Deep vein thrombosis associated with major lower extremity amputation

Thesis

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In General Surgery

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Khaled Alaaeldin Mostaf Aboshiesha

List of Contents

List of Abbreviations

Abbrev.	Full-term
ABI	: Ankle-brachial index
ACCP	**:** American College Of Chest Physicians
ADP	**:** Adenosine diphosphate
APC	**:** Activated protein C
ATP	**:** Adenosine triphosphate
BMI	**:** Body mass index
Ca	**:** Calcium
CRP	**:** C-reactive protein
CTPH	**:** Chronic thromboembolic pulmonary hypertension
DVT	**:** Deep vein thrombosis
FDPs	**:** Fibrin degradation products
HIT	**:** Heparin-induced thrombocytopenia
HMWK	**:** High-molecular-weight kininogen
LMWH	**:** Low-molecular-weight heparin
PAIs	**:** Plasminogen- activator inhibitors
PE	**:** Pulmonary embolism
PTS	**:** Post-thrombotic syndrome
TAX2	**:** Thromboxane A2
TF	**:** Tissue factor
TFPI	**:** Tissue factor pathway inhibitor
TGF- α	**:** Tumour growth factor-α
UFH	**:** Unfractionated heparin
u-PA	**:** Urokinase plasminogen activator
VKA	**:** Vitamin K antagonist

List of Tables

List of Figures

Abstract

Introduction

Venous thromboembolism (VTE) is a disease that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). It is a common lethal disorder that affects hospitalized and nonhospitalized patients, is often overlooked, and results in long-term complications including chronic thromboembolic pulmonary hypertension (CTPH) and the post-thrombotic syndrome (PTS) ***(Coldhaber, 1992).***

Venous thromboembolism results from a combination of hereditary and acquired risk factors, also known as thrombophilia or hypercoagulable states. In addition, vessel wall damage, venous stasis, and increased activation of clotting factors first described by Rudolf Virchow more than a century ago remain the fundamental basis for our understanding of thrombosis ***(Anderson et al, 1991)***.

Venous thromboembolism is the third most common cardiovascular illness after acute coronary syndrome and stroke. Although the exact incidence of VTE is unknown. Pulmonary embolism is the third most common cause of hospital-related death and the most common preventable cause of hospital-related death ***(Heit, 2005)***.

In the EU, It has been noted that VTE is responsible for more than twice the number of deaths than those caused by AIDS, breast cancer, prostate cancer and road traffic accidents combined ***(Cohen et al., 2007).***

VTE can lead to serious long-term complications, including:

- Post-thrombotic syndrome (PTS)
- Thrombo-embolic pulmonary hypertension (CTPH)

PTS is the most common complication of DVT and typically causes chronic pain and swelling in the affected leg, and in severe cases can result in venous ulcers. After symptomatic DVT, 20–50% of patients develop PTS ***(Geerts et al., 2008).***

CTEPH is a serious long-term complication of PE, but it can be difficult to diagnose because clinical symptoms and signs are non-specific or absent in early CTEPH. Many of the symptoms are similar to those for acute PE, including dyspnoea, chestpain, presyncope or syncope and/or haemoptysis. CTEPH causes the right side of the heart to work harder than normal owing to abnormally high blood pressure in the arteries of the lungs. This can lead to heart failure and other serious consequences ***(Heit et al., 2005).***

The main goals of treatment for DVT include prevention of PE, the PTS, and recurrent thrombosis. Once VTE is suspected, anticoagulation should be started immediately unless there is a contraindication. Different types of anticoagulant can be used including unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), or fondaparinux followed by an oral anticoagulant (vitamin K antagonist [VKA]), Direct thrombin inhibitors ***(Birdwell et al., 2000)***.

Aim of the Work

The aim of this work is to determine the risk of deep venous thrombosis associated with major lower extremity amputation and whether there is need for anticoagulation prophylaxis with this kind of procedure. Caprini score was used to assess the risk factors for developing deep vein thrombosis. The aim is to determine the integrity for the Caprini score for determining the need for anticoagulation prophylaxis in patient undergoing major lower extremity amputation.

Chapter (1)
Physiology of the Coagulation System

Introduction:

The concept of blood coagulation dates back to the 1960's when Davie, Ratnoff and Macfarlane described the "waterfall" and "cascade" theories showing the fundamental principle of a cascade of proenzymes leading to the activation of some enzymes. Usually, the process of coagulation is controlled by several inhibitors that limit the clot formation, which prevents more propagation of the thrombus. This thrombo-haemmorhagic balance is maintained in the body by some complicated interactions between the coagulation and the fibrinolytic system as well as the platelets and the blood vessel wall ***(Achneck et al., 2010).***

Haemostasis is defined as the arrest of bleeding. It comes from Greek, where, haeme means blood and stasis means to stop. When a vessel is injured or ruptured, haemostasis occurs by several mechanisms:

(1) Vascular constriction,

(2) Formation of a platelet plug,

(3) Formation of a blood clot as a result of blood coagulation

(4) The growth of fibrous tissue into the blood clot which closes the hole in the vessel permanently ***(Anderson et al., 2006)*.**

Steps of coagulation:

1. Vascular Constriction:

After a blood vessel has been cut or ruptured, the trauma to the vessel wall itself causes the smooth muscle in the wall to contract immediately; this causes instant reduction of the flow of blood from the ruptured vessel. The contraction results from **(1)** local myogenic spasm, **(2)** local autacoid factors released from the traumatized tissues and platelets, and **(3)** nervous reflexes. Initiation of the nervous reflexes are is by pain nerve impulses or sensory impulses that originate from the traumatized blood vessel or the tissues nearby ***(Anderson et al., 2006).***

In the resting state, blood is actively maintained in a liquid form by endothelial cells and circulating plasma protein inhibitors. When the vascular integrity is disrupted or the endothelium becomes inflammed, the thrombotic activity of the endothelial cells is triggered. This occurs through secreting platelet activating factor, a substance that induces platelet aggregation and synthesizes Von Willebrand factor (VWF), which is a cofactor for adherence of platelets to the

subendothelium. The endothelium is also able to secrete plasminogen activator inhibitor which inhibits the fibrinolytic system ***(Dittman and Majerus, 2001)***.

Damage to the endothelium exposes blood to a highly thrombogenic subendothelial connective tissue which initiates the clot formation. This connective tissue consists of various types of compounds including fibrillar collagen, which is a potent stimulus for the activation and adhesion of platelets. Simultaneously, subendothelial components convert inactive coagulation factors into powerful enzymes, initiating an intrinsic stimulation of the plasma coagulation system ***(Edward and Juan, 2000)*.**

2. Formation of the platelet plug:

Platelets have an over-expanding role in hemostasis. Beside their role when vascular integrity is disturbed, they also maintain the integrity of normal endothelium. This is why patients with platelet deficiencies have a tendency to develop purpuric bleeding ***(Edward and Juan, 2000)*.**