Risk factors for Deep Vein Thrombosis in a South African public hospital

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Declaration

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LITERATURE REVIEW

Deep vein thrombosis (DVT) represents the formation of blood clots within the deep venous system. It is a common and dangerous disease in the most serious since clots can propagate from the deep veins leading to a fatal pulmonary embolus. DVT can be difficult to detect and may be confused with many other conditions.[1] It is not an easy diagnosis to make because lots of other conditions mimic DVTs, for example lower limb oedema, cellulitis and Bakers cyst. Over 200,000 South Africans suffer from DVT each year, because most DVT is occult, the true incidence is unknown. [2] The patients will suffer from acute and/or chronic complications such as stasis dermatitis and venous ulcers. While the degree of morbidity is significant, mortality rates are equally problematic. Thromboembolic disease is annually responsible for 20,000 deaths in South Africa. [3]

1. Pathophysiology of Thrombosis

There are different theories trying to explain the pathophysiology behind thrombosis. [1, 4] Rudolf Virchow, (a German pathologist in the 1800s) defined the types of conditions that could predispose patients to abnormal thrombus formation. These categories of risk factors, called "Virchow's triad," are[1, 4, 5]:

- Hypercoagulability
- Venous stasis
- Endothelial damage.

i. Hypercoagulable states

The most common causes of hypercoagulability include mutations in factor V and deficiencies in protein C or protein S. Protein C and its cofactor protein S, are Vitamin K-dependent and work by inhibiting factors V and VIII. When a deficiency of one of them develops or procoagulation factors are not properly inhibited, a tendency for the development of thrombus results.[6, 7] Deficiencies of antithrombin III and hyperhomocysteinemia are less common genetic causes of hypercoagulability.[8,9] Pregnancy and the post-partum period are associated with an increased risk of DVT due to hypercoagulability . Other causes of hypercoagulability include: Autoimmune diseases such as Systemic lupus erythematosus (SLE); [10] Malignancy especially Adenocarcinoma of the visceral organs and lung cancer; and medications such as chemotherapy agents and Oestrogens. Polycythemia increases the risk for DVT due to an increased haematocrit .[11] Obesity has been thought in the past to be a unique risk factor for DVT .[1, 12] Smoking has been associated with an increased risk of thrombosis. [12]

ii. Venous stasis

Any decrease in venous flow, results in stasis of the blood, which predisposes to venous thromboembolism for example: immobility, local pressure, congestive heart failure, shock and venous obstruction. Immobility implies long trip for more than 6 hours by airplanes, cars or trains associated with assuming one position without moving the lower limbs.[12] There is a clear association between the incidence of DVT and the systemic venous pooling seen in Congestive heart failure.[13]

iii. Endothelial damage

Local damage to the intimal wall of a vein can occur because of inflammation, infection, local trauma, or indwelling catheters. However, vessel wall damage is less important in venous thrombosis formation than in arterial thrombosis formation. Examples of low-grade chronic vessel injury that increase the baseline propensity for thrombosis may include endothelial injury due to chemotherapy, hyperhomocysteinemia, vasculitis, or antiphospholipid syndrome.[14] The greatest risk factor for venous thrombosis is previous thromboembolic disease.

Major surgery and multisystem trauma often require 2 or more classic risk factors for DVT (e.g. activation of clotting factors, immobility and local damage) and together they are responsible for up to 40% of all thromboembolic disease. The rate of postoperative DVT in non-anticoagulated patients is 70% after non-elective hip surgery, 48% after elective orthopaedic surgery and 12% after elective general surgery.[15] Upper extremity DVT is far less common than lower extremity DVT and is most often associated with the presence of a central venous line. The subclavian vein is the most common place to develop upper extremity DVT followed by the axillary and brachial veins.[15,16] Effort thrombosis is a syndrome of DVT unique to the upper extremity, typically occurring in young males after strenuous or unusual exercises.[16]

2. Risk factors for DVT

There are numerous recognised risk factors for DVT. The most widely accepted are not discussed in detail, but are listed under the clinical decision rule section below.

i. Clinical Decision Rules

Here we have defined a clinical decision rule as *a clinical tool that quantifies the contributions that various components of the patient's history and physical examination make toward the diagnosis.*[17]

In 2006, Scarvelis and Wells conducted a comprehensive review of the DVT literature by searching MEDLINE from 1966 to April 1997. They concluded that the diagnostic properties of the clinical

examination are poor. The sensitivity of the clinical examination ranges from 60% to 96%, and the specificity ranges from 20% to 72%.[18] Additionally, they concluded the use of a clinical prediction guide that includes specific factors from both the history and physical examination in combination with non-invasive tests will simplify diagnosis of patients with suspected DVT. [18] The scoring system they developed has become widely known as the *Wells score*, which enable physicians to reliably stratify their patients into high-, moderate-, or low-risk categories. Combining this with the results of objective testing greatly simplifies the clinical workup of patients with suspected DVT. Wells score is shown in the table. A total score of two or higher indicates that the probability of deep-vein thrombosis is likely; a total score of less than two indicates that the probability of deep-vein thrombosis is unlikely. In patients with symptoms in both legs, use the more symptomatic leg.[18-21]
Wells score is one of the most commonly used criteria to guide further investigations for DVT in emergency centres (EC). [22] However, it is not the only one - Landefeld and colleagues[23] developed another clinical decision rule, but it was based upon a very small sample and its uptake has been very poor. It will not be discussed further. The Wells score has never been validated in South Africa.

Clinical Characteristic	**Score**
Active cancer (patient receiving treatment for cancer within previous the 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recent bedridden for greater than 3 days or major surgery within the previous 12 weeks requiring general or regional anaesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (no varicose)	1
Previously documented deep-vein thrombosis	1
Alternative diagnosis at least as likely as deep-vein thrombosis	-2

Table: Wells score for DVT risk stratification[18]

ii. Other risk factors

TB

According to The Global TB Control Report 2009, the African Region which accounted for an estimated 12% of the world population contributed 22% of notified TB cases. Case notification rates have increased from 82:100,000 in 1990 to 158:100,000 in 2007 [24] Pulmonary tuberculosis (PTB) is one of the most prevalent chronic infectious diseases in South Africa and worldwide.[25] The mortality rate in pulmonary tuberculosis is high in those with advanced disease and in the presence of complications. Deep vein thrombosis is reported as a systemic haematological complication in patients with PTB. Reactive thrombocytosis, elevations in plasma fibrinogen degradation products (FDP), tissue plasminogen inhibitors with depressed antithrombin III levels appear to favour the development of DVT in PTB.[26] Many studies have also demonstrated that these haematological parameters worsen during the first 2 weeks of anti-TB therapy in many cases, but they normalize after a month of anti-tuberculosis therapy.[27] Thrombosis have been reported in patients with intra-abdominal lymphadenopathy of tubercular aetiology.[28] The high frequency of anti-phospholipid antibodies and Protein-S deficiency in patients with tuberculosis is also mentioned in the literature.[28] Studies have also demonstrated a possible association between DVT and use of Rifampicin containing regimens. This does not contraindicate the use of this drug in patients at risk, but such patients should be monitored. [29]

Pulmonary tuberculosis is characterized by an acute phase response and leads to a series of cellular and molecular interactions that profoundly alter haemostasis .[30] One series of patients with active pulmonary tuberculosis has shown anaemia, leucocytosis, thrombocytosis, elevation in plasma fibrinogen, factor VIII, plasminogen activator inhibitor-1 with depressed antithrombin III and protein C levels. Fibrinogen and factor VIII levels had decreased to normal levels, protein C and antithrombin III levels had increased to normal levels, and there was no difference in plasminogen activator inhibitor-1 levels. None of the patients, however, developed DVT. The hypercoagulable state in tuberculosis has been described variously as an increased number of platelets, an increase in platelet adhesiveness, hyperfibrinogenemia and a decrease in fibrinolysis.[30] Tuberculosis patients have lower levels of anticoagulation factors (protein C, protein S, antithrombin III), with elevation in plasma fibrinogen, factor VIII, plasminogen activator inhibitor-1 and D-dimers. White[31] found a 4.7-fold increased incidence of DVT in the rifampicin arm of a study as compared with another anti-TB regime but could not elucidate the mechanism. In most patients, diagnosis of TB was made in the first 2 weeks after admission and start of therapy. Through enzyme induction, rifampicin could theoretically alter the balance of procoagulant and anticoagulant proteins produced by the liver. Decreased production and increased clearance of anticoagulant proteins may favour

hypercoagulability .[31]

HIV

Infection with the Human Immunodeficiency Virus (HIV) is still a major health problem worldwide. According to the latest statistics about HIV/AIDS an estimated 5.6 million people were living with HIV and AIDS in South Africa in 2009, more than in any other country. It is believed that in 2009 an estimated 310,000 South Africans died of AIDS.[32] Haematological and vascular complications of HIV/AIDS are frequently reported. The incidence was increased two to ten fold in comparison with a healthy population of the same age.[33] A two- to10-fold increased incidence of VTE is described in HIV-infected patients. [34] An increased risk of venous thrombotic disease in HIV-infected patients could be explained by the presence of a hypercoagulable state characterized by an increase in pro-coagulant factors.[35] HIV-infected patients are at increased risk of venous and arterial thrombosis. In this Study [35], 109 consecutive HIV-infected patients in the study and tested them twice for currently known thrombophilic abnormalities at an interval of at least 3 months (median, 3 months; range, 3-12 months). After HIV infection was diagnosed, 16% of the patients experienced symptomatic thrombosis (venous, 10%; arterial, 6%). Multiple acquired and persistent thrombophilic abnormalities are more frequently observed in HIV-infected patients than in the healthy population. The frequencies of these thrombophilic abnormalities increase with the progression to AIDS. These findings may contribute to the high prevalence of venous and arterial thrombosis in HIV-infected patients.[35] In a case series that described the thrombotic complications of patients infected with HIV, it was noted that the patients were characterized by a relatively young age at the time of thrombosis, a predominance of elevated levels of lipids, a history of malignancy, and an advanced CDC HIV classification, but not by a low CD4 cell count or an elevated HIV load.[35]

3. Diagnosis of DVT

In addition to the history and physical examination findings as detailed in the Wells score, diagnosis of DVT is then dependent upon further testing. Testing is guided by the pre-test probability of DVT, but the details of that stratification are not discussed further here. The 2 main testing modalities are

expanded upon below.

i. D-Dimer

A simple blood test measures the degradation product of factor XIII cross linked fibrin. It reflects on-going activation of the haemostatic system. It can be used as rule out test when the pre-test probability of DVT is low[36], but has little diagnostic yield with an intermediate or high pre test probability.

ii. Duplex Ultrasound

All other diagnostic measures are imaging based: venography, duplex Ultrasound, CT scan and MRI. Venography is traditionally held as the gold standard for evaluating DVT, but it has largely been supplanted by duplex venous ultrasonography[37] due to its several disadvantages: it is an invasive procedure, requires the intravenous injection of contrast, and some patients may develop an allergic reaction to the contrast or it may cause nephrotoxicity. Additionally, 2-3% of patients develop DVT secondary to venography.[38] CT and MRI have reasonable accuracy – although no higher than well done ultrasound - but are not affordable in our setting and so are not explored further.

Duplex Ultrasound consists of evaluating for vein collapsibility under ultrasound transducer compression and evaluating blood flow with both colour and spectral Doppler. It is performed on the entire proximal deep venous system where accessible. It is an inexpensive, quick and non-invasive test. Ultrasound can be limited in its utility by the operator's skills and the patient size: in obese patients or those with severe lower limb oedema it may be virtually impossible to visualize the clot on ultrasound. It has a sensitivity of 95% for proximal DVT, 65% sensitivity for distal DVT, and combined specificity of 94%[38] ; the diagnosis of distal or calf DVT is frequently difficult and time-consuming, with sensitivity for isolated calf vein thrombosis in the range of 40-90% [39] Ultrasound may however identify a substantial alternative diagnosis, such as a ruptured Baker's cyst, cellulitis and presence of hematoma .[40]

In South Africa duplex ultrasound is the most commonly utilized test to evaluate for the presence of DVT.

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MOTIVATION FOR THE STUDY

The evidence suggests an association between HIV, TB and DVT. There are no studies of this link in the Southern African setting, where the incidence of both of these conditions (HIV and TB) is high. We therefore undertook a study to define the incidence of HIV and TB in patients with confirmed DVT in this setting.

AIM

The aim of this study is to describe the incidence of HIV, TB and the more commonly accepted risk factors in patients with confirmed DVT in a South African public hospital.

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Risk factors for Deep Vein Thrombosis in a South African public hospital

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African Relevance:

- HIV and TB are affecting many patients in this continent.
- The reality of high rate of patients with DVT diagnosed with HIV, TB, or both.

Keywords:

DVT, Risk factors, HIV, TB

Abstract

1. *Objective*

   To identify the presence of risk factors for DVT in a population of South African public healthcare system patients with confirmed DVT.

2. *Methods:*

   A retrospective review of patients with ultrasound confirmed DVT at GF Jooste, a Cape Town public hospital. Medical notes were reviewed for the presence of established risk factors, TB and HIV.

3. *Results*

   Eight hundred and sixty five (865) patients with suspected DVT were identified; 685 had confirmed DVT. 610 had complete records; 62.6% were female. The location of DVT was in lower limbs in 97 % of patients and in upper limbs in 3%. HIV status was positive in 393 (64.4%), negative in 53 (8.6%) and unknown in 164 (26.8%). TB status was positive in 339 (55.5%) and negative in the rest. In addition, 264 patients were positive for both HIV and TB; 135 patients were unknown to have HIV or TB.

4. Conclusion

   It appears that the risk of developing DVT is high in patients with HIV or TB. More research is required to optimally define the risk factors in our population in order to develop a DVT scoring system.

African Relevance:

- HIV and TB are affecting many patients in this continent.
- The reality of high rate of patients with DVT diagnosed with HIV, TB, or both.

INTRODUCTION

Deep vein thrombosis is caused by clot formation in the deep veins of the body. Virchow's Triad encapsulates the main pathophysiologic issues in DVT development: hypercoagulable states, venous stasis and local damage to the intimal wall of the vein[2]. Traditionally described risk factors for DVT include: immobility, thrombophilia, surgery, pregnancy, recent injury, cancer, congestive heart failure, oral contraceptives, previous history of DVT or pulmonary embolism (PE), smoking, advanced age and obesity [3]. However, there is no literature describing the prevalence of these risk factors in patients with DVT the South African context. Recent reports note an increase in the incidence of DVT's in HIV positive individuals[4]; one study showed that thrombotic events are four times more common in HIV-infected than the general population, and these occur at a younger age[5]. Lijfering showed that the reasons for this increased rate of thrombosis include protein C and protein F deficiency, increased factor VIII and high fibrinogen concentrations[6].There is good literature to suggest that the occurrence of DVT is much higher in patients with Tuberculosis (TB) infection than in the general population[7-9]. This is thought to be due to the molecular interactions of the acute phase response which alter haemostasis, combined with the immobility superimposed with the illness[8]. TB patients appear to develop a reactive thrombocytosis, elevated plasma fibrinogen levels, impaired fibrinolysis and a decrease in antithrombin III, a ll of which contribute to thrombogenicity[9].

Diagnosis of DVT

Well's criteria are internationally accepted as a reliable clinical prediction rule to calculate an individual's risk of having a DVT (Table 1) [10]. A score of two or higher indicates that the probability of a DVT is likely and that further testing is required. However, they have never been validated within South Africa; they also exclude two very common and important risk factors: HIV and TB.

Table 1 near here

In addition to the role of d-dimer, which is not considered further here, numerous imaging modalities can be used to diagnose DVT, including contrast venography, compression and colour flow duplex ultrasound, magnetic resonance venography and computed tomographic venography[11]. Contrast venography is the gold standard, but is time consuming, requires a high degree of technical expertise and is invasive. For these reasons, even though ultrasound is less sensitive and specific, it has replaced venography as the initial imaging of choice[11]. Duplex Ultrasound consists of evaluating for vein collapsibility under ultrasound transducer compression and evaluating blood flow with both colour and spectral Doppler. It is performed on the entire proximal deep venous system where

accessible.

Ultrasound has a reported sensitivity of 95% for proximal and 65% for distal DVT, and a specificity of 94%[12] (although some studies claim a sensitivity for diagnosis of isolated calf vein thrombosis between 40-90%[14]).It is a relatively inexpensive, quick and non-invasive test, but is limited by the operator's skills and the patient size (in obese patients or those with severe lower limb oedema it may be virtually impossible to visualize the clot on ultrasound). The diagnosis of distal or calf DVT is frequently difficult and time-consuming with ultrasound[13, 14; but a significant alternative diagnosis, such as a ruptured Baker's cyst, cellulitis or haematoma may easily be diagnosed using ultrasound.[15, 16] In South Africa, duplex ultrasound is the most commonly utilized test to evaluate for the presence of DVT: confirmation of DVT is determined by a positive compression and/or colour flow duplex ultrasound.

Given the lack of locally relevant information on the relationship between DVT and HIV and TB, we undertook a study to describe the incidence of these 2 risk factors in patients with DVTs in a South African population.

METHODS

GF Jooste is a busy urban 224 bed district hospital situated in one of the city's most violent township areas. It has a high rate of HIV and TB in its patient catchment area. It runs an emergency centre which sees around 40,000 patients per year.

We retrospectively reviewed medical records of all patients with a confirmed DVT presenting to the ultrasound department of GF Jooste hospital, Cape Town from 1 April 2008 to 30 April 2011. The ultrasound registers were reviewed by the primary researcher, to identify patients undergoing ultrasound for suspected DVT. All such patients were reviewed and those with positive findings were identified and formed the study population.

Medical records were retrieved on all patients with positive scans; patients with missing or incomplete records were excluded from the analysis. A standardized data capture form was used to collect age, sex, site of DVT (upper or lower limbs), risk factors for DVT, HIV status (positive, negative or unknown) and TB status (positive, negative). Data were entered into a Microsoft Excel 2010 (© Microsoft, Richmond VA) spread sheet and data analysed using Stata 10 (©Statacorp, College Station, Tx).

This study was granted ethics approval by the Research Ethics Committee, University of Cape Town (REF: 020/2012)

RESULTS

Eight hundred and sixty-five patients with suspected DVT were identified from the ultrasound register during the study period: 685 had confirmed DVT. Of these, 610 had available medical records of DVT, 48 records were missing and 27 records were conflicting and therefore unusable. Therefore the total study sample was 610 patients.

Figure near here

The median age for the group was 37 years (interquartile range 15 - 88 years). Of the patients who had DVT, 62.6% were female. The location of DVT was in lower limbs in 97 % (male 95%, female 99%); all others occurred in the upper limbs.

HIV stats was recorded as positive in 393 (64.4%), negative in 53 (8.6%) and unknown in 164 (26.8%); TB status was positive in 339 (55.5%). A total of 264 patients were both HIV and TB positive; 137 patients were not known to have HIV or TB. **Table 2** contains details of other commonly identified risk factors in this population.

Table 2 near here

DISCUSSION

We conducted this descriptive study trying to find the commonest risk factors of DVT among the South African population and to show the possible association between HIV and TB, as independent risk factors of DVT. South Africa ranks fourth in the world in terms of absolute TB cases after India, China and Indonesia. TB is the most common opportunistic infection in HIV infected people.[17] Approximately 5.6 million South Africans were living with HIV in 2009 of which roughly 1 million people are currently accessing antiretroviral treatment.[18] The prevalence of HIV in South Africa is currently between 11% and 19%.[19] The HIV epidemic in South Africa has a significant impact on the burden of tuberculosis. TB notification rates have increased to 1500 / 100 000 populations more commonly in poverty stricken areas.[20]

GF Jooste Hospital currently provides district and regional services to more than 1 million people. This population presents a good sample of the South African population with different races and age groups. A 2003 survey of medical admissions to GF Jooste hospital showed that approximately 32.3% of surveyed patients were HIV positive and most of them (85.2%) had WHO Stage III disease or AIDS. [21] With regards to the tuberculosis-related burden of disease, 20.6% of surveyed patients had undiagnosed active TB and 33.4% were on TB treatment at the time of discharge, transfer or death.[21]

Our findings clearly show that in most cases of DVT the patient is HIV positive or has TB or both. More than 64% had HIV and more than 55% had TB: 43.2% were positive for both HIV and TB. This suggests a clear association between both of these conditions and the development of DVT.

Nearly two thirds of patients were female: this is not representative of the EC population, which is closer to half female. Only 14 of these patients were pregnant, but insufficient other clinical information were captured to allow deductions to be made as to why this female predominance is seen.

Upper limb DVT was found in 3%: all of them were secondary to previous central line insertion.

The commonest "traditional" risk factors for DVT were immobility and history of previous DVT / PE (8.7%, 4.3% respectively). History of cancer, CCF and obesity were found in 3-4% of patients.

LIMITATIONS

As this is a retrospective records review including only patients identified from the ultrasound. This study is limited by the documented patient information and work-up done by the managing medical staff. As such it is expected that there may be occasions when risk factors and/or comorbidities have not been accurately recorded. Therefore our reported incidence rates may be at the lower end of the real rates.

Some records were not available at the time of review. This could have affected the incidence rate in either direction. However, there is no reason to suppose that the 11% missing records were different in any way to the records retrieved.

The use of ultrasound as diagnostic measure also has its limitations, as it is not the gold standard for the diagnosis of DVT. However, it is standard practice in most countries today, and has performance characteristics suitable to allow reasonable interpretation of its results.

The study was conducted at one centre (GF Jooste hospital) in the Western Cape and may not reflect the results in different centres.

CONCLUSION

This is the first study reporting the incidence of HIV and TB in patients with DVT in a South African setting. We have demonstrated a very high rate of infection with either of both pathogens in this population. More research is required to determine whether this association is repeated in other parts of the region.

1. **Funding**

The study was funded by the researcher.

2. Conflict of interest

The authors declare that there is no conflict of interest.

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Figure: patient identification

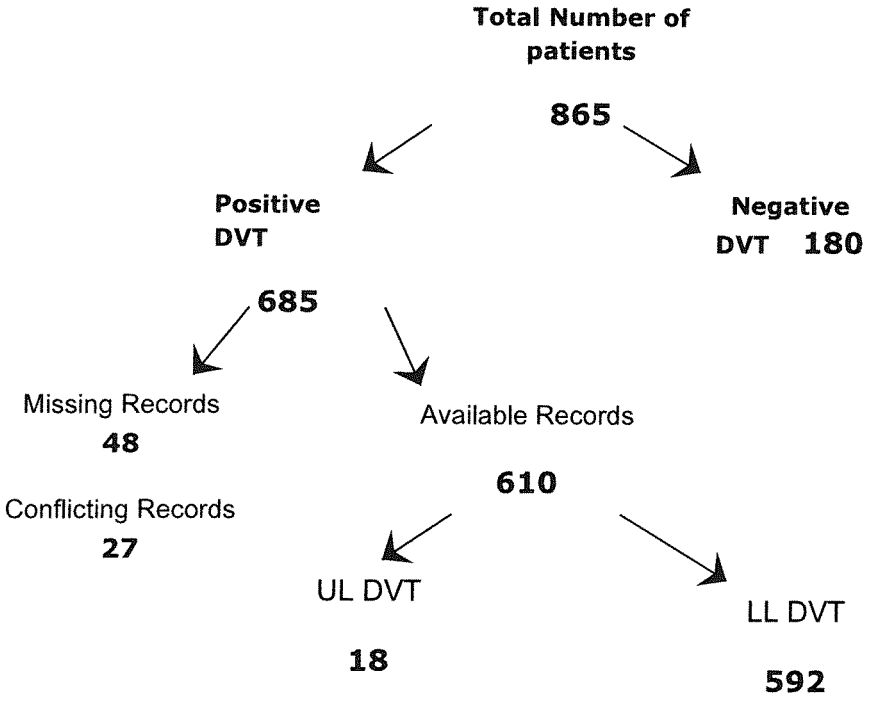

Table 1: Wells Clinical Model for Predicting Pre-test Probability for DVT [10]

CLINICAL CHARACTERISTIC	SCORE
Active cancer (patient receiving treatment for cancer within previous the 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recent bedridden for greater than 3 days or major surgery within the previous 12 weeks requiring general or regional anaesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibia tuberosity)	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (no varicose)	1
Previously documented deep-vein thrombosis	1
Alternative diagnosis at least as likely as deep-vein thrombosis	-2

Table 2: Risk factors for DVT

RISK FACTORS	n (%)
HIV	393 (64.43)
TB	339 (55.57)
IMMOBILITY	53 (8.69)
PREVIOUS DVT/PE	26 (4.26)
CANCER	25 (4.10)
CCF	22 (3.61)
OBESITY	19 (3.11)
RECENT SURGERY	3 (0.49)
PREGNANCY	14 (2.30)
TRAUMA	10 (1.64)
SMOKING	11 (1.80)
NO RISK FACTORS	17 (2.79)

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Case Reports: Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. Case reports should be structured as follow: Introduction, Case report and Discussion. They should not contain an exhaustive review of the literature. A structured abstract (see Preparation below) is required. Maximum length: 1,000 words, plus abstract (max 150 words) and references (max 10), and 1 table or figure.

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- ☐ Author names, affiliations and contribution
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Risk factors for Deep Vein Thrombosis in the South African Population

Research Proposal
February 2012

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In partial completion of the degree MMed in Emergency Medicine

TABLE OF CONTENTS

1. Introduction

1.1. Literature Review

It is estimated that over 200,000 South Africans suffer from deep vein thrombosis (DVT) each year, but because DVT is occult the true incidence is unknown[1].

Deep vein thrombosis is caused by thrombus formation in the deep veins of the body. Virchow's Triad describes the risk factors for DVT to include hypercoagulable states, venous stasis and local damage to the intimal wall of the vein[2].

Traditional risk factors for DVT include: immobility, thrombophilia, surgery, pregnancy, recent injury, cancer, congestive heart failure, oral contraceptives, previous history of DVT or PE (pulmonary embolism), smoking, age and obesity[3]. No literature describes the prevalence of the aforementioned risk factors for DVT in the South African population.

More recently an increase in the incidence of DVT's in patients with HIV (Human immunodeficiency virus) has been described[4] with one study showing that thrombotic events are four times more common in HIV-infected individuals than the general population and occur among these HIV infected patients despite their younger age[5]. Lijfering et al[6] showed that reasons for this increased incidence of thrombosis included protein C and protein F deficiency, increased factor VIII concentrations and high fibrinogen concentrations.

There is also literature supporting the occurrence of DVT in patients with Tuberculosis (TB) infection[7, 8, and 9]. This is thought to be due to the molecular interactions of the acute phase response that alters haemostasis combined with the immobility superimposed with the illness[8]. These changes that occur in patients with TB appear to include a reactive thrombocytosis, elevated plasma fibrinogen with impaired fibrinolysis and a decrease in antithrombin III[9].

Well's criteria for DVT[10] is an internationally accepted clinical prediction tool to calculate an individual's risk of having a DVT. A score of two or higher indicates that the probability of a DVT is likely and that further testing is required.

Wells et al Clinical Model For Predicting Pre-test Probability For DVT [10]	
Clinical Characteristic	**Score**
Active cancer (patient receiving treatment for cancer within previous the 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recent bedridden for greater than 3 days or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibia tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (no varicose)	1
Previously documented deep-vein thrombosis	1
Alternative diagnosis at least as likely as deep-vein thrombosis	-2

Well's criteria has never been validated within South Africa and also excludes the 2 independent risk factors which affects the South African population and which this study is looking at, namely HIV and TB.

There are numerous modalities available that can be used to diagnose DVT. These modalities include: contrast venography, compression and colourflow duplex ultrasound, magnetic resonance venography and computed tomographic venography[11]. Contrast venography is the gold-standard, but is time consuming, requires a high degree of technical expertise and is invasive. For these reasons, even though ultrasound is less sensitive and specific, it has replaced venography as the initial imaging of choice[11]. For this study, confirmation of the presence of DVT shall be determined by a positive compression and/or colour flow duplex ultrasound.

1.2. Aim

The aim of this study is to describe the risk factors present in patients with deep vein thrombosis in a Western Cape Hospital population

1.3. Objectives

1.3.1. To evaluate what traditional risk factors for DVT are present in Western Cape patients with ultrasound confirmed Deep Vein Thrombosis.

1.3.2. To evaluate the presence of HIV and/or TB in Western Cape patients with ultrasound confirmed DVT.

2. Methods

2.1. Study design

This will be a retrospective descriptive study. A review of the ultrasound registers over a 36 month period at GF Jooste will be done. All patients who have undergone ultrasound by sonographers and/or radiologists for suspected DVT will be reviewed and those with positive findings will be identified. Folders will then be requested for those patients with ultrasound confirmed DVTs. The data capture sheet will then be filled in using the information gained from the patients' folders. The names of the patients will not be kept, only the information from the files will be stored with study numbers (not folder numbers).

2.2. Study population

The ultrasound registers over a 36 month period at GF Jooste Hospital will be reviewed for patients undergoing ultrasound for suspected DVT. Those patients with positive findings will form the study population. It is estimated that the study population will be approximately 550 patients.

2.3. Sampling

2.3.1. Inclusion criteria

All patients with deep vein thrombosis as identified by ultrasounds done by sonographers and/or radiologists over a 36 month period at the above hospital will form the study population.

2.3.2. Exclusion criteria

Patients under the age of 18 will be excluded from the study. Patients whose folders are missing will be excluded from the study population.

2.4. Data collection and management

The primary investigator shall request the folders of those patients with positive DVTs. The primary investigator shall then complete the data capture sheet using only study numbers and not folder numbers or any other identifying characteristics. The data capture sheets shall then be entered into a password protected computer and stored by the primary investigator.

2.5. Timeline

Ethics Mar 2012, Data Capturing April 2012, Write up May 2012

3. Statistical analysis

Data will be collated in a Microsoft Excel database. Statistical analysis will be done with the help of UCT statisticians. Simple descriptive statistics (means and medians and standard deviations) will be used to describe the demographic data. The assistance of a statistician will be sought to determine potential statistical associations between key variables.

4. Ethical and legal considerations

This will be a retrospective folder review. The data collected will be anonymous. The folder numbers will initially be used to track data information, but thereafter no patient identifying characteristics will be recorded. Only the primary researcher will have access to patients' folders and data sheets while recording the information. All patients will only be identified by study numbers. These study numbers will not be cross referenced with patient's names or folder numbers. Patient consent will not be required as the study does not involve any intervention or recording of patient details.

This study will seek approval from the University of Cape Town Ethics Committee. Furthermore, permission for access to ultrasound records and patient medical records will be obtained from the above listed hospital administrator and the Provincial Department of Health.

5. Limitations

As this is a folder review, this study will be limited by the patient information recorded and workup done by the medical staff that managed the patient. As such it is expected that there may be many occasions when all risk factors and/or comorbidities have not been included and/or excluded.

6. Resources

6.1. Budget

Printing costs	40 x 50c	R 20.00
Transport costs		R 500
Total		R520

The study will be funded by the researcher.

7. Reporting and implementation of results

The results of this study will be written up and submitted to a peer reviewed journal for publication for dissemination of information of risk factors for DVT in the South African population.

References

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APPENDICES:

APPENDIX A: ETHICS APPROVAL LETTER

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: sharella.thomas@uct.ac.za

15 March 2012

HREC REF: 118/2012

Dr A Mohammed
Emergency Medicine
Department of Surgery

Dear Dr Mohammed

PROJECT TITLE: RISK FACTORS FOR DEEP VEIN THROMBOSIS IN THE SOUTH AFRICAN POPULATION.

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year till the 30th March 2013.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010) if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

APPENDIX B: DATA COLLECTION SHEET

Study No	Demo-graphics		Site of DVT	Risk factors for DVT												
	Age	Sex	R = Right L = Left F = Femoral P = Popliteal I = Iliac S = Subclavian (If other site, then site to be recorded)	HIV	TB	Cancer (ongoing or within 6 months)	Previous DVT or PE	Recent surgery	Pregnancy	immobility	Congestive heart failure	Trauma or fracture/injury	Thrombophilia	Smoking	obesity	Other
1																
2																

CODE USED FOR RISK FACTORS WHILE DATA CAPTURING:

Y = Yes (Recorded in notes as being present or diagnosed at the time of DVT diagnosis)

N = No (Recorded in notes as not being present – as a negative finding)
U = Unknown (Not recorded as being present or absent – so unknown)
S = Suspected (When the condition was suspected by the treating clinicians, but not confirmed. This may occur for example in HIV infection when the patient refused testing)