



### Deep Vein Thrombosis: Risk Factors and Prevention in Surgical Patients

*Deep Vein Thrombosis: Facteurs de risque et de prévention dans les patients chirurgicaux*

D. C. Obalum\*, S. O. Giwa, T. O. Adekoya-Cole, C. N. Ogo, G. O. Enweluzo

#### ABSTRACT

**BACKGROUND:** Deep vein thrombosis (DVT) is a cause of preventable morbidity and mortality in hospitalized surgical patients. The occurrence of the disease is related to presence of risk factors, which are related primarily to trauma, venous stasis and hyper-coagulability. DVT seems not to be taken seriously by many surgeons in Nigeria. This is despite comprehensive studies that show no real differences in racial demography of the disease.

**OBJECTIVE:** To highlight the importance of physician awareness about DVT especially its risks and prevention methods.

**METHODS:** A detailed literature search was completed to extrapolate articles that described DVT risks and prevention. This involved hand and online searches. Specific search terms used included DVT/risk factors/prevention. The searches generated 468 papers. Of these 57 papers were included in the review.

**RESULTS:** Predominant risk factors for DVT include middle or old age, prolonged surgery, trauma, confinement, presence of malignancy and insertion of deep venous catheters. In women, contraceptive use, hormone replacement therapy, pregnancy and the puerperium are a additional risk factors. Prophylactic measures include those directed at eliminating venous stasis and those directed at changes in blood coagulability.

**CONCLUSION:** Deep Venous Thrombosis is a common disease with fatal and serious long term burdensome complications. We must target primary and secondary prophylaxis to improve survival and reduce morbidity from this preventable disease. *WAJM 2009; 28(2): 77–82.*

**Keywords:** Deep Vein Thrombosis, Venous Thrombosis, Phlebothrombosis.

#### RESUME

**CONTEXTE:** La thrombose veineuse profonde (TVP) est une cause évitable de morbidité et de mortalité chez les patients chirurgicaux hospitalisés. L'apparition de la maladie est liée à la présence de facteurs de risque, qui sont principalement liées à un traumatisme, la stase veineuse et hyper-coagulation. Thrombose veineuse profonde ne semble pas être pris au sérieux par beaucoup de chirurgiens au Nigeria. Ceci en dépit des études approfondies qui montrent pas vraiment de différences raciales dans la démographie de la maladie.

**OBJECTIF:** mettre en évidence l'importance du médecin de la thrombose veineuse profonde prise de conscience sur les risques et en particulier les méthodes de prévention.

**MÉTHODES:** Une recherche bibliographique a été réalisée pour extrapoler des articles qui décrit les risques et de prévention de la thrombose veineuse profonde. Il s'agissait de la main et les recherches en ligne. Des termes de recherche utilisés comprenaient la thrombose veineuse profonde /facteurs de risque et de prévention. La recherche a généré 468 documents. Sur ces 57 documents ont été inclus dans l'étude.

**RÉSULTATS:** prédominance des facteurs de risque de thrombose veineuse profonde des moyens ou la vieillesse, des périodes prolongées de chirurgie, de traumatologie, de confinement, de la présence d'une tumeur maligne et l'insertion des cathéters veineux profond. Chez les femmes, l'utilisation de la contraception, traitement hormonal substitutif, la grossesse et la puerperum sont un des facteurs de risque supplémentaires. Mesures prophylactiques comprennent celles qui visent à éliminer la stase veineuse et celles qui visent les changements de coagulation du sang.

**CONCLUSION:** thrombose veineuse profonde est une maladie mortelle et lourde de graves complications à long terme. Nous devons cibler la prophylaxie primaire et secondaire afin d'améliorer la survie et de réduire la morbidité de cette maladie évitable. *WAJM 2009; 28(2): 77–82.*

**Mots-clés:** thrombose veineuse profonde, thrombose veineuse, Phlébothrombose

## INTRODUCTION

Deep vein thrombosis (DVT) carries a serious risk of fatal pulmonary embolism and complications of recurrence, post-phlebotic syndrome, ulcers and varicose veins. In surgical patients with malignant disease undergoing chemotherapy and radiotherapy, thromboembolism is the second commonest cause of death.<sup>1</sup> DVT develops in 50–60% of patients undergoing elective hip replacement without prophylaxis and fatal pulmonary embolism occurs in 1–5%.<sup>2</sup>

Deep vein thrombosis is predominantly a disease of middle age and the elderly.<sup>3,4</sup> It is very rare before the age of 20 years<sup>3,5</sup> and rare before 40 years.<sup>6</sup> Incidence rates are higher in women especially during childbearing years.<sup>7</sup> Average annual incidence rate in the United States of America (USA) is reported to be 117 per 100,000<sup>3</sup> with 50,000 to 100,000 or more fatal pulmonary embolism annually.<sup>8,9</sup> Venous thrombosis is more common in Europe and USA than in Asia and Africa. Incidence of DVT is reported as 20–35% in western countries,<sup>10</sup> 9.6% in Sudan<sup>11</sup> and 12% in Malaysia.<sup>12</sup> The difference in incidence has been attributed to differences in genes, diet, fibrinolytic activity and climate.<sup>4,7,13</sup> This may have contributed to the less attention given to this problem in our environment.

There is a relative paucity of information about DVT in most African populations including Nigeria.<sup>4</sup> Many studies have shown comprehensively that in comparison to whites of European

origin, the prevalence of DVT is similar or higher among African-Americans and lower among Asians and Native Americans.<sup>14</sup> Racial differences notwithstanding, DVT is a multifactorial disease involving both environmental and genetic factors as well as genetic and environmental interactions<sup>15</sup> culminating in a triad of damage to blood vessel wall, decrease in rate of blood flow and change in composition of blood, ultimately a thrombus is formed. These events are largely preventable. However studies show that the use of DVT prophylaxis in hospitalized patients is dismal.<sup>16</sup> Figures as low as 32% utilization of prophylaxis in high risk patients have been reported in USA.<sup>17</sup> Even among those surgeons who believe that the prophylaxis against DVT is desirable, consensus on the agent to be used remains difficult to reach.<sup>18</sup>

This review examines the risk factors and methods for prevention of DVT. It aims to answer some questions raised by Ruckley:<sup>6</sup> What prophylaxis against thrombo-embolism should I provide for my patients? What is the risk of DVT? Does the risk of thromboembolism outweigh the risk of the prophylactic method? Should I limit prophylaxis to a selected group and if so how do I recognize those at special risk?

### Risk Factors For DVT

Prevention aims to improve survival, avoid recurrence, prevent complications and reduce health care costs.<sup>15</sup> To prevent DVT, persons at risk must be identified. It is preferable to confine prophylaxis to

those at greatest risk of DVT in order to minimize work load, cost,<sup>19</sup> and the hazards of the methods of prophylaxis.<sup>6</sup>

DVT risk is associated with the presence of some specific factors as shown on Table 1. This risk increases geometrically if these factors are multiple in a patient as is found in many hospitalized patients. Commencing a patient on prophylaxis against DVT depends on the risk level; therefore an assessment of this risk is important on admission to the hospital. No single factor predicts the risk of developing DVT as there is a considerable overlap in pre-operative clinical and laboratory measurements between patients who did and those who did not develop DVT. This is consistent with the multi-factorial aetiology of DVT.<sup>20</sup> There are individualized risk assessment and stratification models,<sup>21</sup> but generally patients aged over 40 years in hospital confinement for up to 3 days with one or more risk factors should be considered for prophylaxis.

The risk factors of DVT include patient age over 40 years, surgery lasting more than 1 hour, trauma, hospital or nursing home confinement, malignancy, deep vein catheterization, varicose veins, extremity paresis and long haul air travel lasting for over 6 hours.<sup>22</sup> In women, contraceptive use and hormone therapy<sup>23</sup> as well as pregnancy and puerperium<sup>24</sup> increase the risk of DVT. Patients with malignancies are generally at high risk of developing DVT. Those on chemotherapy are even at a higher risk<sup>25</sup> and the risk appears to be higher for those with

**Table 1: Pharmacological Agents for DVT Prophylaxis**

Mechanism of action	Agent	Average Dose	Remarks	
Alpha adrenergic agonist: increases tone of vein wall Increased endothelial fibrinolytic activity Antiplatelet adhesion	Dihydroergotamine	500 microgram 8 hourly	Risk of ergotism	
	Dextran 40 or dextran 70	500ml infusion daily	Allergenic	
	Acetylsalicylic acid	75mg orally daily	Unreliable	
Anticoagulation	Inhibition of coagulation factor synthesis	Warfarin	10mg daily for 2days, then 5mg daily	Difficult to reverse, drug interactions, requires monitoring
		Inhibition of coagulation cascade	Unfractionated heparin	5000u subcutaneous 8 hourly
	Low molecular weight heparin (Enoxaparin)	40mg subcutaneous 24 hourly	More expensive	

leukemia, lymphomas, brain and liver cancers.<sup>26</sup> Confinement in hospitals and nursing homes causes 150- fold increase in incidence of DVT<sup>27</sup> with such patients accounting for about 60% of DVTs in a community.<sup>28</sup>

Among hospitalized surgical patients such risk is higher with infection, duration of surgery for more than one hour, patient age over 40 years, cancer and past history of DVT.<sup>29</sup> Generally, prior DVT increases the risk of another DVT by up to 30%.<sup>30</sup> Patient with history of cerebrovascular accident, especially when they have paraplegia have a 60% risk of DVT.<sup>31</sup> Critically ill patients generally have multiple risk factors and high rate of DVT.<sup>32</sup>

Major surgeries of cardiovascular, orthopaedic, neurosurgical and pelvic nature that last for several hours carry higher risk of DVT.<sup>33</sup> Similarly; obesity,<sup>34</sup> age over 65 years<sup>33</sup> and poor anaesthetic status<sup>35</sup> further increase the risk of DVT in these patients.

### Prophylaxis for DVT

The prevention of DVT remains a problem despite the development of several prevention regimes. This has been due to the lack of essential knowledge on the exact nature of the 'trigger mechanism' which initiates thrombosis in the leg and the absence of sensitive and accurate technique for measuring with precision the effects of prophylaxis. To some extent, the second difficulty has been overcome by using the 125 Iodine – labeled fibrinogen test. It is now possible to determine the true incidence of this disease and the effectiveness of a specific regime of prevention can be judged with greater accuracy. The main attempts to prevent deep vein thrombosis can be categorized under two groups; those directed at eliminating stasis in the deep veins and those directed at counteracting changes in blood coagulability.

### Elimination of Stasis

**Mechanical Methods:** Mechanical methods of prophylaxis include exercises, graduated compression stockings, electrical stimulation and pneumatic compression. These methods are preferred for patients at risk of bleeding with anticoagulants. Such patients may

have active or recent gastrointestinal bleeding, haemorrhagic stroke or thrombocytopenia. Their effectiveness against DVT may be limited by their removal because of discomfort or visits to bathroom. Physiologically, ambulation, encouraging rhythmic active and passive exercises of the limbs among inpatients to improve blood flow in the limbs, discourages stasis and is effective against DVT.<sup>36</sup>

Wearing of graduated compression elastic stockings by patients will also reduce the chances of venous stasis<sup>37</sup> and are important in the prevention of DVT in post-operative patients.<sup>37</sup> These stockings reduce venous thromboembolism in hospitalized post-operative patients by about 50%.<sup>38</sup> Used alone, compression stocking is reported to reduce the incidence of post-operative DVT by approximately 60%, and when used in combination with low dose heparin or intermittent calf compression, they further reduce the incidence by up to 85%.<sup>37</sup> This is equally important in patients with a history of DVT as it reduces the risk of recurrence and incidence of post-phlebotic syndrome by about 50%.<sup>39</sup> Graduated stockings provides a cheap, safe and effective method of prophylaxis against DVT.<sup>40</sup> Sigel *et al*<sup>41</sup> in 1975 demonstrated that when graduated compression was applied to the lower limb by external pressures of 18mmHg at the ankle decreasing to 8mmHg at the upper thigh, mean femoral vein blood flow velocity was increased by 138%. This is the principle applied in thrombo-embolic deterrent (TED) stocking. It effectively reduces pooling of blood in the soleal sinuses and discourages thrombogenesis.<sup>40</sup> Below knee compression stockings with a compression pressure of 18mmHg at the ankle reducing to 14mmHg at the upper calf is as effective in increasing deep venous velocity as a full length pressure gradient from 18mmHg at the ankle to 8mmHg at the upper thigh.<sup>42</sup> Interestingly, a study comparing above and below knee stockings showed that below knee stocking was more effective in reducing post-operative DVT (1.7% of DVT occurrence in below knee versus 7.1% in above knee).<sup>42</sup>

Electrical stimulation of the calf muscles during operation is effective

against DVT.<sup>43</sup> Two electrodes are applied to the calf and a low voltage is used to contract the muscles every 2–4 seconds. This method originally recommended by Doran and White reduces intra-operative venous pooling in the calves.<sup>44</sup> It is simple, cheap and free from side effects, and can be combined with Pharmacological agents.<sup>45</sup>

Another method, pneumatic compression of the calf, involves encasing the legs in a plastic material and rhythmically alternating the pressure to squeeze the calf muscles and increase venous return. In practice an electrical pump inflates each legging alternately so that compression at 40–45 mmHg for 1 min is achieved, followed by a relaxation for 1min. The advantage of this method is that it can be used not only during surgery but also in the post-operative period. Pneumatic compression devices reduce venous stasis and are effective in reducing the risk of DVT in patients after surgery.<sup>38</sup>

**Pharmacological:** Dihydroergotamine is an alpha adrenergic receptor stimulant that increases the tone of vein walls and improves outflow from the calf veins. It has been found successful in decreasing incidence of DVT when used in combination with low dose heparin during hip surgery<sup>46</sup>. It is however not without the risk of possible ergotism.<sup>47</sup>

**Counteracting Blood Coagulability:** Blood coagulability is counteracted by pharmacological agents that are broadly classified into groups based on mode of action.

**Platelet Function:** It has been suggested that adhesions of platelets to sub-endothelial connective tissue at the site of presumed damage to venous endothelium and subsequent events leading to platelets aggregation may account for thrombus formation. If this platelet aggregation can be prevented, it is conceivable that the thrombus will not form. Agents that have been studied to inhibit this pathway include dipyridamole, and acetyl salicylic acid sulphinpyrazone, hydroxychloroquine, flurbiprofen and ticlopidine. Unfortunately, antiplatelet agents have proved disappointing.

Aspirin, the most widely tested appears to be ineffective in women<sup>48</sup> and there is continuing uncertainty regarding dosage.<sup>6</sup>

**Coagulation Mechanism:** To block the coagulation sequence two different types of drugs have been used: oral anticoagulants, which act by reducing synthesis in the liver of various clotting factors like prothrombin, factor X and others, and heparin which act by increasing factor X inhibitor activity. Unfractionated heparin and low molecular weight heparin (LMWH) provide effective DVT prophylaxis in surgical patients.<sup>49</sup> The heparins can reduce by up to 80% the risk of post-operative DVT in patients with malignant disease undergoing surgery who have a very high risk of DVT.<sup>50</sup> Heparins are however, associated with 2% absolute increase in incidence of bleeding complications mostly at the operations site resulting to wound haematoma.<sup>49</sup> The heparins demands skilled nursing time, is unpleasant to the patient and compared to other methods relatively expensive. There is no significant difference between unfractionated heparin and LMWH in reducing risk of DVT, but patients receiving LMWH have a lower rate of bleeding complications.<sup>51</sup> Also the once daily dosing regimen of LMWH is more convenient when compared with the 8 hourly regimen of unfractionated heparin. The use LMWH therefore simplifies administration schedules and improves efficacy.<sup>52</sup> They may become the agents of choice.<sup>53</sup> Unfractionated heparin however is relatively less expensive than LMWH.

Oral anticoagulants like warfarin, though effective, require laboratory control and monitoring. Their effects are not easily reversible and they are incompatible with a number of other drugs.<sup>6</sup>

**Venous Endothelium:** The third group of drugs act on the endothelium to increase naturally occurring fibrinolytic activity in the body. Thrombosis may be due in part to a local or generalized imbalance between coagulation and fibrinolysis. A shift in the balance towards fibrinolysis could prevent thrombosis or rapidly lyse

recent thrombi, while impairment of fibrinolysis could encourage the growth of the thrombus. Dextran 40 and dextran 70 falls into this group and its infusion is effective in reducing the incidence of DVT and pulmonary embolism. It is an established DVT prophylaxis agent.<sup>45</sup> Dextran are allergenic and should be used with caution.

For hospitalized surgical patients, a protocol of oral anticoagulant therapy starting before operation or immediately after admission to hospital is the most effective and proven method of preventing DVT in patients at risk. The draw back is that despite strict laboratory control, the risk of haemorrhage is real during and after surgery. Low dose, low molecular weight heparin given subcutaneously two hours before operation, twelve hours after, then daily for seven days is the acceptable regime<sup>54</sup>. This prophylaxis is well tolerated by patients, and it is devoid of side effects, requires no special monitoring and does not result in excessive bleeding during or after surgery

#### **Recommendations to improve the prescription of DVT Prophylaxis by Surgeons**

Due to the poor application of DVT prophylaxis in at risk patients, we recommend hospital-based interventions and evidence-based educational programmes that show hospital statistics of the DVT problem. These have been shown to increase the use of prophylaxis by clinicians.<sup>55</sup> Also, use of computerized programmes that identify patients that are at high risk (based on the risk factors from clerking entries) and prompts the clinician to consider DVT prophylaxis use, have been found to increase actual use of prophylaxis.<sup>56</sup>

Recommended guide lines for DVT prophylaxis in hospitalized patients have been published by the thromboembolic risk factors (THRIFT) consensus group.<sup>57</sup> It recommended strongly the use of unfractionated heparin or LMWH in acutely ill hospitalized patients with multiple risk factors. Some recommended pharmacological agents, their doses and remarks are shown on Table 1. It is also recommended that mechanical prophylactic methods for patients at

increased risk of bleeding.

#### **CONCLUSION**

Deep venous thrombosis is a preventable problem in surgical patients. Its prophylaxis is based on the assumption that a lower incidence of DVT will lead to a lower incidence of PE. The efficacy, simplicity of use, freedom from complications and relatively low cost make thrombo-embolic deterrent (TED) stockings the most suitable method for routine DVT prophylaxis, for hospitalized patients aged over 40 years. However, for patients at high risk such as the obese with varicose veins, the elderly with malignancy and those undergoing major surgeries; pharmacological and mechanical methods should be combined. We have tried to address all aspects of DVT risk factors and prevention in surgical patients leaving out pulmonary embolism; believing that if we can prevent DVT, there will be no thrombo-embolism. It is our hope that this review will help health care providers improve their practice in preventing DVT.

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