



**Case:**

Ms. NM is an 82 year-old woman with history Alzheimer's dementia admitted to the hospital with worsening shortness of breath. At baseline, NM requires help with activities of daily living. She speaks fluently; however, her conversation is not contextually correct. To evaluate the patient's dyspnea, the emergency room physician ordered a CT of the chest. In addition to revealing multiple pulmonary emboli, the CT scan also showed a left-upper-quadrant mass. To better evaluate the mass, a CT abdomen was ordered. This showed a left upper quadrant mass with intra- and extra-peritoneal metastases suspicious for gastrointestinal stromal tumor versus sarcomatous mass. The palliative care team was consulted for goals of care. Following guidelines proposed by the CLOT trial<sup>1</sup>, the primary team started the patient on dalteparin (Fragmin<sup>TM</sup>), a low-molecular-weight heparin (LMWH), for anti-coagulation with the plan to continue LMWH anti-coagulation for at least six months. After discussion with the patient's family, palliative care team and primary team, the patient's daughter decided to forgo chemotherapy or surgical intervention for the patient. Thus, the patient's goals of care were concurrent with a hospice philosophy of care. Unfortunately, the cost of dalteparin was prohibitive to hospice care, and thus, the patient was discharged with palliative home care.

**Discussion:**

Venous thromboembolism (VTE) is a common complication of malignancy which carries a poor prognosis. Patients who are diagnosed with malignancy and VTE concurrently have a 12% one-year survival rate.<sup>2</sup> Thus, the management of VTE in the setting of malignancy is important for internal medicine physicians. The following questions may help guide decision-making:

***What is the best treatment for VTE in the setting of malignancy?***

Evidence-based treatment recommendations stem from several randomized controlled trials. The CLOT trial<sup>1</sup> is a randomized controlled trial which compares two therapies for VTE in cancer patients: dalteparin for 5-7 days followed by warfarin for six months versus dalteparin alone for six months. This study included patients with active cancer as defined by those patients with a diagnosis of cancer within six months of enrollment, treatment of

cancer within six months of enrollment or recurrent or metastatic cancer. Exclusion criteria included a weight less than 40 kg, increased creatinine, high risk of bleeding, patients confined to bed greater than 50% of the day, and inability to reach a treatment center easily. This study demonstrated a decreased risk for recurrent VTE in patients maintained on LMWH versus oral anticoagulation with a number needed to treat (NNT) of 13.

A Cochrane review<sup>3</sup> on the topic of anti-coagulation for VTE in patients with cancer identified eight randomized controlled trials with moderate quality evidence. This review showed a statistically significant decrease in recurrent VTE with a relative risk of 0.51 (CI 0.35-0.74)

***Does treating VTE with LMWH translate into improved survival?***

Neither the CLOT trial nor the Cochrane review showed a survival benefit from LMWH anti-coagulation versus oral anti-coagulation in patients with malignancy.

***Besides decreasing the risk of recurrent VTE, what other benefits are there to treating VTE in patients with advanced cancer who are hospice eligible?***

The advantages of treating VTE with LMWH versus oral anti-coagulation include a predictable pharmacokinetic profile, avoidance of drug-warfarin interactions and the decreased need for regular laboratory tests.<sup>4</sup> Treating VTE in patients with advanced cancer has symptomatic benefit in preventing post-phlebotic syndrome associated with lower extremity clot propagation.

***What are the limitations of applying this data to patients with advanced cancer who are hospice eligible?***

The generalizability of these findings is limited. These trials excluded patients in bed greater than 50% of the day, patients with prognosis less than three months and/or those with difficulty traveling to treatment centers. Thus, these results may not reflect the results of a hospice or palliative care population. They would not apply, for example to the patient in the case above. She would have been excluded based on her age, her functional status and her estimated prognosis.

***What are the financial and social costs of treating VTE with LMWH?***

A six month supply of warfarin costs approximately \$0.11/day compared to a cost of approximately \$100/day for

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enoxaparin (Lovenox™) or dalteparin (Fragmin™). This cost comparison does not take into account the cost of laboratory tests to monitor INR in patients on oral anticoagulation nor administration costs for patients unable to self-administer daily injections of LMWH. In this case, the hospice could not afford to pay for LMWH and thus declined to admit the patient. The benefits of hospice for this patient are likely considerable. Hospice care has been associated with improved symptom management and family bereavement outcomes.

***How is this relevant to primary care practice?***

Primary care physicians often follow hospice patients and may resume care of cancer patients after anti-neoplastic treatment options are exhausted. Physicians face a treatment decision in managing the complication of VTE in these patients. In this population, the benefits and costs of continuing a medication which requires the discontinuation of hospice services should be analyzed critically and weighed on an individual level.

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**References:**

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