

# **Primary Prophylaxis of Venous Thromboembolism in Malignant Patients**

*Essay*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

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*Candidate*

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## List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
<b>ACCP</b>	: American College of Chest Physician
<b>aPTT</b>	: Activated partial thromboplastin time
<b>ASCO</b>	: American Society of Clinical Oncology
<b>ATIII</b>	: Antithrombin III
<b>CDT</b>	: Catheter directed therapy
<b>CFV</b>	: Common femoral vein
<b>CHF</b>	: Congestive heart failure
<b>CIV</b>	: Common iliac vein
<b>COPD</b>	: Chronic obstructive pulmonary disease
<b>CT</b>	: Computed tomography
<b>CTV</b>	: Computed tomographic venography
<b>CVC</b>	: Central venous catheter
<b>DVT</b>	: Deep vein thrombosis
<b>FDA</b>	: Food and Drugs Association
<b>FV</b>	: Femoral vein
<b>GCS</b>	: Graduated compression stocking
<b>GSV</b>	: Great saphenous vein
<b>HIT</b>	: Heparin induced thrombocytopenia
<b>HRT</b>	: Hormone replacement therapy
<b>INR</b>	: International normalized ratio
<b>IPC</b>	: Intermittent pneumatic compression

<b>IVC</b>	: Inferior vena cava
<b>IVCF</b>	: Inferior vena cava filter
<b>LMWH</b>	: Low molecular weight heparin
<b>MAUDE</b>	: Manufacturer and User Facility Device Experience
<b>MRI</b>	: Magnetic resonance imaging
<b>MRV</b>	: Magnetic resonance venography
<b>NCCN</b>	: National Comprehensive Cancer Network
<b>NOACs</b>	: New oral anticoagulants
<b>PE</b>	: Pulmonary embolism
<b>PMT</b>	: Pharmacomechanical thrombectomy and thrombolysis
<b>SFV</b>	: Superficial femoral vein
<b>SSV</b>	: Short saphenous vein
<b>SVC</b>	: Superior vena cava
<b>TF</b>	: Tissue factor
<b>TFPI</b>	: Tissue factor pathway inhibitor
<b>UEDVT</b>	: Upper extremity deep venous thrombosis
<b>UFH</b>	: Unfractionated Heparin
<b>VT</b>	: Venous Thrombosis
<b>VTE</b>	: Venous thromboembolism

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### **Abstract**

**Background:** There are many recognized risk factors for venous thrombo-embolism which include immobilization, surgery, malignancy, trauma, pregnancy history of previous attacks of venous thrombo-embolism and oral contraceptive drugs. Deep venous thrombosis may have a lot of complications which gives impact on short-term life especially in patients with cancer like pulmonary embolism and postthrombotic syndrome. Thus, we have aiming to prevention, early diagnosis and treatment of deep venous thrombosis.

**Aim of the Study:** The aim of this study is to focus on the efficacy of preventive measures in reduction of deep venous thrombosis in malignancy as well as its lethal complications. Clinical trials have shown that thromboprophylaxis reduces the incidence of symptomatic venous thrombosis in cancer patients. An increase in major bleeding events was suggested but not confirmed in most recent trials. However, as the incidence of venous thrombosis is relatively not low in general cancer population, thromboprophylaxis should not be recommended for all cancer outpatients. Instead, to optimize the risk/benefit ratio.

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**Key words:** Venous thrombo-embolism, malignancy, postthrombotic syndrome, pulmonary embolism

## Introduction

The complications of acute deep venous thrombosis, pulmonary embolism and post-thrombotic syndrome are one of the most common causes of hospital death. Approximately 300,000 die per year in United States from pulmonary embolism, the majority of which results from deep venous thrombosis (*Silva, 2001*).

Understanding underlying epidemiology, pathophysiology and natural history in deep venous thrombosis is essential in guiding appropriate prophylaxis, diagnosis and treatment. Deep venous thrombosis is usually silent in nature in most of hospitalized patients and usually presented by non-specific symptoms and signs (*Haeger, 2000*).

Components of triad described by Rudolf Virchow for risk factor of Deep venous thrombosis which includes abnormalities of thrombosis, abnormalities of blood flow and vascular injury remains applicable today (*Sue et al., 2005*).

There are many recognized risk factors for venous thrombo-embolism which include immobilization, surgery, malignancy, trauma, pregnancy history of previous attacks of venous thrombo-embolism and oral contraceptive drugs (*Cogo et al., 2004*).

Malignancy is considered one of the most important risk factors of the deep venous thrombosis and this is what we are going to focus in this research. Patients with cancer are at increased risk of venous thrombo-embolism. Approximately 15% of malignancies are complicated by venous thrombo-embolisms with higher prevalence in autopsy studies (*Maxwell and Bennett, 2012*).

Thrombogenic mechanisms associated with cancer may be heterogenous, but likely they involve substances that are directly or indirectly activate coagulation. About 90% of patients with cancer have abnormal coagulation parameters including increased coagulation factors, fibrinogen and thrombocytosis. Levels of coagulation inhibitors, antithrombin, protein C & S may be reduced in malignancy (*Falanga et al., 2010*).

The role of cancer treatment related factors including chemotherapy has been a focus of recent investigations because most cases of venous thrombo-embolism in the oncology settings occur in ambulatory patients (*Kirwan et al., 2003*).

Deep venous thrombosis may have a lot of complications which gives impact on short-term life especially in patients with cancer like pulmonary embolism and postthrombotic syndrome. Thus, we have aiming to prevention, early diagnosis and treatment of deep venous thrombosis (*Amit, 2007*).

Clinical trials have shown that thromboprophylaxis reduces the incidence of symptomatic venous thrombosis in cancer patients. An increase in major bleeding events was suggested but not confirmed in most recent trials. However, as the incidence of venous thrombosis is relatively not low in general cancer population, thromboprophylaxis should not be recommended for all cancer outpatients. Instead, to optimize the risk/benefit ratio (*Crobash et al., 2014*).

## **Aim of the Work**

**T**he aim of this study is to focus on the efficacy of preventive measures in reduction of deep venous thrombosis in malignancy as well as its lethal complications.

## Chapter (1)

# Anatomy

### Venous Anatomy

**T**he veins of the lower extremity are classified according to their relationship to the muscular fascia and are located in either the superficial or deep compartment. The venous system of lower limb includes deep veins which lie beneath the muscular fascia and drain the lower extremity muscles; the superficial veins, which are above the deep fascia drain the cutaneous microcirculation, and the perforating veins. That penetrate the muscular fascia and connect the superficial and deep veins (*Caggiati et al., 2002*).

Superficial veins are large, relatively thick-walled, muscular structures that lie just under the skin within the subcutaneous fascial layer. In the extremities they form a complex network of collecting veins that gather blood from the skin and superficial fascia, passively directing it into the deep system through truncal or perforating veins. Among the superficial veins are the great and small saphenous veins of the leg, the cephalic and basilic veins of the arm, and the external jugular veins of the neck (*Caggiati et al., 2002*).

The deep veins, on the other hand, are thin-walled and less muscular and lie within the deep fascia usually in close proximity to a bone. Deep veins accompany arteries