practice and support nurses in the delivery of high quality treatment and care to myeloma patients and families.

Nursing Best Practice Guide series:

- ★ Complementary therapies
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ABOUT THE MYELOMA ACADEMY

The Myeloma Academy provides healthcare professionals involved in the treatment and care of myeloma patients with access to comprehensive accredited learning resources and tools in an innovative online environment and through educational events.

It supports the education and continual professional development of myeloma healthcare professionals so they can provide optimum patient-centred treatment and care within the current UK health and policy environment.

For more information visit:
www.myeloma-academy.org.uk or by email **academy@myeloma.org.uk**

ABOUT MYELOMA UK

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma.

Our mission is to provide information and support to people affected by myeloma and to improve standards of treatment and care through research, education, campaigning and raising awareness.

For more information about Myeloma UK and what we do, please visit **www.myeloma.org.uk** or contact us at **myelomauk@myeloma.org.uk** or **+44 (0)131 557 3332.**

Appendix I

Example of a VTE risk assessment proforma for myeloma patients

STEP ONE: REVIEW THROMBOSIS RISK FACTORS and tick each box that applies – any tick should prompt consideration of pharmacological prophylaxis with aspirin, dalteparin or warfarin.	
Individual risk factors	Tick
Personal or family history of VTE	
Acute medical illness e.g. infection, acute renal failure, vomiting or dehydration	
Comorbidities: cardiac, diabetes, chronic renal impairment, chronic inflammatory disease	
Obesity (BMI ≥ 30)	
Immobility (acute or chronic)	
Thrombophilias, myeloproliferative disorders, haemoglobinopathies	
Recent surgery (within 6 weeks): neuro-, trauma, orthopaedic, general, any other anaesthesia	
Medications: erythropoiesis stimulating agents, HRT, tamoxifen/stilboestrol	
Myeloma-risk factors	
At diagnosis	
Hyperviscosity	
Myeloma therapy	
Revlimid or thalidomide	
Doxorubicin	
High-dose steroid (≥ 480mg/month dexamethasone or equivalent)	
Combination chemotherapy	
STEP TWO: if none of the boxes from Step One is ticked, the patient is at low risk of a VTE and no intervention is required.	
Patient at low risk of a VTE	
STEP THREE: REVIEW BLEEDING RISK FACTORS and tick each box that applies – any tick should prompt clinicians to consider if bleeding risk is sufficient to preclude pharmacological prophylaxis.	
Active bleeding	
Haemophilia or other known bleeding disorder	
Platelet count <100 $x10^9$/l	
Acute stroke in previous month (haemorrhagic or ischaemic)	
Blood pressure >200mmHg systolic or >120mmHg diastolic	
Severe liver disease (abnormal PT or known varices)	
Severe renal disease (CrCl <30ml/min)	
Undergoing procedure or intervention with high bleeding risk	
STEP FOUR: if thromboprophylaxis is indicated, review if there are ANY SPECIFIC CONTRAINDICATIONS OR CAUTIONS TO ASPIRIN OR DALTEPARIN use.	
Hypersensitivity to heparin/ LMWH/ aspirin or history of HIT	
Bacterial endocarditis / pericarditis (liaise with Cardiology) risk	
Current or recent history of peptic ulcer disease	

Appendix I continued

Example of a VTE risk assessment proforma for myeloma patients

STEP FIVE: select appropriate thromboprophylaxis if required – tick chosen strategy.		
Aspirin 75mg od. po	Only for those on lenalidomide with ≤ 1 additional risk factors	
Dalteparin 5000units od. SC	For those with 1 or 2 additional risk factors ★ Is the weight <45kg or BMI >40; or CrCl <30ml/min? (consider dose reduction)	
Dalteparin 200units/kg od. SC (24hr max 18,000 units)	For those with 3 additional risk factors ★ Are there any bleeding risk factors? (divide dose) ★ Is weight >100kg (seek advice re dosing) ★ Is CrCl less than 30mL/min? Treatment dose dalteparin should generally be avoided – seek haemostasis advice	
Warfarin (target INR 2.5)	For those with 3 additional risk factors	

*Taken from London Cancer - Guidelines for the treatment of multiple myeloma[19].

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Notes

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Myeloma UK **22 Logie Mill,**
Beaverbank Business Park, Edinburgh EH7 4HG
Myeloma Infoline: 0800 980 3332
www.myeloma.org.uk Charity No: SC 026116